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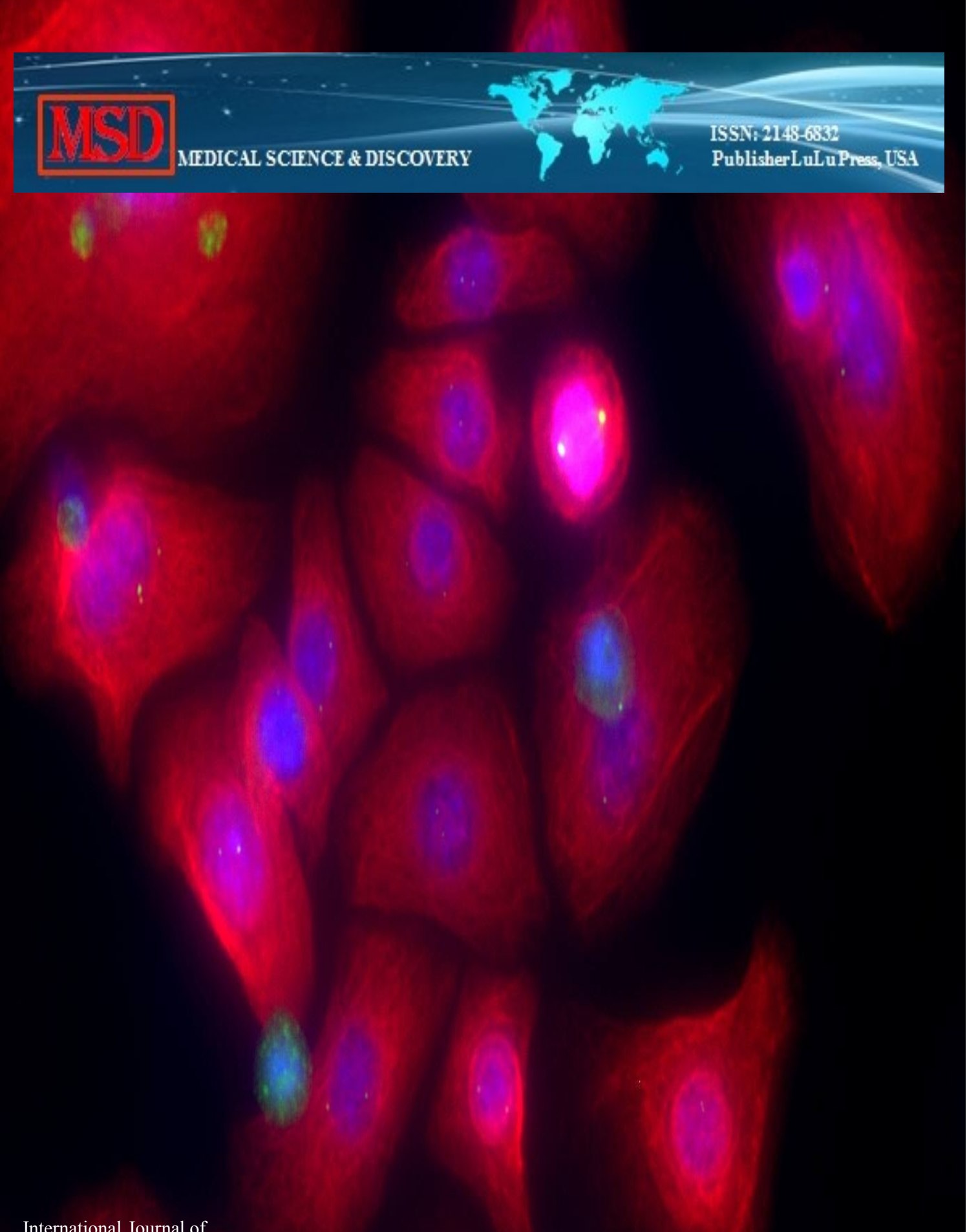

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Hypothesis Doi: 10.17546/msd.59888

Believing (faith or hypnosis) impacts on the healing of warts performed by neurophysiological mediators

Huseyin Guducuoglu[1], Serap Gunes Bilgili[2], Mehmet Arslan[3]

Abstract

Background: Faith and hypnosis methods are applied in many experimental cancer treatments. Practices of religious and psychological healing have a major role in the recovery of tumors. Healing warts by prayer has been used for years, particularly in the Turkish society.
The Hypothesis: This hypothesis maintains that believing is one of the key concepts in the recovery of tumors and also focuses on the effect of believing on the recovery of warts
Evaluation Hypothesis: In people who believe, nerve, endocrine and immune system is activated. NK and T cells in the periphery cause destruction in the wart tissue and also lead to healing in all tissues. According to our hypothesis, believing is the actual trigger for the healing of warts. Both the prayer and the hypnosis methods, in terms of cancer improvement, have been shown in many publications in the literature and have brought a new dimension to cancer recovery.
Conclusion: We hypothesize that believing (prayer or hypnosis) can be effective on the healing of warts through the stimulation of the immune system.

Key words: Warts healing, Believing, Hypnosis

Introduction

The National Center for Complementary and Alternative Medicine (NCCAM) defines complementary and alternative medicine (CAM) as “a group of diverse medical and health care systems, practices, and products that are not presently considered to be part of conventional medicine” (1). Over the last years, the use of CAM for dermatological diseases has remarkably increased (2). Moreover, a significant relationship has been found between some forms of unconventional therapy and some skin disorders, including generalized pruritus and application of cologne, warts and spiritual healing; fungal infections and application of henna, psoriasis and herbal therapy, or spiritual healing; alopecia areata and application of garlic, acne and application of lemon juice, clay, or cosmetics (3).

In the treatment of warts, prayer is a method of unconventional therapy and is frequently used by many people. There is also another concept named ‘‘intercessory prayer’’, which means that a person performs prayer for the benefit of another person. Many people believe that intercessory prayer is very effective in recovering from illnesses (4,5), particularly in the Turkish society (6). In a study on the use of hypnoanalysis, 33 of 41 (80%) consecutive patients were cured, two were lost to follow-up, and six did not respond to treatment (7). Another study investigated the effect of hypnosis on immunity in order to find out whether this effect is the key mechanism in the hypnotic treatment of the genital infection caused by human papillomavirus (HPV). The study reported that hypnosis and medical therapy resulted in a statistically significant reduction both in the surface areas and the numbers of lesions (8).

The hypothesis

Believing is a crucial part of prayer and hypnosis. When the person truly believes in prayer, some molecules trigger immune responses in the brain and consequently some molecules are synthesized in the brain and induce a variety of immune system cells in the body. As a result, the disappearance of warts becomes obvious. Moreover, when the person focuses on believing while performing prayers or hypnosis, a number of mediators are secreted from the brain (immunoregulatory neuropeptides) and these mediators facilitate the healing of cancer cells by activating several immune system cells such as NK and T cells.

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Evaluation of the hypothesis

Most people discuss the effectivity of the procedures used in cancer treatment, but they still ignore the real power of immunity. In some societies, people employ religious methods to eradicate tumors, particularly warts. Nevertheless, to date, no correlation, such as a relationship between the immune response and the eradication of warts, has been clearly explained in any study. However, since medical treatment is the primary method of choice in tumor therapy, believing (prayer or hypnosis) can be used a supportive therapy for enhancing the immunological effects during the healing process.

Traditional methods are commonly used for the eradication of lesions like warts. It is claimed that believing in the prayer method is the key to success in the recovery of warts. Both the prayer and the hypnosis method, in terms of cancer improvement, have been shown in many publications in the literature and have brought a new dimension to cancer recovery. This dimension will open new doors for the intensive studies to be undertaken on the effectivity of believing on the neurophysiological mediators and cancer recovery.

Discussion

Hypnosis and prayer employ the same path for providing effects on the recovery of illnesses. Barabasz et al. suggest the following hypnotic method for both groups; “Your body has the capacity to overcome the wart virus and to heal the infection. Focus your attention and concentrate on the involved area [pause]. Soon, you may notice a sensation of warmth in the surrounding skin [pause]. Your blood vessels dilate to bring in more and more antibodies and white blood cells; more lymphocytes and natural killer cells [pause]. The virus will be destroyed and carried away [pause]. Protein and oxygen will increase to help build the new, normal, healing tissue as the warts disappear. When you feel the increased warmth, a finger will rise [after observation of finger raise] good. Now your inner mind will lock in on this and maintain this special warmth until the warts are all healed and your skin becomes normal in every way” (8).

In the prayer method, believing in God and the prayers is the key to the healing of warts. A similar study reported that the participants prayed to God via an intercessor (an imam) and their warts were thus recovered. The study also reported that no effects were seen in the participants who did not trust the intercessor’s prayers (5). Therefore, believing is a key issue both for prayer and hypnosis.

When the person truly believes in prayer, the nervous, endocrine, and immune systems interact to adapt to infection, inflammation, and tissue injury. Neural control is mediated in several ways: through the neuroendocrine regulation of the secretion of hypothalamic and pituitary hormones, autonomic nervous system-induced activation of epinephrine secretion and of peripheral sympathetic fibers that innervate lymphoid tissue, and sensory neurons that secrete immunoregulatory neuropeptides such as substance P and somatostatin. These regulatory interactions influence the manifestations and course of disease (9). Substance P and other neuropeptides activate neurokinin-1 receptors, leading to plasma protein extravasation from post-capillary venules. Substance P is a neuropeptide that is released from nerve endings in many tissues and plays an important role in immunological and inflammatory states, and it is also a mediator of tissue injury, asthma, arthritis, allergy and autoimmune diseases (10).

In a similar way, products of hypothalamic-pituitary-adrenal activation may be important factors contributing to the resistance of the negative feedback of cortisol on CRH and ACTH secretion associated with depression, and these products may be involved in psychological distress through their effects on serotonin (11). Serotonin, as a neurotransmitter, is thought to cause depression and serotonin reuptake inhibitors, which increase the availability of this transmitter in the synaptic cleft and alleviate the symptoms. Melatonin, which is a hormone secreted by the pineal gland, is best known for its functions in synchronizing the circadian clock and has been implicated in the pathogenesis of cancer. Melatonin is a product of serotonin metabolism. In the biosynthesis of melatonin, the rate-limiting step is the conversion of serotonin to N-acetylserotonin, catalyzed by N-acetyltransferase (12).

HPV-associated malignancies and breast cancers may be more susceptible to immune effects and to the modulation caused by stress and psychological factors. Developments in cancer immunology call attention to other scenarios as well. Accordingly, although a competent immune response may favor eradication of malignant foci, the increased selection pressure may also yield more aggressive and resistant tumor cells. Animal models of cancer progression are instrumental in suggesting neuroendocrine and immunological mediators of stress effects on specific aspects of cancer progression, especially with respect to the role of Natural Killer (NK) cell activity (13).

Very preliminary data seem to show that lymphocyte proliferation and activation may be influenced by the psychological status of the patients. Some cancers like lung cancer may depend not only on tumor characteristics, but also on the psychospiritual status of the individual patient by influencing the immune and neuroendocrine functions, which plays a fundamental role in the control of neoplastic growth (14). Psychoneuroimmunology is the study of interaction between psychological processes and the nervous and immune systems of the

human body. Communication between the mind and the skin involves the psycho-immuno-endocrine-cutaneous system, encompassing the activities of the brain, the immune system and the skin, with participation of different neuropeptides, interleukins, and immune system messengers (15).

Immunity leading to wart regression is essentially universal but poorly understood. Cellular and cytotoxic immunity provided by T cells and NK cells are necessary for the control of HPV infections, but the exact mechanisms are unknown (16). For the past few decades, scientific investigations on CAM have remarkably advanced and partly supported their medical efficacy through preclinical and clinical experiments. In particular, many investigators have suggested that NK cell activation is one of the critical mechanisms for the biological effects induced by various CAM agents (17). Therefore, NK and T cells are likely to have a major role in the destruction of warts and thus further studies on wart healing are warranted to focus on these cells.

This hypothesis takes its virtue from the common believing among Turkish people that warts heal via prayers without using any medical treatment. This hypothesis is unique because it will provide important suggestions for future studies.

Conflict of Interest

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Anesthesia Management of Patients with Mental Retardation

Muhammed Bilal Cegin[1], Nureddin Yuzkat[1*]

Abstract

Mental retardation is a condition likely to develop secondarily to several genetic diseases or to some negative conditions and diseases that occur before, during or after birth. Anaesthetic practices start with the preoperative visit of a patient and are then followed by premedication, preoperative preparation, intraoperative procedures and postoperative periods. All these steps with mentally retarded patients involve separate characteristics. The MR patients must be kept under observation in the recovery rooms for longer periods of time and must also be definitely re-evaluated by an experienced anaesthetist before being transferred to the service department. Since there may be several challenges/difficulties likely to be experienced at each stage of the mentally retarded patients' anaesthesia, far more care and patience is required. A pre-anaesthetic evaluation involving a physical examination in depth and a detailed questioning should be performed. During the pre-medication period, a little amount of midazolam mixed with a proper drink can be used. Prior to applying the neuromuscle blocking agents, the airway opening must be maintained. In the presence of muscular dystrophies, the doses of neuromuscular blocking agents must be equalized. The MR patients must be kept under observation in the recovery rooms for longer periods of time and must also be definitely re-evaluated by an experienced anaesthetist before being transferred to the service department.

Key words: Anesthesia management, Mental retardation, Intelligence quotient

Introduction

The patients with mental retardation have a special place in anesthetic management. Mentallly retarded patients meight be seen at both operation rooms and outpatient anesthesia managements. There are a limited number of data in the literature about the anesthetic management of mentally retarded patients. We think this article would be helpful for recognition of mental retardation.

Definition and Classification: Mental retardation (MR) is a condition likely to develop secondarily to several genetic diseases or to some negative conditions and diseases that occur before, during or after birth. According to the data of The World Health Organization (WHO), 3% of the world's population consists of mentally retarded people at various levels. Patients usually show themselves with intellectual deficiencies (ID), retardation in mentality and social inadaptability. Such disorders may develop in association with the exposure of the intrauterine to toxic substances, infections experienced during the gestational period, problems faced at the time of birth, or a trauma, infection or other diseases experienced in any period after birth/delivery (1).

Mental retardation is defined according to the Intelligence Quotient (IQ) scores, or by being categorized with the terms like trainable, educable and totally in need of care (Table 1). Despite this, dealing with each individual and caring for them with the help of an independent evaluation in the classification process would be a better and more accurate aproach (2)

Anaesthesia: Anaesthetic practices start with the preoperative visit of a patient and are then followed by premedication, preoperative preparation, intraoperative procedures and postoperative periods. At each step of these procedures, the patient and patient relatives must be informed about the processes to take place and the complications that may ocur (3) . All these steps with mentally retarded patients involve separate characteristics.

Preoperative visit comprises the steps, such as the specification of the drugs used by the patient, previously-undergone operations, whether or not the patient has a medical record as to allergy or intubation difficulty, etc., physical examination, consultations to be performed by the involved branches and determining the method of anaesthesia (4,5).

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Table 1. DSM-IV classification of Mentally Retarded patients according to their IQ level (1)

IQ of 100 and above	Normal
IQ is between 70-100	Dull normal
IQ is between 50-70	Mild mental retardation (trained)
IQ is between 40-50	Moderate mental retardation (taught)
IQ is between 25-40	Severe mental retardation (partially trained)
IQ below 25	Heavy mental retardation (total care is required)

These patients in question are generally syndromic ones. Therefore, in addition to MR, there are also comorbid (additional) diseases in these patients as part of these syndromes. This condition must be taken into consideration during the preoperative preparation period. Unfortunately, such a process could be rather challenging for these patients due to cooperation and communication disorders. The role of the family is of great importance in taking the medical history of these patients.

During the examination of the patient, the physician should be quite patient. Under the circumstances in which the physician's patience is challenged or there is a rather limited time, the systemic examination should be left to the consulting physicians and proper conditions and platforms should be observed.

In a MR-syndromic patient, the fact that cardiovascular and craniofacial abnormalities likely to cause difficulty in maintaining the airways/breathing, disorders in the endocrine and electrolyte balance, and musculoskeletal anomalies may occur must be kept in mind and an in-depth analsis ansd necessary consultations related to the involved branch should also be performed. Separately, it must also be kept in mind that in the diseases like Rett syndrome accompanied by MR, the risk of developing an intraoperative malign hyperthermia is higher than the other patients, according to which the preoperative preparations must be carefully planned (6-9).

One of the most important parts of the pre-anaesthetic examination is the evaluation of the airways. In this patient population, the possibility to encounter such conditions as the worst Mallampati score that complicates intubation, thyromental distance, extension difficulty of the head and micrognathia is higher when compared with those in the normal patient population (3).

While determining the method of anaesthesia in the patients with MR, the type of the surgery, the mental retardation degree of the patient and the requests of the patient and patient relatives should be taken into consideration. In MR patients, it is hard to apply the regional anaesthetic techniques and ensure the adaptation of the patient in the course of the operation. For such reasons, selecting one of the general anaesthetic methods in these patients would be a far better approach (10).

Premedication provides serenity, mental comfort, euphoria and a slumber by eliminating the fear, anxiety and excitement in MR patients. Separately, the pressure of the undesired reflex actions, such as preoperative nausea, cardiac dysrhythmia and laryngospasm reduce the necessary anaesthetic dose by decreasing the metabolic activity and eventually allow for a calm waking up and comfortable recovery as well as minimizing the secretions in the respiratory tract and ensures avoiding toxic doses by diminishing the local anaesthetic requirement (5).

The preferable way in applying the drugs for premedication in these patients is the intake. In mentally retarded patients difficult to be persuaded to take drugs orally, the intramuscular way or intravenous ways could be used. (10).

For this purpose, hypnotic sedatives, tranquilizers and narcotic analgesic anxiolytics are used. Apart from this, antihistaminics are also benefited from in order to maintain a sedative effect. Antiemetics, anticholinergics, antiacids and H_2 receptor blockers can also be used in premedication. One of the most applied and recommended agents used for the purpose of sedation is midazolam (0.1-0.2 mg kg).

Another agent or agents like Ketamine can be added to Midazolam, as well. (11). In the patients unable to be convinced to take the drugs orally, neurolept analgesia agents like Ketamine (5-12 mg/kg) or haloperidol, droperidol (2-2.5 mg) can also be preferred (10).

In MR patients, in order to boost the adaptation of the patient to the hospital, premedication could be provided in the patient's home prior to visiting the hospital.

Chan et al. had practised premedication on a 36-year-old MR patient with Down and Treacher-Collins syndrome in his house to avoid any aggressive attittudes before being taken to the hospital. To that end, 10 mg of lorazepam and 1000 mg of ketamine were added into the milk to be given to the patient orally and hence, the sedation was ensured. Thus, the preparations for teeth and ear surgery to be performed in the hospital were made safely (12).

However, such sort of a practice is not that common since the follow-up would be rather difficult at home and as these patients may have comorbid/additional pathologies, as well, and the risks likely to be confronted may be more than expected.

Table 2. Some drug using in sedation (14-17). **nasal dose*

	Oral	Rectal	Intravenous (IV)	Intramuscular (IM)
Midazolam (mg/kg)	0.2-03*	0.05-0,5	0.01-0.1	0.07-0.15
Propofol (mg/kg)	-	-	1,5-2,5	-
Fentanyl (µg/kg)	-	-	0,5-1,5	50-100
Ketamine(mg/kg)	3-10	-	0,2-0,8	2-4

We did not come across a similar practice in the literature, either.

In MR patients, apart from the operating room, anaesthetics are most frequently required in the magnetic resonance imaging process. Due to the fact that the procedure in the magnetic resonance imaging takes a long time and is rather noisy besides the fact that the patient has to totally stay motionless throughout the process, anaesthesia is a mandatory optional way in this respect.

Throughout the procedure, a deep sedation, a rapid recovery and providing patient security are essential. Different methods of sedation can be used to that end (Table 2). Performing a premedication on MR patients in a convenient atmosphere will boost the patient adaptation prior to being taken to the magnetic resonance imaging unit. In the centers where there are no recovery units, the whole team should be quite patient, and patient security must never be risked just to save time (13).

Peri-operative Preparation: Before the MR patients are brought into the operating room, difficult airway instruments, vascular accesses, the fluids to be transferred to the patient, including the induction drugs must all be ready along with all the preparations made. Hence, the unnecessary loss of time must be avodided prior to induction after the patient has been taken onto the operating table. The patient taken into the operating room is now sedated, peaceful or sleepy.

After the routine monitorization of the patient brought to the operating table (electrocardiography, non-invasive tension arterial and peripheral oxygen saturation), a preoxygenation with a mask is performed. The preoxygenation in particular is of great impoortance in these patients, since anaesthesia will allow for an extra period of time in order to cope with the airway problems likely to occur in the wake of induction.

Apart from the additional monitorization that may be required during the surgical procedure in MR patients, there is no other additional procedure to be performed. For the sake of avoiding the unnecessary use of agents during the intraoperative period, and again, for avoiding wakefulness and for the standardization of the anaesthetic depth, a bispectral index monitorization and follow-up can be performed.

However, in a study conducted by Ponnudurai et al. in 2010, it was put forward that no difference was observed in terms of the bispectral index among the groups during the intraoperative period (18).

IV method is preferred for induction in the patients accepting to have their sedation level vascular access established.

On the other hand, the inhalation anaesthetics can be preferred for induction in the patients whose vascular accesses cannot be established. Sevoflurane can be used to that end. Sevoflurane becomes prominent in induction when compared to the other inhalation agents due to its fast effects and nice aroma as well as having no irritant effect on the airways. For this purpose, 4-8% sevoflurane and 50% of oxygen/nitrogen mixture can be performed.

There are various options for the IV general anaesthetic agent following the induction through the inhalation anesthetics. Among these are propofol (1.5-3 mg/kg), thiopental (4-7 mg/kg), ketamine (1-2mg/kg), and etomidate (0.3-0.5mg/kg).

It must always be kept in mind that of these agents, ketaminine must be very carefully used in the patients with intracranial pressure increase, while thiopentalin must be carefullly used in those in hypotensive shock, and etomidate must be very carefully used in the patients with a medical record of epileptic seizure (1,5).

As for the narcotic analgesics, there is no different condition in the MR patients compared to the other patient populations. Prior to preparing the muscle-relaxing agent, the fact that the openness of the patient's airways could be ensured must be verified and the difficult airway must be excluded. For this purpose, in the wake of the induction of the general anaesthetic agent, the Cormack Classification involving laryngoscopy and epiglottis and the inspection of the vocal cords must be rapidly performed. After having determined that there is no problem for intubation, muscle relaxants can be made (19).

Almost one fourth of the patietns with mental retardation have a medical record of epileptic seizure (20). Due to the anti-epileptics used for a long time by the patients, the patients' susceptibility to the drugs metabolized due to the liver enzyme induction may have diminished.

For this reason, it must be particularly kept in mind that there may be a little nonsusceptibility to the non-depolarizing neuromuscular blocking agents of steroid structure, and the dose adjustment must be performed if required.

The depolarizing neuromuscular blocking agents must not be used in the case of muscular dystrophia that accompanies the MR patients more

frequently than the normal patient populations. Much care must be taken in the cannulation procedures required during the perioperative period.

In another study conducted by Sulemanji et al. (21). in 2009 on the cannulation of pediatric patients, where two patient populations- one with Down syndrome an one without Down syndrome- who had undergone a cardiac surgery were compared, it was stated that the arterial and venous cannulation in the population with the Down syndrome had been more challenging. In MR patients, the ultrasonography can be used for the purpose of noticing the anatomic variations during the central venous cannulation as well as the ease of procedures and avoidance of complications.

Recovery: In the recovery rooms, the MR patients pose a problem all by themselves. The limited number of health personnel in charge of these units and the challenge to take simultaneous care of more than one patient can cause some deficits in the necessary care and patience to be shown to these types of patients. The standard measurements/assessments that we use while evaluating the airway reflexes of the normal patients, such as opening the mouth and keeping it open, raising the head, and shaking hands, may not be used so often in this patient population in question. Instead, the patients must be kept under observation for longer periods of time and be referred to the involved service department to have their adequate muscle activities and the presence of their respiratory capacity observed. The patient should be re-evaluated by an experienced anaesthetist before leaving the recovery room (22).

Conclusion

In summary, since there may be several challenges/difficulties likely to be experienced at each stage of the mentally retarded patients' anaesthesia, far more care and patience is required. A pre-anaesthetic evaluation involving a physical examination in depth and a detailed questioning should be performed.

During the pre-medication period, a little amount of midazolam mixed with a proper drink can be used. The anaesthesia induction can be provided with the help of one of the inhalation anaesthetics, sevoflurane. Prior to applying the neuromuscle blocking agents, the airway opening must be maintained. In the presence of muscular dystrophies, the doses of neuromuscular blocking agents must be equalized.

Ultrasonography can be used in the course of the interventional procedures. The MR patients must be kept under observation in the recovery rooms for longer periods of time and must also be definitely re-evaluated by an experienced anaesthetist before being transferred to the service department

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Effect of acetaminofen versus lornoxicam administration on oxidative stress in rat hepatic and renal tissues

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Abstract

Background: The aim of study was to assess the oxidative status in rat hepatic and renal tissues after intraperitoneal administration of acetaminophen (AP) versus lornoxicam (L).
Materials and Methods: For this purpose 18 Wistar Albino rats were randomly divided into 3 groups; each group consists of 6 rats. Group Control (Group C) remain untreated, comprises healthy rats. Group AP received AP (100 mg kg-1) and Group L received L (1.3 mg kg-1) intraperitoneally. Oxidative status was evaluated by MDA, SOD, GST and CAT in hepatic and renal tissues. Furthermore histopathalogical evaluation was performed in both tissues.
Results: The lornoxicam received rats (Group L) showed significantly increased level of MDA and GST [(p=0.015), (p=0.048) respectively],decreased level of SOD (p=0.02)in liver tissue. Renal tissue MDA, SOD and GST activity and CAT levels were similar in groups [(p=0.168), (p=0.270), (p=0.686) respectively]. Histopathalogically Group AP and Group L more damaged than in Group C. Hepatic injury was moderate level in two groups. Minimal injury was observed in group AP. Renal injury in group L more than the Group AP.
Conclusion: The results suggest that hepatotoxic effects of lornoxicam more than the AP while no remarkable difference nephrotoxicity.

Key words: Oxidative Stress, Acetaminophen, Lornoxicam, Rat, Hepatic, Renal

Introduction

Nonsteroidal anti-inflammatory drug (NSAID)'s and acetaminophen (AP) have been used as an analgesic (1,2). Acetaminophen is normally metabolized in the liver and kidney by cytochrome P450 enzymes which differ somewhat in character between the liver and kidney.

In spite of no toxicity is observed with therapeutic doses of AP both clinical and experimental studies revealed that even much lower doses can produce renal damage (2). Nephrotoxicity is a major complication of AP exerts acute and chronic nephrotoxic effects. AP toxicity is dependent on the bioactivation by CYT enzymes to N-acetyl p-benzoquinoneimine (NAPQI) depletion of GSH, adduct formation to target proteins and oxidative stress. Although the sequence of biochemical changes associated with AP toxicity is believed to be proportional to the degree of covalent binding of AP to target proteins.

The cytotoxicity of NAPQI can be dependent on its metabolism via one-electron reduction followed by reoxidation. This redox cycle reaction can reduce molecular oxygen to superoxide anion with a consequent formation of hydrogen peroxide and hydroxyl radical. In addition to reactive oxygen species, AP toxicity can increase reactive nitrogen species generation, and these oxidative species can induce lipid peroxidation, protein oxidation, and DNA fragmentation; hence are a potential cause of cell death. Renal tissue is the secondary while liver the first target organ of AP toxicity. Oxidative stress is an important component of the AP hepatotoxicity (2,3). AP produces necrosis of the centrilobular cells of the liver and often causes liver failure when taken in overdose (3). Non-steroidal anti-inflammatory drug may cause to reduce the renal blood flow, glomerular filtration rate, retention of water and sodium and may also cause hyperkalemia (4) the administration of single dose of lornoxicam on rats in our previous

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study, revealed that liver and renal blood flow was decreased but this was not statistically significant. On the other hand paracetamol did not cause any alterations (5).

Recent reports described liver injures in association with cycloxygenase ranging from acute liver failure to varying degree of transient cholestatic liver injury (6).

Lornoxicam (chlorotenoxicam), a NSAID drug of the oxicam class with analgesic, anti-inflammatory and antioxidant properties, is available in oral and parenteral formulations (7). Anti-inflammatory and analgesic properties of lornoxicam have greater potency (8).

Many other drugs in addition to AP such as L are known to induce oxidative stress and the cause side effects during their metabolism in the liver. Although side effects of lornoxicam have beenwell documented in previous studies (9,10), comparison with lornoxicam and AP has not been investigated to the best of our knowledge. The purpose of this study was to determine the effects of intraperitoneally administered single dose AP versus L on oxidative stress in rat renal and hepatic tissue in terms of MDA, SOD, GST activity, CAT levels and tissue histopathalogy

Material and method

Animals and study Design

This study was conducted in the Physiology laboratory of Kırıkkale University upon the consent of the Experimental Animals Ethics Committee of Kırıkkale University. The experiments were conducted in accordance with ethical guidelines for investigations in laboratory animals.

In the study, 18 male Wistar Albino Rats 250-300 gr in weight, raised under the same enviromental conditions, were used. The rats were kept under 20-21 oC at cycles of 12-hour daylight and 12-hour darkness and had free access to food until 2 hours before the anaesthesia procedure.

Three groups of rats were formed as the study and control groups. Randomized 6 rats were grouped as control and no surgical procedure was performed (Group C, n=6). The study groups were administered lornoxicam (Xefo® Abi İbrahim İlaç San ve Tic A.Ş, İstanbul, Turkey) 1.3 mg kg-1 intraperitoneally (Group L) and another study groups were administered i.v. paracetamol (Perfalgan®Bristol-Myers Squibb Pharmaceuticals Ltd, UK) 100 mg kg-1 intraperitoneally (Group AP).

Thirty minutes after lornoxicam and iv paracetamol administration, the rats were weighed and then anaesthetized with ketamine (Ketalar®100 mg mL-1, Pfizer, İstanbul, Turkey), and the euthanasia via intraabdominal blood uptake was performed.

Histopathological evaluation

The semi-qualitative evaluation technique, which was used by Abdel-Wahhab et al (11) and Sen et al (10) was employed for the evaluation of structural changes in control and experimental groups. The slides for control and experimental groups were examined and assigned semi-qualitatively for severity of changes using scores on a scale of none (-), mild (+), moderate (++) and severe (+++) damage.

Biochemical Analysis

The liver and renal tissues were first washed with cold deionized water to discard blood contamination and then homogenized in a homogenizator. Measurements on cell contest require an initial preparation of the tissues. The preparation procedure may involve grinding of the tissue in a ground glass tissue blender using a rotor driven by a simple electric motor. The homogenizator as a tissue blender similar to the typical kitchen blender is used to emulsify and pulverize the tissue (Heidolph Instruments GMBH&CO KGDiax 900 Germany®) at 1000 U for about 3 min. After centrifugation at 10 000 g for about 60 min, the upper clear layer was taken.

MDA levels were determined using the method of Van Ye et al. (12) based on the reaction of MDA with thiobarbituric acid (TBA). In the TBA test reaction, MDA and TBA react in acid pH to form a pink pigment with an absorption maximum at 532 nm. Arbitrary values obtained were compared with a series of standard solutions (1,1,3,3-tetraethoxypropane). Results were expressed as nmol/mg.protein.

Part of the homogenate was extracted in ethanol/chloroform mixture (5/3 v/v) to discard the lipid fraction, which caused interferences in the activity measurements of T-SOD, CAT and GST activities. After centrifugation at 10.000 x g for 60 min, the upper clear layer was removed and used for the T-SOD, CAT, GST analyses.

In the upper clear layer, T-SOD, CAT and GST enzyme activities were measured as described Durak, et al (13), Aebi (14) and Habig et al (15), methods respectively. One unit of SOD activity was defined as the enzyme protein amount causing 50% inhibition in NBTH2 reduction rate and result were expressed in U/mg protein. The CAT activity method is based on the measurement of absorbance decrease due to H2O2 consumption at 240 nm. The GST activity method is based on the measurement of absorbance changes at 340 nm due to formation of GSH-CDNB complex. PON1 activity toward

paraoxon was assessed by adding samples to 2 mL Tris/HCl buffer containing CaCl2, paraoxon (O,O-diethyl-O-p- nitrophenylphosphate), and NaCl. Rate of generation of p-nitrophenol was determined at 405 nm and 25 °C in a spectrophotometer.

Increases in absorbance were recorded at 30-sec intervals during 5 min after 30 sec of initial pre-incubation. Enzymatic activity was calculated from molar extinction coefficient (17,000 L/mol.cm).

Statistical analysis

All variables were expressed as median and range. Differences between groups were evaluated by Kruskal–Wallis variance analysis followed by a post-hoc Mann–Whitney U-test.P-values <0.05 were considered statistically significant. All data were entered into and processed by SPSS 20.0 for Windows statistical package

Results

In present study hepatic tissue MDA, SOD, GST enzyme activity was showed significant difference in groups [(p=0.015), (p=0.002), (p=0.048) respectively]. MDA and GST enzyme activity is higher in Group L than in Group AP [(p=0.014), (p=0.048) respectively, SOD activity was lowest in Group AP, and lower in Group L than in Group C [(p=0.011), (p=0.003), (Table 1)]. But CAT and GST enzyme level in hepatic tissue was similar to that of in Group AP and Group L (Table 1).

Renal tissue MDA, SOD, GST activity and CAT levels were similar in groups [(p=0.168), (p=0.270), (p=0.673), (p=0.686) respectively (Table 2)].

Histopathological results

Liver

In the control group, the histopathological evaluation of the liver tissue showed hepatocytes in a radial pattern extending along vena centralis and a normal architecture of sinusoids.

Hepatocyte cordons had a homogenous distribution pattern. Congestion in vena centralis, sinusoidal dilatation and minimal cellular changes were observed. In addition mild non-specific inflammatory cells and mild dilatation of sinusoids were appearent in portal area (Figure 1, Table 3).

Histological sections obtained from lornoxicam showed a significant hepatic degeneration, sinusoidal dilatation, picnotic and hyperchromatic cells, focal necrosis sites and mononuclear cell infiltration, Kuppfer cell hyperplasia, inflammation, congestion and ballooning of peripheral hepatocytes. Necrotic and apoptotic appearance, degenerative changes, vasocongestion and bleeding areas were evident/appearent on hepatocytes around vena centralis. (Figure 2a, 2b, Table 3).

In the paracetamol group the alignment of the sinusoids were irregular. The size of the hepatocytes and hepatocyte cordons around vena centralis were similar with the control group. Vacuoles were noted around sinusoids adjacent to paranchimal cells.

Congestion in vena centralis and dilatation of sinusoids were observed as well as minimal cellular changes. In some areas mild nonspecific inflammatory cells, mild dilatation of sinusoids and mild hydrophilic degeneration of hepatocytes were identified. There were basophilic areas with an irregular structures in the cytoplasm of hepatocytes. (Figure 3, Table 3).

Kidney

The semislides obtained from the control group revealed no abnormal changes from the normal histological structures. (Figure 4).

In the lornoxicam group the most noticeable findings were the vacualizations in proximal tubular epithelium and the reduction in brush border. Tubules comprising vacuoles in basal localization and transparent tubules were also remarkable.

Browman distance and enlargement and congestion in blood vessels between tubules were observed. Abundant increase in mesangial matrix, glomerular hyperthrophy, thickening of basement membrane were not detected. Dilated tubules were mostly seen in distal tubules Bleeding areas, inflammatory cells, disseminated tubular cells were also observed. Glucogenic vacuolization (Armani-Ebstein lesions), degeneration and detachment of brush border of tubular epithelium, particles in tubular epithelial cell cytoplasm were detected in proximal tubules. (Figure 5).

In the paracetamol group loss of brush border and microvillus and focal vacualizations were identified. Infiltrations, vasocongestion, asymmetrical proximal tubules, bleeding areas, thickened basal membrane and shortening of brush border were also observed.

Dilatation of tubules was rare. Tubular degeneration was seen in some certain tubulus and was not common. The tubules which doesn't have a certain vacuolization had a normal structure. Narrowing in browmann distance, increase in mesangial matrix and glomerular hypertrophy were not observed. (Figure 6).

Table 1. Oxidative status parameters in rat hepatic tissue [Mean±SD]

	Group C (n=6)	Group AP (n=6)	Group L (n=6)	P**
MDA (nmol/mg prot)	2,28±1,00	4,35±2,33	6,05±2,33*	0,015
SOD(U/mg protein)	383,35±91,27	238,63±58,48*	258,89±42,14*	0,002
GST (Liver) (IU/mg prot)	17,75±5,15	25,73±8,69*	26,73±4,58*	0,048
CAT (IU/mg prot)	5920,67±1700,42	6463,86±1932,57	7458,86±1010,15	0,234

P**: p< 0.05 (with Kruskal Wallis test)
*p<0.05: Comparison with Group C

Table 2. Oxidative status parameters in rat kidney tissues [Mean±SD]

	Group C (n=6)	Group AP (n=6)	Group L (n=6)	P**
MDA (nmol/mg prot)	7,82±2,58	9,43±1,66	10,42±2,88	0,168
SOD(U/mg protein)	95,48±40,03	62,94±32,87	82,40±33,16	0,270
GST (IU/mg prot)	1,14±0,27	1,00±0,31	1,07±0,25	0,673

P**: Kruskal Wallis test

Table 3. Comparison of histological changes in rat liver by means of semi-qualitative evaluation

	Group C (n=6)	Group AP (n=6)	Group L (n=6)
Hepatocyte degeneration	-	+	+++
Sinusoidal dilatation	+	++	++
Pcynotic nucleus	-	+	++
Cell pre necrosis	-	+	++
MN cellular infiltration in the parenchyme	+	++	+++

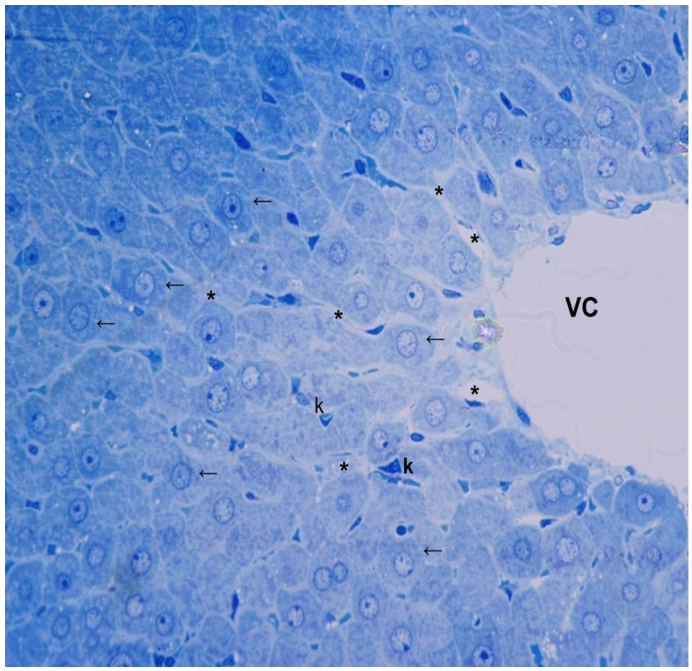

Figure 1: A slide of liver tissue obtained from the control group (vc: vena centralis, * dilated sinusoids Toluidine blue.x40)

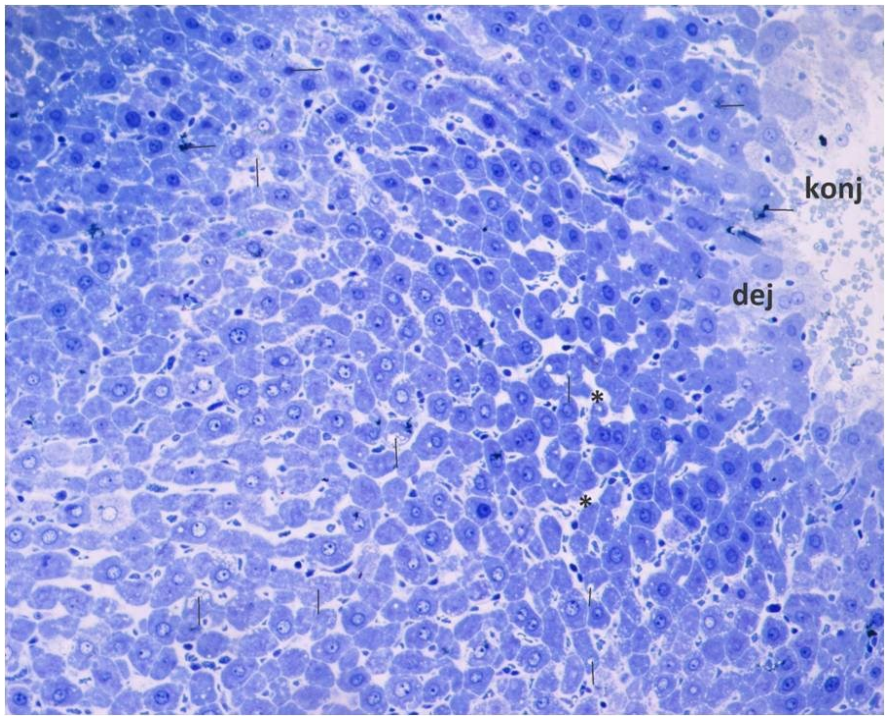

Figure 2a: Hepatoycte and vena centralis degeneration in lornoxicam group)(centrolobular damage)sinusoidal dilatation, (*) Picnotic and hyperchromatic nüclei(←) Vacuolar degeneration (↑)(Toluidine blue.x20)

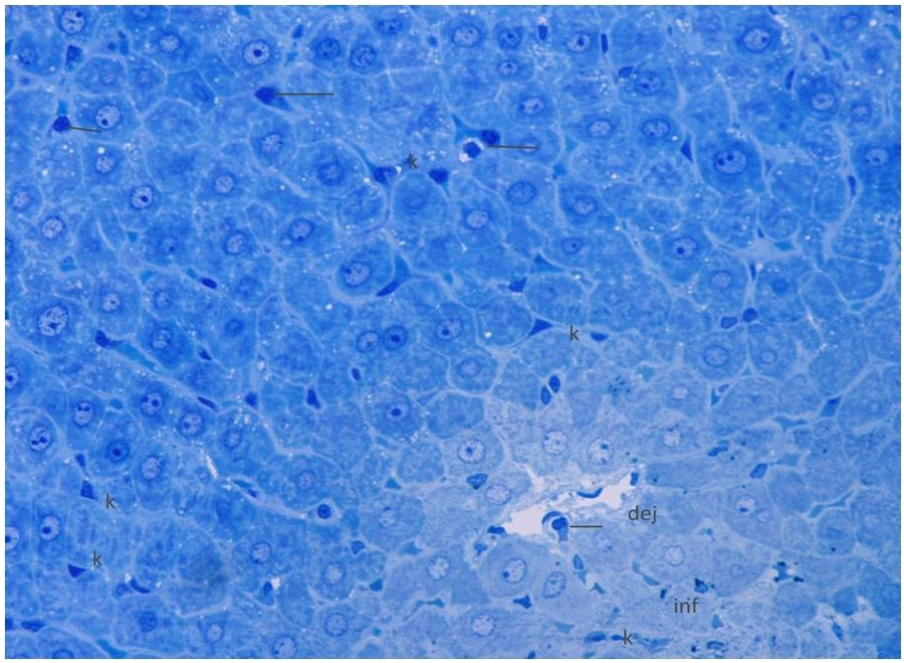

Figure 2b: Necrotic and apoptotic appearance of hepatocytes around vena centralis in the semislides obtained from the lornoxicam group (nec), Kupffer cell hyperplasia (k), Picnotic and hyperchromatic nuclei (←), sinusoidal dilatation (*)Toluidine blue.x40)

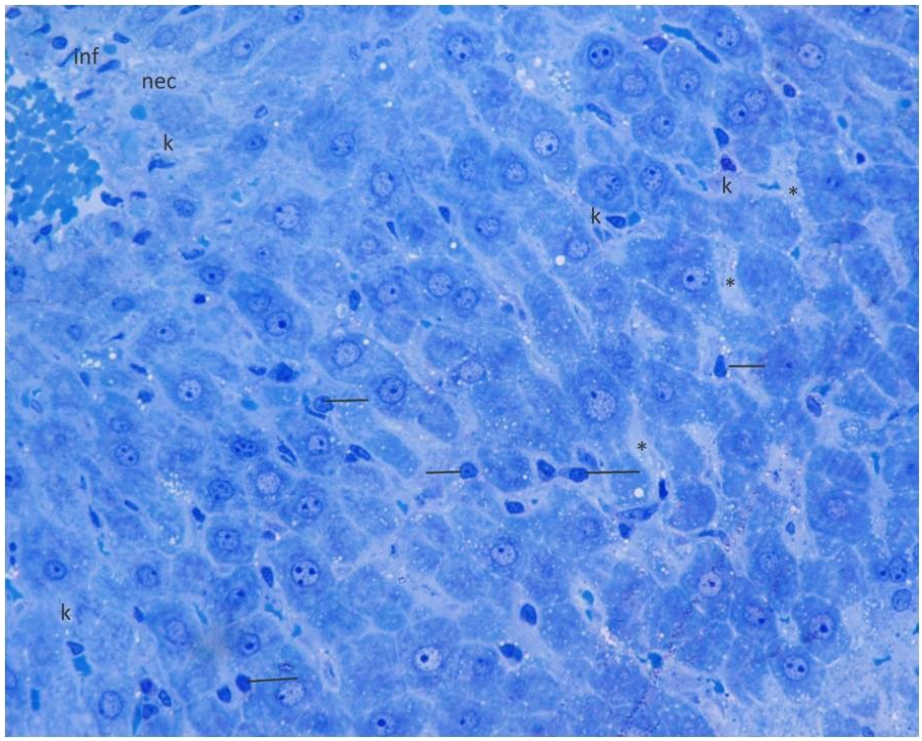

Figure 3: (Hydrophylic degeneration of hepatocytes around vena centralis in acetaminophen group, necrotic and apoptotic appearance, Kuppfer cell hyperplasia(k), picnotic and hyperchromatic nuclei(←), sinusoidal dilatation(*)Toluidine blue.x40)

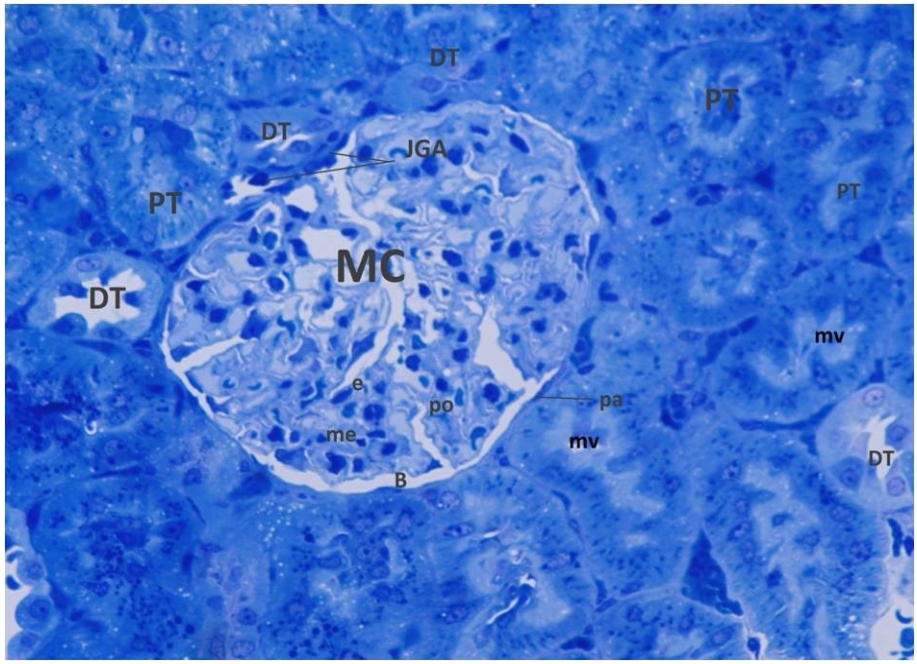

Figure 4: (Proximal and distal tubules of kidney tissue in control group MC: malpighian corpuscle, B: Bowman's gap, pa:parietal fascia, po: podocyte nucleus, e:endothelium, me: mesangial cell, mv: brush border of the proximal tubule, JGA: juxta glomerular apparatus) (Toluidine blue.x40)

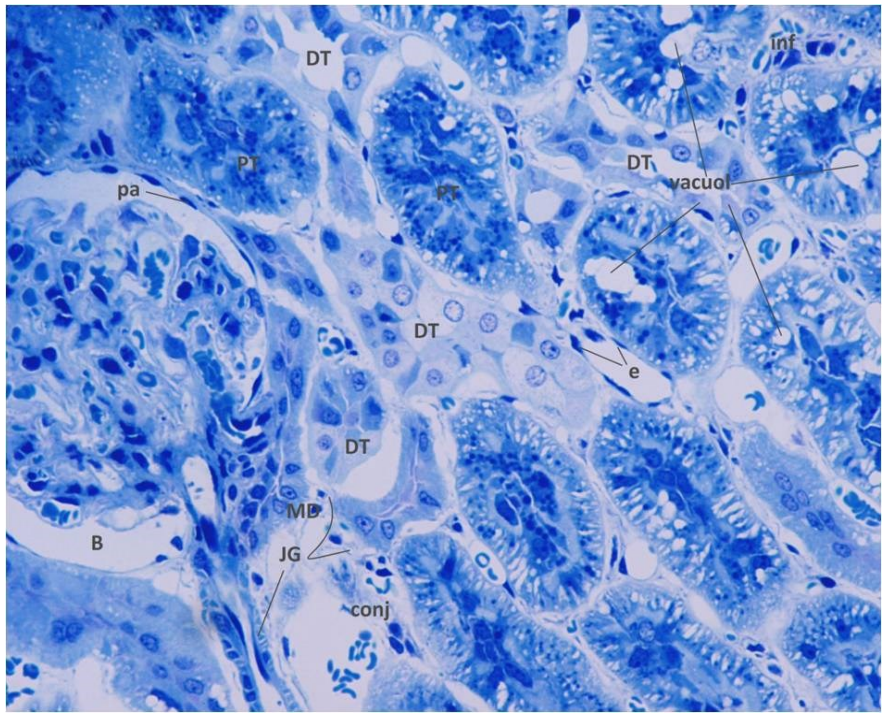

Figure 5: Malpighi corpuscule in the semislide of lornoxicam group, proximal and distal tubules. PT: Proximal tubule, DT: Distal tubule, B: Bowman's gap, pa: squamous epithelium of parietal fascia, e: endothelium, MD: macula densa and JG: juxtaglomerular cells, conj: congestion, inf: inflammation, vacuole: diffuse proximal tubule vacuolization (increase in the number and size of vacuoles) (Toluidine blue.x40)

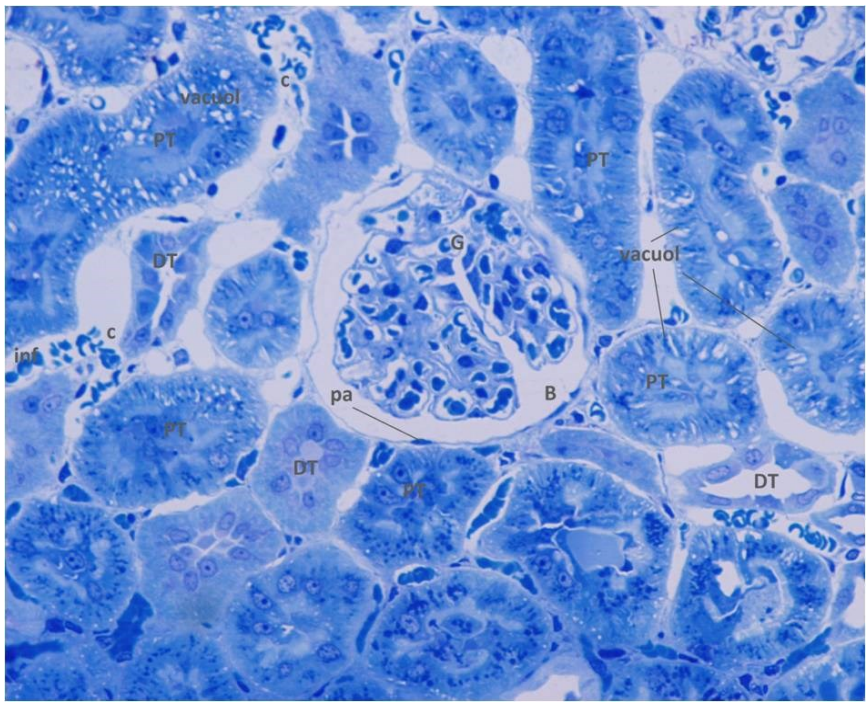

Figure 6: Renal cortex including malpighi corpuscule, proximal and distal tubules are shown in the semislide obtained from acetaminophen group. G: glomerulus, PT: proximal tubule, DT: distal tubule, B: Bowman's gap, pa: squamous epithelium of parietal fascia, c: congestion, inf: inflammation, vacuole: vacuolization of focal proximal tubule) (Toluidine blue.x40)

Discussion

Acetaminophen-Liver

Acetaminophen is the most commonly used medication worldwide because of its efficacy and safety profile. There have been several reports in the literature that suggest that acetaminophen leads to liver damage and failure (16-18). It is important to note that the doses leading to liver failure are within therapeutic range (19).

Acetaminophen produces hepatic necrosis due to the chemical reactions and interactions among hepatocytes. Acetaminophen is regarded as hepatotoxin (20). The toxicity occurs by a complex sequence of events. These include prothein, oxidative stress, calcium imbalance, changes in transcription ways, signals leading to inflammation and apoptosis. (21)

The studies on lipid peroxidation, antioxidant enzymes (glutathione peroxidase, superoxide dismutase and catalase) have been found to be of great importance in the assessment of liver damage (22).

Oxidative stress is reported to constitute a major mechanism in the pathogenesis of PCM-induced liver andrenal damage in experimental animals (23).

Oxidative damage has been reported as a mechanism contributing to acetaminophen toxicity (24). Koçak et al (24) reported that there was no statistically significant difference in terms of lipid peroxidation levels under low doses of acetaminophen(5, 10 ve 20 mg/kg) in comparison with control group. A slight increase was found in MDA levels in high dose of acetaminophen administration (100, 200 ve 500 mg/kg) in comparison with control and low dose groups. However this finding was reported not to be statistically significant. SOD values were also found to be similar.

Koçak et al. (24) concluded that intraperitoneal administration of acetaminophen (5, 10 ve 20 mg/kg) had no acute toxicity on liver.

Lores et al (25) found no significant change in SOD efficiacy following 375 mg/kg acetaminophen administration, while a 40-53% decrease ws reported in GSH-Px efficacy.

In an experimental study by Ranivce et al a significant increase was reported in GPx levels following paracetamol use (26).

Lipid peroxidation in acute acetaminophen toxicity is controversial (27). In the present study a mild increase in MDA levels were observed, whereas there was no significant difference among groups. Our results correlate with the findings of Knight et al (28), who reported no significant change following 300 mg/kg paracetamol use. Paracetamol-treated animals showed alterations in the antioxidant status of the tissues, which is manifested as an abnormal histopathology like cloudy swelling, centrilobular fatty changes, steatosis, fatty vacuolization and individual hepatocytic necrosis of hepatic cells (26).

Koçak et al. (24) demonstrated mononuclear cell infiltration around portal vein, picnotic and hyperchromatic cells and granular and vacuolar degeneration in hepatocytes following administration of 100 mg/kg acetaminophen use.

In the present study vacuolar structures were in the parenchymal cells adjacent to the sinusoids. Congestion of vena centralis, sinusoidal dilatation and minimal cellular changes were also evident in some areas. Mild non-specific inflammatory cells on portal areas, mild dilatation of sinusoids and mild hydrophilic degeneration of hepatocytes were observed.

Acetaminophen-Kidney

Renal failure secondary to analgesic and antipyretic drug use has been frequently reported in the literature. However renal failure following paracetamol and flurbiprophen administration in therapeutic doses has rarely been reported (17,18).

Gökçeoğlu et al (19) reported four cases of acute tubulointerstitial nephritis. The findings of the biopsy specimen obtained from the first case revealed moderate interstitial inflammation, lenfocyte infiltration, moderate interstiyel fibrosis, tubular necrosis, mild tubular atrophy. Mild interstitial inflammation, lenfocyte and eosinofil infiltration, mild interstitial fibrozis, tubular atrophy were reported for the second biopsy specimen of the second patient. Immunofluorescent evaluation was reported to be negative for both cases.

In these two cases the paracetamol dosage was in therapeutic limits and the usage period was short. However the medical history of the patients included antibiotic usage combined with paracetamol use (19).

In the present study the slides of paracetamol group revealed infiltration centers, vasocongestion, asymmetrical proximal tubules, bleeding areas, thickened basement membrane and shortening of brush border. Tubular dilatation was rare. New tubulus formations were present. Tubular degeneration was observed at some tubules and was not common. The tubules presenting cloudy vacuolization were in normal architecture. Narrowing of Browman distance, increase in mesangial matrix and glomerular hyperthrophy were not observed.

Linares et al. (29) reported that, during kidney injury, superoxide radicals are generated at the site of damage and modulate SOD and CAT, resulting in the loss of activity and accumulation of superoxide

radical, which damages kidney. SOD and CAT are the most important enzymes involved in ameliorating the effects of oxygen metabolism.

Availability of paracetamol as an over counter medication alone and in combination with other prescription creates a situation that may lead to exposure to excessive quantities of the drug (30). Insensitive individuals, such as persons with renal insufficiency, therapeutic doses of paracetamol have also been implicated in kidney damage (31).

In the present study Significant increases were detected in SOD and CAT levels in rat kidney tissues. However there was no significant difference among groups.

Lornoxicam-Liver

Kathleen and Michael (32) reported adverse effects with NASIDs used in dog and rats which include gastrointestinal bleeding, ulceration and platelet dysfunction nephrotoxicity, hepatotoxicity. Which results in fulminant hepatic failure and acute tubular necrosis (10).

As a possible mechanism, production of cytochrome p450-mediated metabolic activation, un coupling of oxidative phosphorylation, mitochondrial permeability transition and generation of reactive oxygen species have been suggested (33).

Sen et al. (10) who also reported that CAT and GSH levels increased in LOR-treated group compared to those in control groups.

Hummdi et al. (34) reported that hepatocytes degradation and necrosis surrounding the portal area as well as lost their nuclei with cirrhosis of the space around the portal vein and increase the thickness of theartery and the expansion of the of lymph duct also observed.

LeBail et al. (35) investigations consistent with the current study, they attribute hypertrophy of Kupffer's cells to the defense activity of these cells in the phagocytosis of red blood cells infected and cellular debris. The hypertrophy of endothelial lining cells due to their important role in inflammatory reactions against injuries and damages tissue.

In the current study histological sections obtained from lornoxicam showed a significant hepatic degeneration, sinusoidal dilatation, picnotic and hyperchromatic cells, focal necrosis sites and mononuclear cell infiltration, Kuppfer cell hyperplasia, inflammation, congestion and ballooning of peripheral hepatocytes. Necrotic and apoptotic appearance, degenerative changes, vasocongestion and bleeding areas were appearent on hepatocytes around vena centralis.

Lornoxicam-Kidney

Rabab et al. (36) reported that the kidney showed congestion in tauft of glomuruli associated with the degeneration in the lining epithelium of the renal tubules. Focal inflammatory cell infiltration between the tubules with therapeutic dose.

Radhofer–Welte and Rabasseda (37) studied the clinico pathological changes of the kidney by effect oflornoxicam as renal papillary necrosis but the kidney associated changes were notcompletely reversible during recovery period. Aydin et al. (38) determined that th elesion of the kidney varied from degeneration and epithelial cell necrosis in epithelial linning of some tubules with mononuclear cell infiltration in the interstatium, eosinophilic secretion in the tubules lumen.

In the current study the lornoxicam group showed vacuolisations and decrease in brush border of proximal tubulus epithelium. Tubules comprising vacuolar in multiple sizes and transparent tubules were remarkable. Enlargement of browman distance and blood vessels and congestion of blood vessels were significant. Tubular dilatation was generally observed in distal tubules. Bleeding areas, inflammatory cells, and diffuse tubule cells were also observed

Conclusion

These results suggest that lornoxicam may cause unfavorable pathological changes in the liver and kidney more than acetaminophen, and that further studies are needed to identify the nephrotoxic and hepatotoxic effect in patient with renal or hepatic deficiency.

Lornoxicam and acetaminophen were cause to mild to moderate reversible injury in rat hepatic or renal tissue. Acetaminophen or lornoxicam induced oxidative stress in rat hepatic tissue more than in renal tissue. Further studies are required to understand toxic effect of acetaminophen or lornoxicamin renal or hepatic deficiency patients

Conflict of Interest

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Coronary Artery Bypass surgery and sexual function

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Abstract

Objectives: To evaluate the influences of coronary artery by-pass surgery (CABS) on sexual function(SF) and the comorbidities on the impact of CABS on SF.
Methods: The data of 112 patients who underwent CABS and interviewed by full form of IIEF questionnaire before and 6 months after CABS were retrospectively evaluated. We specifically analyzed and compared the preoperative and postoperative (PAP) IIEF questionnaire(IQ) results to determine the influences of CABS on SF. Furthermore, we separately analyzed the same PAP data in diabetic, hypertensive and both diabetic and hypertensive subgroups and compared the data in each group to find possible influences of the comorbidities on the impact of CABS on SF.
Results: The mean age was 61,7±9,1. The number of patients without erectile dysfunction(ED) increased from 3(%2.6) to 7(%6.2), with severe and moderate ED decreased from 85(%75.9) to 33(%29.4), with mild ED increased from 24(%21.4) to 72(%64.2) after CABS, which revealed the severity of ED declined in overall and ED completely improved in some patients after CABS. The total IIEF, erectile function (EF), intercourse satisfaction, orgasmic function and sexual desire scores significantly increased after CABS(P=0,000). Although OS(Overall Satisfaction) had an increase, no statistically significant alteration was found(P= 0,04). The SF most improved in both diabetic and hypertensive group, it was least affected in diabetic group.
Conclusions: CABS had positive impacts on EF and almost all domains of SF. While the lonely presence of diabetes did not significantly affect the impact of CABS on SF, the SF most improved in both diabetic and hypertensive cases after CABS.

Key words: Comorbidities; coronary artery by-pass surgery; sexual function

Introduction

The most common cause of death in the world is cardiovascular disease (CVD) (1,2). Sexual dysfunction (SD) is common in patients with CVD. The reported prevalence of erectile dysfunction (ED) shows an increase from %46 in men with coronary artery disease (CAD) to 84% in men with congestive heart failure (2-4). Age, medical treatments, and cardiovascular risk factors such as hypertension, diabetes mellitus, and dyslipidaemia have been shown to be contributing to impaired sexual function (SF) (5-7). Cardiac surgeries are among the most stressful operations for the patients, and coronary artery bypass surgery (CABS) is one of the most frequent surgical procedure actually used for the treatment of CAD (8,9). Although most of the elderly people remain sexually active and there is an established relation between CAD and male SD, studies analyzing the SF following CABS are limited.

When some studies stated that preoperative erectile function (EF) appeared to be the best predictor of postoperative EF in patients who will undergo CABS, one study suggested that the conventional on-pump CABS surgery could significantly impact SF (9-11). However, resumption of SF is one of the important factors of psychosocial recovery after CABS (12).

The aim of this study was evaluating the SF before and after CABS in patients with CAD, and determining the incidence and types of sexual problems and the possible alterations in SF after CABS in relation with some comorbidities by using full form of International Index of Erectile Function (IIEF) questionnaire, in an effort to obtain data for counselling and rehabilitation of future patients

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Material and method

The data of 112 patients who underwent CABS were retrospectively evaluated. The data of patients who underwent elective CABS, were preoperatively and postoperatively interviewed by using the full form of IIEF questionnaire, had no previous cardiac surgery except for cardiac catheterization and had stable partners with regular intercourse were included in the study. The data of patients with the features that could alter SF such as renal failure, thyroid disease, chronic liver disease, previous pelvic and genitourinary surgeries, and who had previous diagnosis and medical or surgical treatment of ED were excluded from the study.

The patients were interviewed by full form of IIEF questionnaire previous to CABS. This questionnaire consists of 15 questions to evaluate the subgroups of sexual function including total IIEF score, erectile function (EF), orgasmic function (OF), sexual desire (SD), intercourse satisfaction (IS) and overall satisfaction (OS). Scoring the IIEF domain of erectile function provides the classification of each patient as having no (26–30), mild (17–25), moderate (11–16) or severe (0–10) ED. As a result of this evaluation, we have determined the preoperative status of EF and other subgroups of SF in IIEF questionnaire. At 6th month's control, the questionnaire was completed by all patients again and the same data demonstrating postoperative status were also collected. By using preoperative and postoperative data, we specifically analyzed and compared the preoperative and postoperative IIEF questionnaire results with the aim of finding the incidence and severity of ED, determining the possible alterations in all subgroups of SF in IIEF questionnaire related to CABS, and showing the possible influences of CABS on SF.

The descriptive data were also evaluated in the sample. This data included age, body mass index, the comorbidities of diabetes mellitus (DM), hypertension (HT) and both (DM+HT), the severity of vascular disease, alcohol, smoking habit and medical treatments. The patients were grouped into 3 subgroups according to the concomitant comorbidities, such as diabetic (group 1), hypertensive (group 2) and both diabetic and hypertensive (group 3) subgroups. We separately analyzed the same preoperative and postoperative IIEF data in 3 subgroups and compared the data in each group with the aim of finding possible influences of the comorbidities on the impact of CABS on SF results of IIEF questionnaire.

Statistical analysis

All data were reviewed retrospectively. Data are expressed as Mean±SD. The categorical variables were presented as percentage (%). Analytical tests including independent

Student's *T*-tests, Mann Whitney U test and Wilcoxon test were used for comparing the preoperative and postoperative data and evaluating the correlations between the data, as appropriate. A P value <0, 05 was considered significant. SPSS version 16.0 was used for the analyses.

Results

The mean age was 61.7±9.1 years. The sample included 41(36.6%) diabetic, 50 (44.64%) hypertensive and 28 (25%) diabetic and hypertensive patients. 76 (67.8%) patients were with hyperlipidemia. One vessel disease, 2 vessel disease, 3 vessel disease and multivessel disease was determined in 10(8.92%), 33(29.46%), 52(46.42%) and 17(15.17%) patients, respectively. The mean ejection fraction was 58%±17.4. The demographic features of patients were clearly demonstrated in table 1.

Table 1. The demonstration of demographic features of patients

n	(112)
Mean age	61.7±9.1
DM	41 (36.6%)
Hypertension	50 (44.64%)
DM + Hypertension	28 (25%)
Hyperlipidemia	76 (67.85%)
Smoking	85 (75.89%)
Family history	59 (52.67%)
One vessel disease	10 (8.92%)
Two vessel disease	33 (29.46%)
Three vessel disease	52 (46.42%)
Multivessel disease	17 (15.17%)
Mean ejection fraction	58% (SD 17.4)
Beta blocker medication	83 (74.10%)
CCB medication	7 (6.25%)
ACE inhibitor medication	46 (41.07%)
AT2 blocker medication	8 (7.04%)
Statin medication	89 (79.46%)
Diuretic medication	13 (11.60%)
Mean body mass index	28 (SD 3.77)

DM: Diabetes mellitus
CCB: Calcium channel blocker

The analysis of preoperative and postoperative IIEF results showed that severe ED was preoperatively present in 1(0.89%) patient, and it was increased to 8 (7.14%) at 6th month postoperatively. While 84 (75) patients had moderate ED preoperatively, it decreased to 25 (22.32%) at 6th month control after the surgery. However, 24(21.42%) patients were with mild ED preoperatively, this result increased to 72(64.28%) postoperatively. The number of patients without ED increased from 3 (2.6%) to 7 (6.2%). The preoperative and postoperative results of ED were clearly seen in table 2.

The evaluation of IIEF data regarding all subgroups of sexual function in IIEF questionnaire in overall revealed that total IIEF scores significantly increased after the operation (P=0.000). In addition, both of the IIEF scores of EF, IS, OF and SD also significantly increased (P=0.000 in all).

Table 2: The demonstration of pre and postoperative status of erectile dysfunction in the sample. (1., 2., 3., 4., 5. and 15. questions in IIEF -15 questionnaire evaluates the erectile function.)

Severity of ED	Preoperative Erectile Function	Postoperative Erectile Function
Severe ED (IIEF score 6-10)	1 (0.89%)	88 (7.14%)
Moderate ED (IIEF score 11-16)	84 (75%)	25 (22.32%)
Mild ED (IIEF score 17-25)	24 (21.42%)	72 (64.28%)
No ED (IIEF score 26-30)	3 (2.6%)	7 (6.2%)

No significant alteration was occurred in the IIEF score of OS postoperatively (P=0.04). The analysis and comparison of IIEF results in the subgroups of sexual function in IIEF questionnaire in overall was demonstrated in table 3.

Table 3. The comparison of pre and postoperative IIEF scores in overall.

IIEF subgroups	Mean	Mean Diff.	P value
Preop total IIEF	37,47±5,07	9,69	0,000
Postop total IIEF	47,16±11,51		
Preop EF	15,34±2,24	2,74	0,000
PostopEF	18,08±5,39		
Preop IS	9,15±1,21	1,3	0,000
Postop IS	10,45±2,54		
Preop OF	3,78±1,13	3,08	0,000
Postop OF	6,86±2,17		
Preop SD	4,26±0,77	1,23	0,000
Postop SD	5,49±1,99		
Preop OS	4,95±1,68	0,58	0,040
Postop OS	5,53±2,21		

N=112
EF: erectile function,
IS: intercourse satisfaction,
OF: orgasmic function,
SD: sexual desire
OS: overall satisfaction

The analysis of IIEF data in 3 subgroups of the sample regarding the comorbidities declared different results. In group 1, it was seen that there were no statistically significant differences between preoperative and postoperative scores of total IIEF (P=0.226), EF (P=0.328), IS(P=0.161), and SD (P=0.668). While OF score significantly increased from 3.70±1.10 to 6.17±2.34 (P=0.000), OS significantly decreased from 5.34±1.66 to 4.09±1.82 after the operation (P=0.003). In group 2, the scores of total IIEF, EF, IS, OF and SD significantly increased (P=0.000 in all). Although an increase from 4.80±1.69 to 5.82±1.90 was also seen in terms of OS score, it was not found statistically significant (P=0.06). In group 3, total IIEF and EF scores significantly increased from 35.82±6.56 to 56.42±5.97 and from 14.67±2.95 to 22.07±3.37, respectively (P=0.000 in all).

Furthermore, a significant improvement was also seen in other subgroups of sexual function in IIEF questionnaire including IS, OF, SD and OS (P=0.000 in all). The analysis and comparison of preoperative and postoperative IIEF data in 3 subgroups of the sample regarding the comorbidities were shown in table 4

Table 4: Pre and postoperative IIEF scores in 3 sub-groups, regarding to the comorbidities.

	Mean	Mean Diff.	p value
Group 1 n=41			
Preop IIEF	38,04±3,75	2,25	0,226
Postop IIEF	40,19±11,47		
Preop EF	15,65±1,65	-0,8	0,328
PostopEF	14,85±5,11		
Preop IS	9,14±0,96	0,71	0,161
Postop IS	9,85±2,88		
Preop OF	3,70±1,10	2,47	0,000
Postop OF	6,17±2,34		
Preop SD	4,39±0,86	-0,1	0,668
Postop SD	4,29±1,45		
Preop OS	5,34±1,66	-1,25	0,003
Postop OS	4,09±1,82		
Group 2 n=50			
Preop IIEF	37,72±4,73	11,42	0,000
Postop IIEF	49,14±8,93		
Preop EF	15,34±2,07	3,92	0,000
PostopEF	19,26±4,28		
Preop IS	9,32±0,76	1,36	0,000
Postop IS	10,68±2,27		
Preop OF	4,04±1,12	3,04	0,000
Postop OF	7,08±1,98		
Preop SD	4,16±0,65	1,52	0,000
Postop SD	5,68±1,99		
Preop OS	4,80±1,69	1,02	0,060
Postop OS	5,82±1,90		
Group 3 n=28			
Preop IIEF	35,82±6,56	20,6	0,000
Postop IIEF	56,42±5,97		
Preop EF	14,67±2,95	7,4	0,000
PostopEF	22,07±3,37		
Preop IS	8,85±1,89	2,25	0,000
Postop IS	11,10±1,42		
Preop OF	3,35±0,98	4,07	0,000
Postop OF	7,42±2,13		
Preop SD	4,25±0,75	2,42	0,000
Postop SD	6,67±1,76		
Preop OS	4,60±1,49	2,65	0,000
Postop OS	7,25±1,95		

EF: erectile function,
IS: intercourse satisfaction,
OF: orgasmic function,
SD: sexual desire
OS: overall satisfaction

Discussion

CABS is known to cause inflammatory response that is primarily associated with low blood pressure, temperature changes, leukocytosis and tissue edema and can lead to end-organ dysfunction, which may affect the SF (2,13,14). The current technical and technological improvements have rendered CABS more safe, reducing to acceptable levels the surgical risk even in older cases (2.15). Although most of the elderly people are sexually active and there is an established relation between CAD and male SD, studies analyzing the SF following CABS are limited. The most common sexual problems in patients with CAD are faced with include reduced libido, avoidance of sexual activity, and ED (16). When some studies stated that preoperative EF appeared to be the best predictor of postoperative EF in patients who will undergo CABS, one study suggested that the conventional on-pump CABS surgery could significantly impact SF (10,11).

In the present study, we aimed to evaluate the preoperative and postoperative status of SF in patients with CAD, to determine the incidence and types of sexual problems and the possible alterations in SF after CABS in relation with some comorbidities by using the full form of IIEF questionnaire. ED is defined as the inability to achieve an erection in order to maintain satisfactory intercourse. The prevalence of ED in general population is 19–52% (2,17). Atherosclerosis is the most common cause of ED, and the patients with CAD are commonly together with ED that occurs as a result of some potential mechanisms (2,18). ED has significant influences on quality of life. There were only a few studies in literature, which evaluated EF retrospectively before and after CABS, regarding to changes in EF after CABS (19,20). In our study we evaluated EF before and after the surgery. It was found that the number of patients without ED increased 3(%2.6) to 7(%6.2). However, while total account of severe and moderate ED decreased from 85(%75.9) to 33(%29.4), the number of patients with mild ED increased from 24(%21.4) to 72(%64.2). It was clearly seen that the severity of ED declined in overall and also ED completely improved in some patients (n=4) after the surgery. Therefore, we supposed that CABS had positive impacts on EF. In the literature, one study revealed that CABS may have a significant impact on EF (10,21). Nevertheless, some reports declared that CABS does not provide a net gain in SF (10,11). It should be kept in mind that ED may be early marker of CAD, and must prompt every physician to evaluate the patient for CAD (18). Although some previous reports in the literature commonly used the short form of IIEF questionnaire (IIEF-5) and analyzed only EF and/or had commonly no sufficient follow-up period, we used the full form of IIEF questionnaire and also evaluated all sexual components of the sample before and 6 months after CABS. Thus, we could analyses the alterations in other components of sexual function in IIEF questionnaire related to the CABS. The previous literature showed that CABS influenced SF and resumption of sexual activity is an important factor for recovery. In a study, it was found that after the diagnosis of a cardiac disorder or a cardiac intervention, %25 lost their SF completely, %25 of patients had normal SF, and %50 had a decreased SF (22). The previous literature determined that a considerable improvement in comparison to the patients' status before CABS and one study declared that the most common sign of patients' recovery after cardiac surgery is resumption of their social and sexual activity (2,23).

In our study, the evaluation of IIEF data regarding all subgroups of SF in IIEF questionnaire revealed that total IIEF score and IIEF scores of EF, IS, OF and SD significantly increased after the operation (P= 0,000 in all). Although an increase were also seen in terms of OS, no statistically significant alteration was found (P= 0,04). The improvement of the majority of subgroups of SF in IIEF questionnaire showed that CABS had positive impacts on SF of patients with CAD. Vascular disorders are one of the organic causes of SF so it is not surprising that the patients with CAD have SD. The association between ED and cardiovascular risk factors has been previously reported by several authors (2,24-27). Both ED and CAD share the same risk factors including aging, diabetes mellitus, hypertension, hyperlipidemia and smoking (19,27-29). Although there are some reports addressing the predictive factors of SF following CABS; they did not evaluate the impacts of each vascular RFs on sexual function after CABS (10,11). In our study, the sample were divided in 3 subgroups according to the comorbidities, including diabetic (group 1), hypertensive (group 2) and both diabetic and hypertensive (group 3) subgroups. The preoperative and postoperative IIEF data were separately determined in 3 subgroups. The comparison of preoperative and postoperative IIEF results in each group with the aim of finding possible influences of the comorbidities on the impact of CABS on sexual function was performed. This analysis revealed different results in each group. In group 1, it was seen that there were no statistically significant differences between preoperative and postoperative scores of total IIEF, EF, IS, and SD. Nevertheless, OS score significantly decreased, while OF score significantly increased in diabetic patients after CABS. In the guidance of these results, it was concluded that CABS had no significant effects on sexual function in diabetic patients with CAD. Nevertheless, while total IIEF, EF, IS, OF and SD scores significantly increased in group 2. These results showed that a significant improvement was occurred in almost all scores of the parameters in hypertensive patients after CABS. Furthermore, all scores of the subgroups of sexual function in IIEF questionnaire significantly improved in group 3 after CABS. In overall, these results revealed that while the sexual function most improved

in both diabetic and hypertensive patients, it was least affected in only diabetic patients after CABS.

Conclusion

The determination of the decline in the severity of ED in overall and the complete improvement of ED in some patients after CABS revealed that CABS had positive impacts on EF in patients with CAD. Furthermore, the demonstration of a significant improvement in the majority of subgroups of SF in IIEF questionnaire was concluded that CABS had also an encompassing positive impact on almost all domains of sexual function in patients with CAD. On the other hand, the analysis of possible influences of the comorbidities on the impact of CABS on sexual function showed that while the lonely presence of diabetes mellitus did not significantly affected the impact of CABS on sexual function, the sexual function most improved in both diabetic and hypertensive cases after CABS. We supposed that these results need to be confirmed by prospective and randomized trials in greater series.

Conflict of Interest

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Retrospective analysis of deep sedation in pediatric population for endoscopic procedures: adverse events and outcomes

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Abstract

Background: Upper gastrointestinal endoscopy (E) and colonoscopy (C) procedures are not well tolerated in pediatric population. General anesthesia or sedation applied during gastroendoscopic procedures. This study is done to review our sedation practice and to evaluate the clinical effectiveness and side effects of an anaesthesiologist administered deep sedation for gastroendoscopic procedures outside the operating room.
Methods: After Institutional Review Board Approval, the charts of all children who underwent endoscopic procedure at the outpatient endoscopy suite under sedation, (Jan 2011- December 2011) were reviewed retrospectively.
Results: Deep sedation was used in 301 procedures, which 255 were endoscopic and 23 were colonoscopic procedures. Twenty-three children had both procedures performed in one session. Demographic details: Age [year, mean]: 10,1±5,1, Gender (M/F): 152/149, Body weight [kg, (mean±SD)]: 35.7±18.7. Severe bradycardia with oxygen desaturation was recorded in two patients. All procedures were carried out successfully. Emergence delirium was seen in only one patient who was the substance user. No significant side effect derived from intervention was observed during the procedures, except one case (perforation of the colon).
Conclusion: Deep sedation applied by anesthesiologist found to be adequately safe and appropriate for children during gastroendoscopic procedures

Key words: Child, Complication, Sedation, Ambulatory Anesthesia

Introduction

In paediatric patients, sedation or sedo-analgesia procedures are required when there is anxiety, fear of medical procedures, behavioural impairment and pain. Upper gastrointestinal endoscopy (E) and colonoscopy (C) frequently performed to diagnose and treat a wide range of gastrointestinal problems. These procedures are not well tolerated in paediatric population. For those reason endoscopic procedures under sedation or general anaesthesia is preferred option.

The aims and objectives of providing care during sedation or general anaesthesia on children are amnesia, motionless, safety, early discharge, and cost effective care. But sedation or general anaesthesia are not complication free applications. Furthermore endoscopic procedures are frequently performed outside the operating room (1-5). Significant complications during such procedures have been reported (6).

There exists a great variation in anaesthesia practice for paediatric endoscopy. Increased awareness of the complications associated with sedation during GI endoscopic procedures in children, the institution of modern monitoring modalities to identify these complications, and the involvement of the anaesthesiologists in looking after these children in, or outside, the operating room is optimal for the safety of these patients (1-8).

We aim to present adverse events and outcomes at endoscopic procedures under deep sedation applied by the anaesthesiologist in paediatric population

Material and method

This study was approved by the institutional review board at Gazi University Faculty of Medicine. The anesthesia database at our hospital during January 2011-December 2011 interval was searched for all patients less than 19 years of age referred for gastro endoscopic procedures under deep sedation. All interventions were performed by same team of the pediatric gastroenterologist. All sedation was given by a staff anesthesiologist. Following demographic and clinical data were obtained:

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age, gender, weight, ASA classification, time of endoscopy procedure, oxygen delivery method, doses of the anesthetics, and hemodynamic variables during sedation, complications, and any therapeutic interventions performed.

Procedural and resuscitative equipment of a size and type appropriate for pediatric use was been readily available during procedures. There were no premedication's prior to the procedure.

For all patients EKG, non-invasive blood pressure and SpO2 monitoring were used. All patients received supplemental O2 at 2-3 l/min through nasal canula. Sedation level was sustained with sedation agent as University of Michigan Sedation Scale (UMSS) (9) scores (3,4).

Post-Anesthetic Discharge Scoring System (PADSS) was used to discharge of the patients from endoscopy suit, and total score≥9 was considered for discharge (10). The effectiveness of intravenous sedation was defined as successful completion of the procedure. Sedation-related complications were defined as desaturation (oxygen saturation<94%), bradycardia (heart rate<20% than initial values), need for supplemental oxygen (above baseline supplementation). Intervention related complications were recorded too.

Statistical analysis

The statistical analyses were performed with SPSS 17.0 software program and $p<0.05$ was considered statistically significant. Data were presented as mean value±standard deviation (SD), (Min-Max), n, (%).

Kolmogorov-Smirnov test was performed for the measurable parameters in order to determine whether the range is normal. Parametric values were evaluated with one-way ANOVA with Bonferroni adjustment. Numerically equality be achieved and non-parametric values were studied with Kruskal-Wallis test and the differences were evaluated with Mann-Whitney U test. HR and SpO2 parameters were analysed using repeated-measures analysis of variance (ANOVA), with Bonferroni's adjustment. Complication and/or side effects were compared using Chi-square and Fisher's exact tests

Results

Three hundred and one procedures (n=255 E, n=23 C, n=23 E+C) were performed on 301 children (Table 1). Supplemental oxygen was given via nasal cannula, ambu or endotracheal intubation (Table 2). Doses of used anesthetics, anesthetic agents or combinations in terms of groups, quantity of the used anesthetic agents and procedure time were shown in Table 3, Table 4 and Table 5 (respectively). Time dependent heart rate and SpO_2 variables were shown in Figure 1 and 2. Complication and/or side effects in terms of E, C, and E+C groups were shown in Table 6. Significant desaturation was recorded in seven patients (lowest SpO_2 values were 55%). Endoscopic intervention was stopped and the children were ventilated 100% O_2 by ambu mask (n=5) or endotracheal tube (n=2) than SpO_2 values were normalized. The procedures were then completed uneventfully. No significant side effect derived from intervention was observed during the procedures except one patient (perforation of the colon) and then endotracheal intubation was attempted. Colonic perforation case was carried out to the operation room for urgent surgical operation. Except this case all procedures were carried out successfully. Severe agitation and delirium was seen during recovery period in one patient who was the substance addicted

Discussion

This retrospective study demonstrates clinical effectiveness and side effects of deep sedation applied by the anesthesiologist for pediatric gastro endoscopic procedures.

The aims and objectives of providing sedation on children for endoscopic procedures are: allowing the children to tolerate the unpleasant procedures, remaining motionless, amnesia, preventing complications, ensuring safety, ensuring early discharge from the facility to home providing high quality and cost effective care. This also requires careful consideration of the patient, the endoscopy facility, and the variables of the procedure itself. Patient factors include age, weight, concurrent diseases, airway assessment, pre-procedure anxiety, and pain tolerance. Procedure variables include the amount of anticipated discomfort, the duration of examination, and how invasive the procedure will be. Although GI endoscopy is generally considered safe, the procedure does have a potential for complications.

For pediatric gastroendoscopic procedures general anesthesia or sedation are applied in anesthesia practice. It is important to recognize that most pediatric sedation are deep and risk and adverse events occur more than adults (1-5).

In our work; parents of the patients were informed of and agree to the administration of anesthesia, including discussion of its benefits, risks, and limitations and possible alternatives. Patient's historic details just like; diseases of major organ systems, snoring, stridor, sleep apnea, allergies, prior adverse reaction to drugs, current medications, time of and type of last oral intake, alcohol, or substance use are obtained by direct questions. Furthermore physical examination (measurement of vital signs, determination of baseline level of consciousness, and assessment of the cardiopulmonary system was performed.

Table 1. Demographic properties and operation data [Mean±SD (Min-Max), n]

Number of the patient (n)	301
Gender (Male/Female)	152/149
Age (Year)	10,16±5,19 (0,25-18)
Weight (kg)	35,74±18,72 (5-83)
ASA (I/II)	265/36
Time of endoscopy procedure (minute)	20,36±12,75 (5-75)

Table 2. Oxygene delivery method [n (%)]

Devices	**n, (%)**
Nasal canula	294 (98)
Ambu	5 (1,4)
Endotracheal entubation	2 (0,6)

Table 3. Doses of anesthetics [n, Mean±SD (Min-Max]

IV Pharmacologic agents	**n**	**Mean±SD (Min-Max)**
Propofol (mg)	261	112,17±60,31 (10-310)
Midazolam (mg)	284	0,91±0,24 (0,5-2)
Ketamine (mg)	144	19,58±13,19 (5-70)
Fentanyl (µg)	2	37,50±17,68 (25-50)

Table 4. Used anesthetic agents or combinations [n, (%)]

Used anesthestic agents	**E (n=255)**	**C (n=23)**	**E+C (n=23)**
Propofol	15	-	-
Midazolam+Propofol	126	11	4
Midazolam+Ketamin	35	1	3
Midazolam+Ketamin+Propofol	77	11	16
Sevoflurane	2	-	-

Table 5. Quantity of the used anesthetic agents and procedure time [Mean±SD (Min-Max)]

	E (n=255)	**C (n=23)**	**E+C (n=23)**	**p****
Propofol (mg)	104,29±53,26 (10-270)	167,73±80,23* (40-300)	137,25±71,85* (20-310)	<0,0001
Midazolam (mg)	0,91±0,25 (1-2)	0,91±0,20 (0,5-1)	0,94±0,23 (0,5-1,5)	0,844
Ketamin(mg)	18,28±12,29 (5-70)	15,58±10,32 (5-45)	30,00±15,55$^{\&}$*, (5-60)	0,002
Fentanil (µg)	-	50	25	-
Procedure time (min)	10,06±6,13 (5-45)	37,17±13,38* (10-75)	50,87±10,52*,& (30-75)	<0,0001

p** p<0.05 Kruskal-Wallis Test
*p<0.05 Comparison with Group E
$^{\&}$p<0.05 Comparison with Group C

Table 6. Complication and/or side effects in terms of E, C and EC groups [n (%)]

	E (n=255)	**C (n=23)**	**E+C (n=23)**	**p**
Nausea/vomiting	2 (0,8)	-	-	X^2=0,663, p=0,718
Desaturation (94≤)	5 (2)	1(4,5)	1 (4,5)	X^2=0,829, p=0,661
Bradycardia	1 (0,4)	-	-	-
Respiratory distress	2 (0,8)	1(4,5)	-	X^2=2,024, p=0,364
Allergy	2 (0,8)	1(4,5)	-	-
Colon perforation	-	1(4,5)	-	X^2=2,024, p=0,364

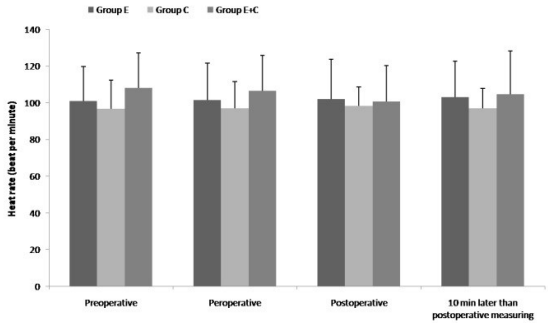

Figure 1. Time dependent heart beat rate in terms of groups

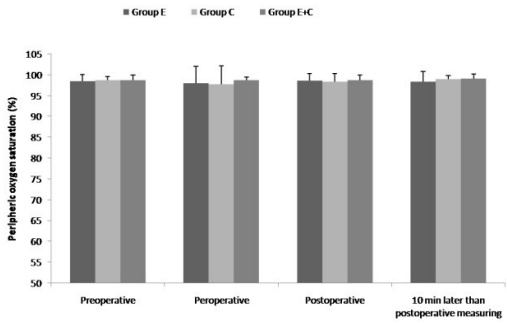

Figure 2. Time dependent SpO2 values in terms of groups

Thakkar et al (4) found that, the younger the age group, the higher the ASA class and intravenous (IV) sedation as risk factors for developing complications. Selection of patients according to this risk stratification may help to prevent or reduce complications associated with the procedure (5). In our series all the patients were in ASA I-II class.

There are no absolute guidelines as to timing of fasting before administration of sedation because of the absence of supporting data with regard to a direct relationship between duration of fasting and risk of pulmonary aspiration. The ASA guidelines recommend that patients should not consume fluids or solid foods for a sufficient period of time so as to permit adequate gastric empting (11, 12). In our clinic; patients were prevented from taking clear fluid, breast milk, light meal or heavy meal orally for 2, 4, 6 to 8 hours (respectively). No patient had pulmonary aspiration related complication in our series.

Monitoring is essential during sedation and recovery period. Pulse oximetry is a valuable tool to pick up oxygen desaturation but may not adequately reflect hypoventilation, apnea, impending hemodynamic instability, or vasoconstrictive shock. In particular, patients may be well saturated with oxygen and still experience significant CO2 retention. Capnography has emerged as a noninvasive way of measuring patient ventilation that may be especially useful in patients undergoing deeper levels of sedation (11-14). Malviya et al (7) picked up desaturation in 5.5% of patients and achieved a reduction in bad outcomes. Hypoxemia secondary to depressed respiratory activity is the most important risk factor for near misses and death during sedation for children undergoing procedures. Early detection may be valuable in avoiding morbidity and mortality in pediatric sedation procedures. In our series patients were observed closely. Desaturation was observed in 7 patients. Although SpO2 was monitored EtCO2 was not monitored causes of technical failure.

Oxygen was administered by nasal cannula in all of our patients. This practice is a matter of debate because it could affect the timely detection of hypoventilation (13,14). On the other hand, the ASA guidelines recommend supplemental oxygen during sedation, and many authors follow this recommendation (11,12).

In our clinic oropharyngeal topical anesthesia just before endoscopy was not used because topical anesthetic agents have been associated with serious adverse effects (aspiration, anaphylactoid reactions) (15).

There aren't exact consensuses about anesthetic management of children for endoscopic procedures, and general anesthesia, sedation, or non-sedation (awake) methods are using1-3. In recent years, 4 levels of sedation were identified, which stretch along a continuum without clear boundaries: minimal sedation or anxiolysis, moderate sedation, deep sedation, and general anesthesia. To date, these levels of sedation have been defined by a patient's response to verbal, light tactile, or painful stimuli, although they are generally also associated with physiologic changes in patient vital signs. Deep sedation is a drug-induced depression of consciousness, during which patients cannot be easily aroused but respond purposefully to repeated or painful stimulation. The ability to maintain ventilator function may be impaired. Patients may require assistance in maintaining a patent airway, and spontaneous ventilation may be inadequate. Cardiovascular function is usually maintained (16). In our series deep sedation level [UMSS scores 3-4 (9)] was intended.

Gastroscopy is a widely-used method for detecting upper gastrointestinal diseases. However, hypoxias, elevations of blood pressure and heart rate have repeatedly been demonstrated during gastroscopy (1-5). These potentially harmful side-effects are sometimes life-threatening, particularly for patients with accompanying disease. Although it has been shown that sedation during gastroscopy helps to prevent the increase in blood pressure and heart rate, hypoxia still remains a potential risk following administration of sedation Administration of sedation incurs additional medical expenditure and risks. The most common serious and life-threatening complications related to sedation are respirator in ethology. Of these, the most serious is aspiration because its consequences may be impossible to correct

or prevent once substantial aspiration has occurred. Even minor episodes of aspiration may result in prolonged coughing, bronchospasm, or pulmonary infections. Thus, avoidance of pulmonary aspiration is critical for safe endoscopic practice. These events are related to the depth of sedation and may result from suppression of respiratory drive in the central nervous system or from airway collapse that occurs with sedation. Cardiovascular complications are less commonly life threatening during endoscopy, and, when life threatening, they most often follow a period of inadequate ventilation and hypoxemia. Nevertheless, the physiologic response to sedation and the physical stress of endoscopy is quite variable. Individual patients have a susceptibility to vagally mediated bradycardia and hypotension that can be precipitated by stretching the sigmoid mesentery during passage of a colonoscope. In other patients, marked tachycardia may develop if the procedure is started when they are inadequately sedated, particularly during upper endoscopic procedures. Hypertension is seen commonly during endoscopic procedures. Although hypotension and hypertension during endoscopy very rarely result in permanent complications, they occasionally reach levels for which corrective action is appropriate. Atrial or ventricular arrhythmias are rarely precipitated by sedation or stress of the procedure (4,5,7,12,17,18). In works of Deenadayalu et al (19) a worldwide multicenter safety review of more than 521,000 patients was conducted. Mask ventilation rates were 0.4:1000 patients for upper endoscopy and 0.1:1000 patients for colonoscopy. Endotracheal intubations, neurologic injuries, and death occurred in 4, 1, and 3 patients, respectively. The 3 deaths occurred in patients with significant comorbid illnesses such as widely metastatic malignancy and polysubstance abuse.

Although gastrointestinal endoscopy occasionally is a safe procedure, significant complication can occur as a result of instrumentation, such as bleeding, perforation and infection. In our series rather than seventeen cases (patients with nausea/vomiting, desaturation, severe bardycardia, respiratory distress, colon perforation, allergy) vital parameters were stable all procedures long. All procedures except one (colonic perforation) carried out successfully.

Sedation is applied by nonanesthesiologist too. Motas et al (20) in a prospective study of pediatric population undergoing sedation by non-anesthesiologists for various procedures reported failure to achieve sedation in 12%-28% using BIS or the UMSS respectively as a monitor of sedation. Malviya et al (7), in another prospective study involving 1140 children sedated by a non-anesthesiologist for various procedures, reported a 20.1% incidence of adverse events. These included inadequate sedation, low oxygen saturation, airway obstruction, apnea needing bag mask ventilation, and excitement and agitation. Lightdale et al (21) prospectively reviewed more than 2300 endoscopic procedures and reported agitation, respiratory events, incomplete procedures, hemorrhage and perforation as adverse events. Agitation was significantly associated with endoscopist-administered sedation. Mamula et al (22) in a retrospective review of conscious sedation in children also reported approximately 20% incidence of non-life threatening adverse events. Levis et al (23) reported a 20% incidence of recall in children following esophago-gastroduodenoscopy, thus increasing their level of anxiety and reluctance to accept subsequent procedures. Thakkar et al (4), in a cross sectional retrospective study of 10.236 upper GI endoscopic procedures in 0-18 year old children reported an overall immediate complication rate of 2.3%. IV sedation with midazolam, fentanyl, meperidine or ketamine was used in 46% of procedures, whereas 54% procedures were performed under GA. Cardiopulmonary complications were reported in 79.9% of procedures, gastrointestinal complications were reported in 18% of procedures, whereas in 5.9% of procedures complications such as prolonged sedation, drug reaction or rash were reported. All complications were non-fatal and most were hypoxia- related and reversible. They identified a younger age, higher ASA class, female sex and IV sedation as risk factors for developing complications. A complication rate of 1.2% was associated with procedures performed under GA as compared to a 3.7% incidence associated with IV sedation. After adjusting with all other variables, they reported IV sedation to be independently associated with a cardiopulmonary complication rate 5.3% times higher when compared to GA. Agostomi et al (24) reported on complication during sedation for gastroendoscopic procedures in 457 pediatric cases. In their series, complication rate 22% (bradycardia), and 4.4% (hypotension). In a study by Barbi and colleagues (25), major desaturation was noted in 0.7% of all the children, and transient desaturation that resolved spontaneously occurred in 12% of all the procedures. Additionally, the study by Yıldızdas¸ et al (26) demonstrated that the use of propofol and midazolam/fentanyl in 126 children had 16.6% incidence of respiratory depression as shown by high end-tidal carbon dioxide (>50 mmHg). The high incidence of respiratory depression reflected the better detection of respiratory depression by the use of end-tidal carbon dioxide. In our series 17 complications or side effects were seen totally.

Conclusion

In conclusion our data suggest that deep sedation (with propofol, midazolam, ketamine, fentanyl, or their combination) which managed from anesthesiologist presents advantages in terms of

safety, and depth of sedation. Although our sedation experiences were not complication free, all sedation related complications were transient and easily treated with no permanent sequelae. We recommend deep sedation for pediatric gastroendoscopic procedures applied by anesthesiologists

Conflict of Interest

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Relationship between premature ventricular complexes and Neutrophil–Lymphocyte Ratio in asymptomatic healthy young men

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Abstract

Background: There is no clear mortality benefit from premature ventricular beat (PVC) suppression in asymptomatic patients. In addition, It has been showed that evidence for structural heart disease consistent with non-ischemic scarring possibly due to inflammation in patients with PVCs. This situation suggests that the mechanisms by which PVCs can be also generated with include clinical and subclinical inflammation. The neutrophil–lymphocyte ratio (NLR) is an easy, cheap, non-invasive, and universally available laboratory marker used to evaluate clinical and subclinical systemic inflammation. We investigated the NLR in asymptomatic healthy young men with PVC (structural heart disease excluded with cardiac magnetic resonance imaging) compared with controls.
Methods: 21 asymptomatic (or atypical complaint) healthy young men with PVCs were recruited into the study as they attended to Diyarbakır Military Hospital for screening from January 2013 to December 2014. The control group consisted of 922 male. Instead of Lown's grading of PVCs, we considered as endpoints > 153 PVC over 24 h (in Holter Electrocardiogram). Data were analysed with the SPSS software version 15.0 for Windows.
Results: There were no significant differences between the 2 groups with respect to
age, gender, body mass index, smoking, as well as glucose, creatinine, total cholesterol, triglyceride, LDL-C, HDL-C, haemoglobin levels, white blood cell count, and red cell distribution width. The NLR was significantly higher among the men with PVC than that of the control group (2.6 ±0.8 vs 2.1 ± 0.7, respectively; P = 0.002).
Conclusions: We found that the NLR is significantly elevated in asymptomatic healthy young men with PVC compared with control group. The increased NLR values might indicate subclinical and clinical inflammation in asymptomatic healthy young men with PVC, and we must consider that there can also be inflammation in the one of the mechanisms of PVCs in humans

Key words: Premature ventricular complexes, neutrophil–lymphocyte ratio, inflammation

Introduction

Premature ventricular complexes (PVC) are a relatively common electrocardiographic abnormality presenting in individuals without overt cardiovascular disease. PVC pathogenesis has traditionally been considered idiopathic and in the absence of severe clinical symptoms or structural cardiac abnormalities, their presence benign (1,2). Recent prospective studies evaluating the prognostic significance of PVC for sudden and total cardiac death in apparently healthy adults directly challenge this view. Among individuals without history of heart disease or stroke, PVC counts independently predicted future cardiac events or sudden cardiac death compared to those without PVC (3-7). But there is no clear mortality benefit from PVC suppression in asymptomatic patients. In addition, It has been showed that evidence for structural heart disease consistent with non-ischemic scarring possibly due to inflammation in patients with PVCs (8). This situation suggests that the mechanisms by which PVCs can be also generated with include clinical and subclinical inflammation as well as re-entry, enhanced normal or abnormal automaticity, triggered activity resulting in after depolarizations and also mortality benefit can be related to inhibit clinical and subclinical inflammation rather than triggered activity.

The neutrophil–lymphocyte ratio (NLR) is an easy, cheap, non-invasive, and universally available laboratory marker used to evaluate clinical and subclinical systemic inflammation (9,10), and also the NLR is related to the severity of coronary heart disease(CHD) and clinical outcome in patients undergoing angiography and is also related to angiographic progression of coronary atherosclerosis, and it is an independent predictor of adverse outcomes

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among patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention (11,12).

To our knowledge, no study investigated the independent relationship between NLR and PVC in asymptomatic healthy young men. We investigated the NLR in healthy young men with PVC (structural heart disease excluded with cardiac magnetic resonance imaging) compared with controls

Material and method

Subjects: Our study is cross-sectional, retrospective, observational analysis (Military personnal screening). 21 asymptomatic (or atypical complaint) healthy young men with PVCs were recruited into the study as they attended to Diyarbakır Military Hospital for screening from January 2013 to December 2014. Insead of Lown's grading of PVCs ,we considered as endpoints > 153 PVC over 24 h (in Holter Electrocardiogram) ,in that elevated risk for sudden cardiac death was reported for high-risk participants in the Cardiovascular Health Study with > 153 PVC over 24 h, or about 6 events/hr (13). Because Lown's grading of PVCs has become clear over the years that this pertains only to acute myocardial infarction and ischemia and bears no prognostic relevance in other situations. The control group consisted of 922 male . Exclusion criteria were , non-sustained ventricular tachycardia(NSVT), sustain ventricular tachycardia (SVT), structural heart disease(with cardiac magnetic resonance imaging, - Philips,3.0T), CHD, valvular heart disease, heart failure, hypertension , peripheral arterial disease, diabetes mellitus, renal or hepatic dysfunction, hematological disorders, history of malignancy, acute or chronic infection, and drug use affecting (e.g alcohol) PVC and NLR.

Blood Sampling: Blood samples were drawn from an antecubital vein by careful after a fasting period of 12 hours. Glucose, creatinine, and lipid profiles were determined by the composition of the sample was calculated in relation to the internal standard using a modification of a commercially available computer program and the results were expressed as mg or mole % and characteristic molar ratios of classes. Hematologic indices were measured within 30 minutes of collecting the blood samples in tubes containing dipotassium EDTA. An automatic blood counter was used for with a Coulter analyser equipped with ZBI counter (Coulter Electronics, Hialeah, Fla).

Echocardiography: All patients were studied by standard Doppler, tissue Doppler, and 2-D echocardiography. All echocardiographic measurements were performed using a commercially available ultrasound system (Philips hd7xe) equipped with a harmonic 4.0-2.5 MHz variable –frequency phased-array transducer. Transthoracic 2-dimensional echocardiography (TTE) was performed in all study subjects according to the published protocol adopted form the recommendations of the American Society of Echocardiography.

Statistical Analysis:

Data were analyzed with the SPSS software version 15.0 for Windows. Continuous variables from the study groups were reported as mean± standard deviation and categorical variables as percentages. To compare continuous variables, the Student t test. Categorical variables were compared using the chi-square test. A two-tailed $P < 0.05$ was considered statistically significant

Results

Clinical and laboratory characteristics of the asymptomatic healthy young men with PVC(structural heart disease excluded with cardiac magnetic resonance imaging) and control group are shown in Table 1. There were no significant differences between the 2 groups with respect to age, gender, body mass index, smoking, as well as glucose, creatinine, total cholesterol, triglyceride, LDL-C, HDL-C, haemoglobin levels, white blood cell count, and red cell distribution width. Neutrophil count was significantly higher among the asymptomatic healthy young men with PVC than that of the control group (4.1 ±0.6 vs 3.7 ±1.1 x 1000/mm3, respectively; P =0.004). Lymphocyte count was significantly lower among the asymptomatic healthy young men with PVC than that of the control group (1.6 ±0.45 vs 1.8 ±0.51 x 1000/mm3, respectively; P =0.009).

The NLR was significantly higher among the men with PVC than that of the control group (2.6 ±0.8 vs 2.1 ± 0.7, respectively; P = 0.002) (Fig.1).

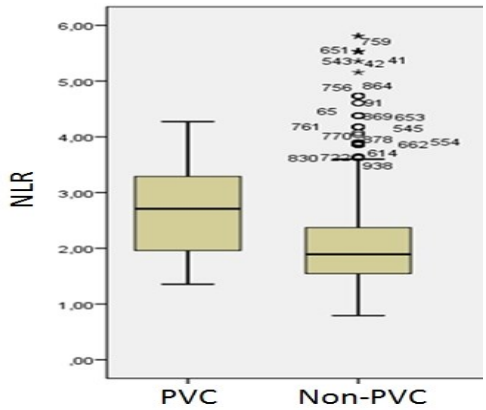

Figure 1: Comparison of the neutrophil-lymphocyte ratio (NLR) of the Asymptomatic Healthy Young Men with PVC and Control group. The NLR was significantly higher among the men with PVC than that of the control group (2.6±0.8 vs 2.1±0.7, respectively, P=0.002).

Discussion

Previously it has been showed that evidence for structural heart disease consistent with non-ischemic scarring possibly due to inflammation in patients with premature ventricular beats (PVCs). We found that the NLR, an indicator of inflammation, is significantly elevated in asymptomatic healthy young men with PVC (structural heart disease excluded with cardiac magnetic resonance imaging) when compared with control group.

Since invasive testing is rarely performed in patients with only simple PVCs, there is little information about the mechanisms of PVCs in humans. Information derived from experiments in animals suggests that the mechanisms by which PVCs are generated include: re-entry, enhanced normal or abnormal automaticity, triggered activity resulting in after depolarisations.

Table 1. Comparison of the clinical and Laboratory characteristics of the asymptomatic healthy Young men with PVC and Control group

	PVC Group n=21	Control Group n=962	P
Age	22.7±2.0	22.6±3.1	0.16
BMI, kg/m2	22.6±1.8	22.7±1.7	0.91
Echocardiography	normal rng	normal rng	
Smoking	%14	19%	0.34
Glucose, mg/dl	97±5	90±5	0.18
Creatinine, mg/dl	1.03 ± 0.10	1.00±0.22	0.06
Total cholesterol, mg/dl	156±35	157 ±24	0.28
Triglycerides, mg/dl	124±69	122±36	0.19
LDL-C, mg/dl	102±17	101±15	0.16
HDL-C, mg/dl	34±3	35±3	0.15
WBC, 1000/mm3	6.57±0.92	6.58±1.28	0.22
Hemoglobin, g/dl	14.5±1.2	14.5±1.1	0.15
RDW, %	14.2±1.2	14.3±1.6	0.14
Neutrophils,	4.1±0.6	3.7±1.1	0.004
Lymphocytes,	1.6±0.45	1.8±0.51	0.009
NLR	2.6±0.8	2.1±0.7	0.002

BMI; body mass index, LDL-C; low-density lipoprotein cholesterol; HDL-C; high-density lipoprotein cholesterol, WBC; white blood cells, RDW; red cell distribution view, NLR; neutrophil–lymphocyte ratio

It has been showed that evidence for structural heart disease consistent with non-ischemic scarring possibly due to inflammation in patients with PVCs (8). However, prophylactic treatment of asymptomatic PVCs in patients without cardiomyopathy has not been shown to improve mortality. This situation suggests that the mechanisms by which PVCs can be also generated with include clinical and subclinical inflammation as well as re-entry, enhanced normal or abnormal automaticity, triggered activity resulting in after depolarisations and also mortality benefit can be related to inhibit clinical and subclinical inflammation rather than triggered activity.

The NLR is easy, cheap, non-invasive, and widely available laboratory marker of systemic clinical and subclinical inflammation. Recently, it gained increased interest due to its role as an independent prognostic factor for many conditions such as uncontrolled hypertension, diabetes mellitus, acute coronary syndromes, valvular heart disease, congenital heart disease, renal or hepatic dysfunction, malignancy, local or systemic infection, and some other inflammatory diseases (14,15).

In our study, the patients with PVC (structural heart disease excluded with cardiac magnetic resonance imaging) and controls were free of CHD. We also excluded non-sustained ventricular tachycardia(NSVT), sustain ventricular tachycardia(SVT), structural heart disease(with cardiac magnetic resonance imaging, - Philips,3.0T), CHD, valvular heart disease, heart failure, hypertension , peripheral arterial disease, diabetes mellitus, renal or hepatic dysfunction, haematological disorders, history of malignancy, acute or chronic infection, and drug use affecting(e.g. alcohol) PVC and NLR.

Limitation

Our study has some limitations. First of it, the number of patients with PVC was small. The second one, our analysis was based on a simple baseline determination at a single time point that may not reflect patient status over long periods.

Conclusion

We found that the NLR is significantly elevated in asymptomatic healthy young men with PVC compared with control group. The increased NLR values might indicate subclinical and clinical inflammation in asymptomatic healthy young men with PVC, and we must consider that there can also be inflammation in the one of the mechanisms of PVCs in humans

Conflict of Interest

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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This study was designed and analysed by the authors. The database was collected from the Diyarbakır Military Hospital registry by the authors

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Case Report Doi: 10.17546/msd.44492

Delayed organophosphate induced polyneuropathy

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Abstract

Intoxication with organophosphate compounds used for pest control is common in Turkey. Organophosphate intoxication may occur during agricultural spraying, transport of organophosphate compounds, or domestic accidents, although suicide attempts are the most common way of intoxication. In this case, we present a 23-year-old woman ingested a fistful of painkillers and drank a sip of unknown syrup after having a quarrel with her family. About 18 days after drug intoxication she began noticing headache and weakness and numbness in her arms and legs. A detailed patient history taken in the emergency department indicated that the syrup she had taken for suicidal purpose was an organophosphate compound. An organophosphate –induced polyneuropathy was primarily considered. In conclusion, organophosphate intoxication should always be remembered in the differential diagnosis of intoxication cases even when no specific compound could be determined.
Keywords: Late onset, organophosphate poisoning, polyneuropathy.

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Introduction

Intoxication with organophosphate compounds used for pest control is common in Turkey (1). Organophosphate intoxication may occur during agricultural spraying, transport of organophosphate compounds, or domestic accidents, although suicide attempts are the most common way of intoxication (2, 3). Organophosphate intoxication may occur via oral, respiratory, transdermal, or parenteral route (4).

Organophosphates irreversibly bind to acetylcholine receptors to inhibit acetylcholine breakdown at neuromuscular junction. As a result, acetylcholine receptors are continually stimulated, leading to cholinergic, nicotinic, and central nervous system signs and symptoms (4).

The clinical picture depends on the type, dose, and route of administration of the culprit compound. Death typically occurs within the first 24 hours, usually due to respiratory failure (3). Some complications of organophosphate intoxication have been reported, including “delayed organophosphate - induced polyneuropathy” that has been only rarely reported (2).

It usually arises 14-18 days after intoxication (2, 4). This paper discusses a rare case of delayed organophosphate - induced polyneuropathy

Case

A 23-year-old woman ingested a fistful of painkillers and drank a sip of unknown syrup after having a quarrel with her family. Four hours later, she had been taken to a nearby hospital with nausea, vomiting, and abdominal pain, where she had been treated for drug intoxication at an intensive care unit for 2 days and discharged uneventfully. About 18 days after drug intoxication she began noticing headache and weakness and numbness in her arms and legs. Her symptoms progressively deteriorated over 2 days and she was admitted to our emergency department with inability to walk.

On admission, her general status was well and she was conscious. Her blood pressure was 100/70 mmHg, pulse rate 86 beats per minute (bpm), respiratory rate 18/minute, and body temperature 36.7°C. Her head and neck examination revealed no abnormality. She had normal respiratory sounds and no rales or ronchi on auscultation. Heart sounds were also normal, with no additional sounds or murmurs. Her abdomen was non-tender and there was no mass lesionon palpation.

Neurological examination revealed mild weakness in both upper extremities; both lower extremities had a 3/5 muscular weakness, reduced deep tendon reflexes, and minimal sensory loss.

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Table 1: Important blood parameters of delayed organophosphate induced polyneuropathy patient

	Value	Normal range
Hemoglobin	12.4 g/dl	(12-16 g/dl)
White Blood Cell (WBC)	13400/µl	(4500-11000/µl),
Platelet	242000/µl	(150000–400000/µl)
Glucose	162 mg/dl	(70-105 mg/dL)
Blood Urea Nitrogen (BUN)	17 mg/dl	(6-21 mg/dl)
Creatinine	1.1 mg/dl	(0.5-1.3 mg/dl)
Alanine transaminase (ALT)	46 U/l	(0-31 U/l)
Aspartate transaminase (AST):	47 IU/l	(0-31 IU/l)
Creatine kinase (CK)	152 IU/l	(22-192 IU/l)
Creatin kinase muscle-brain (CK-MB)	41 IU/l	(0-25 IU/l)
Pseudocholinesterase	2450 U/l	(5400-13200 U/l)

Electrocardiogram (ECG) of patient showed a normal sinus rhythm with a rate of 76 bpm and laboratory examinations were as in Table 1.

A detailed patient history taken in the emergency department indicated that the syrup she had taken for suicidal purpose was an organophosphate compound. An organophosphate – induced polyneuropathy was primarily considered and a neurology consultation was requested with the working diagnosis of delayed organophosphate - induced polyneuropathy. Distinction between acute vs chronic organophosphate intoxication was based on patient history.

The consulting department admitted the patient to hospital and performed an electromyography (EMG), which revealed sensorimotor neuropathy consistent with "delayed organophosphate -induced polyneuropathy". MR examinations revealed no pathology.

The patient was put on steroid therapy and discharged after resolution of much of her symptoms

Discussion

Organophosphates are chemical compounds that are commonly used for pest control in agriculture. Their wide availability and ease of access may sometimes lead to accidental or suicidal ingestions (3). Suicidal ingestions most commonly occur via oral route although parenteral route has also been reported (5).

Pesticide-induced intoxications are common in Turkey. According to 2008 statistics of the National Poison Center of Turkey (NPCT), intoxications caused by agricultural compounds ranked second among all intoxication events, with a rate of 8.34%. Among pesticide intoxications, those occurring with organophosphates rank first.

According to reports, 47.66% of all pesticide intoxications were caused by insecticides and %20.98 of them were secondary to organophosphate compounds (1).

Organophosphates act by inhibiting the cholinesterase enzyme found at nerve endings. Symptoms and course of intoxication depend on the type, amount, and route of ingestion of the culprit compound.

In acute intoxication, majority of cases become symptomatic within first 8 hours while others begin experiencing symptoms within 24 hours (4). Three stages of organophosphate intoxication have been defined. These include the acute cholinergic crisis, the intermediate syndrome, and delayed polyneuropathy (6). Death usually occurs during acute cholinergic crisis or the intermediate syndrome (2).

Acute cholinergic crisis is characterized by muscarinic, nicotinic, and central nervous system signs and symptoms, including weakness, nausea, vomiting, myosis, salivation, altered consciousness, respiratory difficulty, muscle fasciculation's, and bradycardia (2, 4).

The intermediate syndrome usually spans from the first to fourth day of intoxication and is characterized by paralysis of respiratory, cranial, flexor neck and proximal limb muscles. It may culminate into death when it involves respiratory muscles (4).

Delayed organophosphate induced polyneuropathy is typically encountered between 14th and 28th days of intoxication (2, 4). It has been linked to suppression of neuropathy target esterase (NTE) by organophosphates in the nervous tissue (2).

Many lipid-soluble organophosphates may cause delayed polyneuropathy with no signs and symptoms of acute poisoning (4). There is loss of function in the ascending and descending limbs of spinal cord as well as sensory and motor axons of peripheral nerves.

The acute stages of organophosphate-induced polyneuropathy are characterized by leg cramps. This is followed by sensory loss and muscle weakness in legs. Weakness becomes advanced and widespread and deep tendon reflexes become suppressed in later stages (2, 4).

As for the prognosis of polyneuropathy, some functions may be regained over time although some severe cases may have residual sequela, including ataxia, drop foot, and spasticity (7).

This syndrome usually mimics Guillain-Barre syndrome (4). Our patient also had bilateral muscle weakness and sensory loss. Most of the symptoms of our case disappeared by the time of discharge. Many cases with appropriate therapy at the acute intoxication stage may avoid the last stage of the intoxication (2, 4).

Our patient, unfortunately, was not managed appropriately at the acute stage and she was thus at risk of this complication. Delayed organophosphate - induced polyneuropathy has no proven therapy although one study indicated that B complex vitamins and prednisolone may be of some benefit (8). Hence, our case enjoyed a resolution of her symptoms after steroid therapy.

Parkinsonism as a result of basal ganglion injury is another neurological manifestation of organophosphate intoxication. Shahar et al reported a 15-year-old male with extra pyramidal symptoms such as poker face, rest tremor, inability to wink, cogwheel rigidity, and slow walking. He responded to amantadine treatment and his symptoms completely disappeared by 7 days (9).

Organophosphate intoxication is usually diagnosed by history, clinical signs and symptoms, and laboratory test (4). Package of the ingested compound should be inspected to determine the responsible molecule whenever possible (6).

The characteristic garlic-like smell of these compounds may sometimes warn physician. Cholinergic signs and symptoms also help in the diagnostic process. Myosis is the most common sign. The prognostic role of plasma and erythrocyte cholinesterase level measurements is low and does not predict the amount of the antidote or need for ventilatory support. Routine laboratory tests also have limited diagnostic role (4).

Some patients may exhibit signs of pulmonary edema or acute respiratory distress syndrome (ARDS) on chest X-Ray (8). In our case no cholinesterase level measurement had been done at the outside center since she had not been considered to suffer from organophosphate intoxication. Treatment of organophosphate intoxication consists of decontamination, airway control, gastric lavage, and administration of antidotes, atropin and pralidoxime (4). As our patient applied at a later stage, these therapies were not applied.

Karasu et al reported a 29-year-old woman with sub-acute neuropathy 3 weeks after organophosphate ingestion. The authors suggested that organophosphate intoxication should be considered in the differential diagnosis of unilateral distal neuropathy (10). Gulle et al published a 13-year-old male child with polyneuropathy 3 weeks after organophosphate intoxication (11).

Conclusion

In intoxication cases, package of the ingested compound should be inspected to determine the culprit molecule whenever possible.

Organophosphate intoxication should always be remembered in the differential diagnosis of intoxication cases even when no specific compound could be determined since suicidal attempts with agricultural pesticide compounds are common in Turkey.

Early diagnosis and therapy of the deadly organophosphate intoxication may avoid much of the complications and sequel in the long term

Conflict of Interest

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article. This study was presented as poster presentation at the 10th National Emergency Medicine Congress and the 1st Intercontinental Emergency Medicine Congress, 15-18 May 2014, Antalya, Turkey.

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Treatment of postoperative atelectasis with dornase alpha (Pulmozyme®) after congenital heart surgery

Mustafa Hakan Zor[1], Abdullah Ozer[1*], Huseyin Demirtas[1], Yigit Kilic[1], Baris Mardin[1]

Abstract

One year old patient followed with tetralogy of fallot (TOF) was admitted to our service for surgical repair. Ventricular septal defect (VSD) was repaired with a Dacron patch. The infundibular muscle was resected to allow for unobstructed flow of blood to the pulmonary valve and the area above the pulmonary valve was opened with a polytetrafluoroethylene (PTFE) patch. The patient was intubated three times because of the atelectasis occurred in the lungs after the surgery. Atelectasis was treated with nebulised dornase alpha. It avoided the recurrence of atelectasis and the patient was discharged

Key words: Atelectasis, Dornase Alpha (Pulmozyme), Congenital Heart Surgery

Introduction

The prevalence of congenital heart disease (CHD) is between 8 and 10 children per 1000 live births. The average number of cardiovascular surgeries for CHD that are necessary in Brazil is of the order of 23,077 procedures per year, including new-born babies with CHD and cases requiring reoperations (1). Pulmonary complications of postoperative pediatric cardiac surgery observed in the study of Felcar et al. where: atelectasis, pneumonia, pleural effusion, pneumothorax, chylothorax, pulmonary hypertension, pulmonary haemorrhage and diaphragmatic paralysis, whereas the first two aforementioned complications are the more common ones (2). Atelectasis, defined as collapse of a certain region of the lung parenchyma (3) is the most common complication in the postoperative period of cardiac surgery (4) by worsening oxygenation, decreasing pulmonary compliance, leading to inhibition of cough and pulmonary clearance and may lead to respiratory failure and increase pulmonary vascular resistance. Heart surgeries associated with CPB have as adverse effect the increased capillary permeability that causes edema, which results in decreased lung compliance and gas exchange (6) , in addition to lead to airway obstruction, atelectasis, decreased functional residual capacity and, therefore, hypoxemia (5). Pulmonary complications are the most common causes of morbidity and mortality in the postoperative period after congenital heart surgery. Both mechanical and gas exchange abnormalities result in increased ventilator requirements, intensive care unit (ICU) stay and mortality.

Parenchymal lung disease can be caused by a variety of conditions including nosocomial pneumonia, atelectasis and use of cardiopulmonary bypass. Direct surgical trauma to the respiratory system can result in diaphragmatic paralysis, chylothorax, subglottic stenosis or vocal cord paralysis. Disturbances in the pulmonary vasculature can also trigger complications including pulmonary embolism, plastic bronchitis and even pulmonary hypertensive crises in certain at risk populations (7).

Case

One year old female patient followed with tetralogy of fallot (TOF) was admitted to our service for surgical repair. Her weight was eight kilograms. She was diagnosed with TOF in utero by fetal echocardiography at 27 weeks of gestation. After birth her echocardiography and cardiac catheterization findings were intact Interatrial septum, sub aortic ventricular septal defect, dextroposed aorta, right ventricular hypertrophy, hypo-plastic pulmonary artery and dilated ascending aorta. Total correction of TOF was decided. VSD was repaired with a Dacron patch. The infundibular muscle was resected to allow for unobstructed flow of blood to the pulmonary valve and the area above the pulmonary valve was opened with a PTFE patch. On the first postoperative day when she met extubation criteria she was extubated. 6 hours after extubation she had difficulty in breathing. Her arterial blood gas was analysed. She had respiratory acidosis and she was re-entubated.

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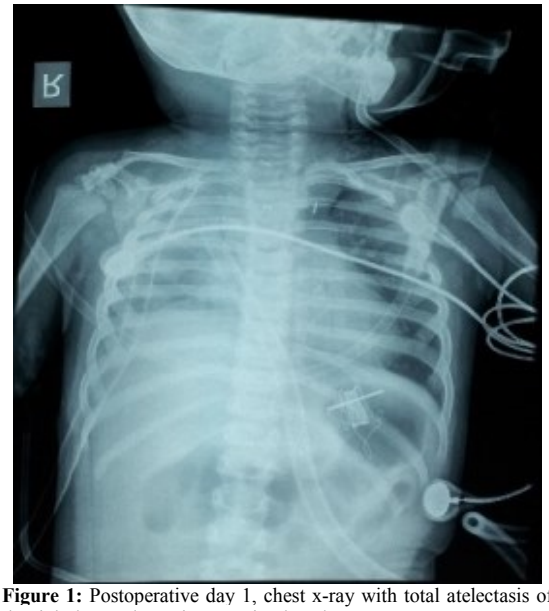

Figure 1: Postoperative day 1, chest x-ray with total atelectasis of the right lung. The patient was intubated

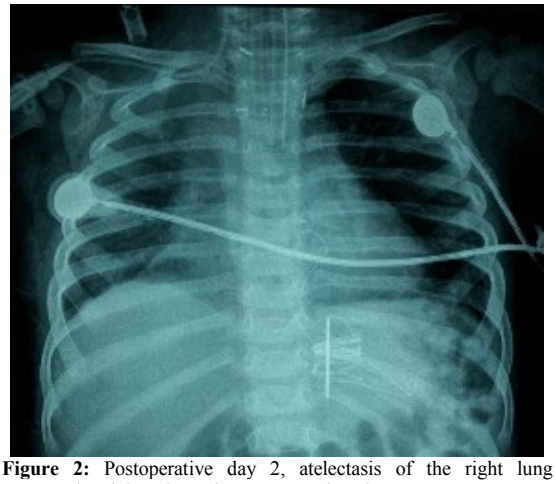

Figure 2: Postoperative day 2, atelectasis of the right lung recovered and then the patient was ex-tubated.

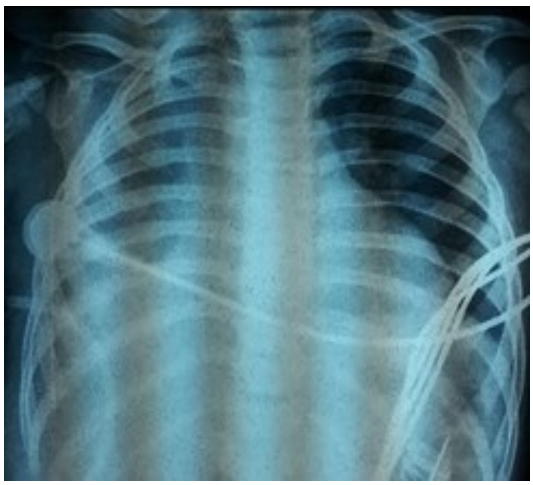

Figure 3: Postoperative day 3, partial collapse of the right lung (recurrent atelectasis) the patient was re-entubated. Pulmozyme treatment was started.

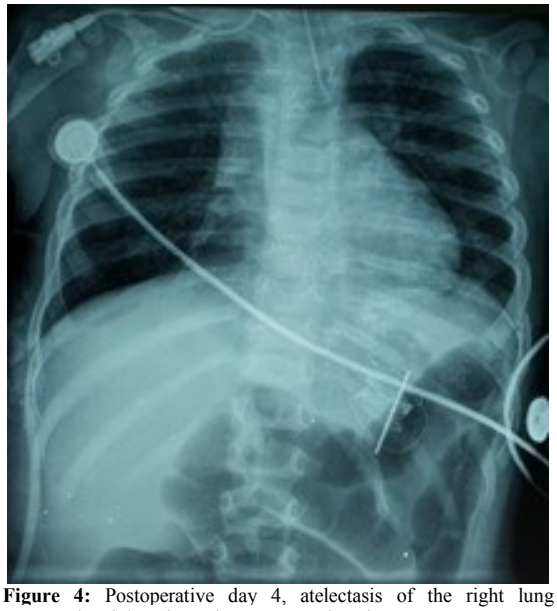

Figure 4: Postoperative day 4, atelectasis of the right lung recovered and then the patient was ex-tubated

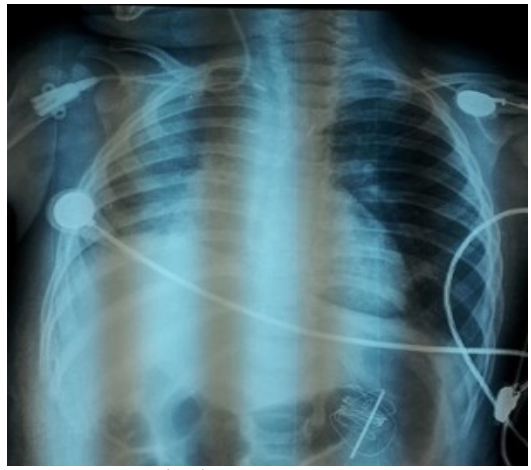

Figure 5 - Postoperative day 5

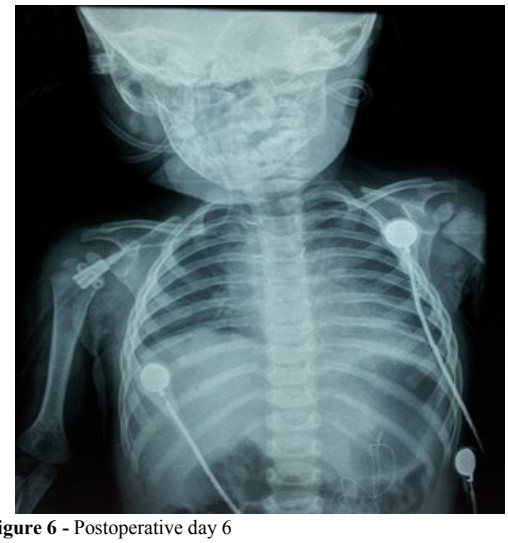

Figure 6 - Postoperative day 6

The chest x ray showed total atelectasis of the right lung. After 17 hours of intubation the atelectasis of the right lung totally recovered on chest x ray. The patient was extubated again. Pulmonary rehabilitation techniques and bronchodilators were used for the treatment of atelectasis. After nine hours she had difficulty in breathing again. She had bradycardia, her oxygen saturation level was at 50% and she was intubated again.

Her chest x ray showed total atelectasis of the right lung. After 15 hours she was extubated again. We started to treat the patient with nebulised Dornase alpha (Pulmozyme®) twice a day. Pulmozyme is a recombinant human deoxyribonuclease I (rhDNase) an enzyme which selectively cleaves DNA. Each ampule has 2.5 mL of the solution. Each mL of aqueous solution contains 1 mg dornase alfa. After administration of 2.5 mg of Dornase alpha twice a day for three days the atelectasis of the right lung started to recover. The patient was discharged from the Intensive Care Unit (ICU) and was followed in the clinic. She was treated with Dornase alpha for three more days in the clinic and then on the fifth day she was discharged from the hospital.

Discussion

Atelectasis resolves with the use of non-invasive mechanical ventilation but after the extubation, by the effect of the spontaneous breathing, lung starts to collapse. Postoperative pain management is important in patients who undergo open heart surgery and aorta surgery. The use of opioid-based analgesics for pain control after cardiac surgery is inevitable. Poorly controlled pain also contributes to hemodynamic instability (8). In fact, several authors have reported that a continuous positive airway pressure, with or without intermittent positive pressure ventilation, alleviates a tracheal collapse (9,10) .

Pulmozyme is a nebulised form of recombinant human DNase I (rhDNase). It is reliable, non-invasive and FDA approved. Recombinant human DNase I (rhDNase) has been shown to depolymerise DNA and thereby reduce the in vitro viscoelasticity of sputum in patients with cystic fibrosis and improved pulmonary function in patients with cystic fibrosis (CF) (11).

Its efficacy has been well documented in cystic fibrosis, whereas case reports have described a beneficial effect in other respiratory disorders. Recombinant human DNase I (rhDNase, Pulmozyme, dornase alpha) has been approved for the management of CF(12,13).

Conclusion

In conclusion, nebulised form of Dornase Alpha (Pulmozyme®) has a positive effect on morbidity and mortality in patients with atelectasis that do not resolve due to pulmonary medication and rehabilitation program after congenital heart surgery

Conflict of Interest: The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Cyst hydatid case ruptured after awake intubation causing difficult airway

Nureddin Yuzkat[1*], Muhammed Bilal Cegin[2]

Abstract

Encountered throughout the history, the Cyst Hydatid is a parasitary disease caused by Echinococcus Granulosus. Cyst hydatid settles in the liver almost at a rate of 60% and about 30% in the lungs. The cysts settling in the lungs are generally solitary and asymptomatic. While the cyst hydatid of the lungs is often seen as solitary, the perforation rate occurring spontaneously in these cases was reported as 0.36%. The iatrogenic perforation is quite rare, like 1% in the studies. In the literature, we could not come across a cyst hydatid case ruptured due to intubation. In this article, we aimed to present a cyst hydatid case that was operated on due to diaphragmatic hernia, instantly getting ruptured after intubation and causing a difficult airway.

Key words: intubation, cyst hydatid, difficult airway, ruptures late onset,

Introduction

Encountered throughout the history, the cyst hydatid is a parasitary disease caused by Echinococcus Granulosus. Its prevalence in Turkey is presumed to be around 50 per 100 thousand (1). Cyst hydatid settles in the liver almost at a rate of 60% and about 30% in the lungs. The cysts settling in the lungs are generally solitary and asymptomatic (2). However, it provides findings in some patients with a symptom or a perforation due to pressure. Perforations may be usually spontaneous or iatrogenic (traumatic, surgical) (3, 4).

In the literature, we could not come across a cyst hydatid case ruptured due to intubation. In this article, we aimed to present a cyst hydatid case that was operated on due to diaphragmatic hernia, instantly getting ruptured after intubation and causing a difficult airway

Case

A 64kg -male patient aged 78 and planned to be taken under operation due to his right diaphragmatic hernia was preoperatively evaluated. His physical examination and laboratory parameters were normal. In his thorax CT, a 72x58mm thick-walled cavitary lesion containing a solid component in the apical upper lobe of the left lung was monitored (Figure 1). The case was taken under operation without performing a premedication. In the operating room, a routine anesthesia monitorization was performed.

His blood pressure was measured as 145/79mmHg, whereas his heart rate was 85 beats/minute and the oxygen saturation was 94%. Then 0.9% fluid was placed through a vascular access. After administering 1mg- iv midazolam to the case, an anesthetic induction with 2.5µg/kg fentanyl, 2mg/kg propofol and 0.6mg/kg rocuronium was performed. An endotracheal intubation with a 37F left-sided double-lumen tube was performed, as well, and the tube level was verified. After observing that both lungs were normally ventilated, the case was strapped to a mechanical ventilator. When the case was given a right-side position for the surgery, first a pressure increase in the mechanical ventilator and then an insufficient tidal volume was noticed.

The pressure was immediately brought under control by performing manual respiration to the case. It was seen that there was a severe resistance in the airways. The left lung sounds/beats could not be received by merely listening. The case had a ventilation problem. The peripheral oxygen saturations dropped down to 72%, whereas the blood pressure went down to 84/50mmHg. The case was given a supine position, an aspiration in tube was performed, and an intraoperative chest radiography (X-ray) was taken. (Figure 2). The left lung was determined to have been totally closed. Then an aspiration with a physiological saline solution was performed once again. A large amount of serous fluid was aspirated. The peripheral oxygen saturations rose up to 92%.

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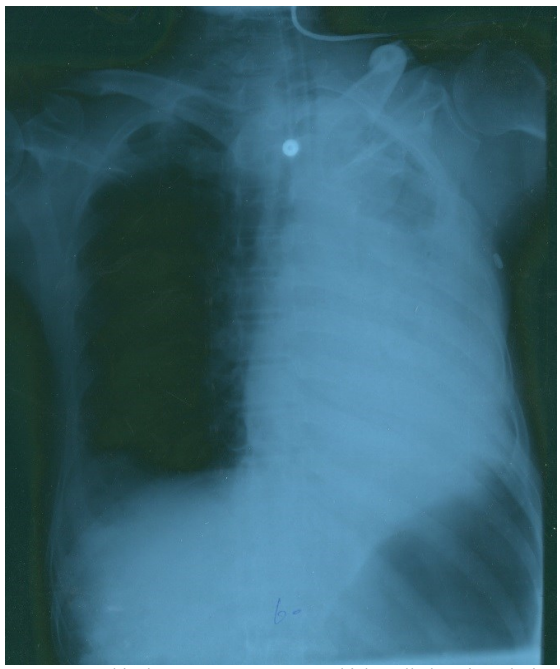

Figure 1: In his thorax CT, a 72x58mm thick-walled cavitary lesion containing a solid component in the apical upper lobe of the left lung

It was understood that the cyst hydatid in left lung was ruptured. The case was administered with both an intravenous fluid replacement and intravenous 80mg methylprednisolone (Prednol-L, Mustafa Nevzat, Turkey) along with 40mg pheniramine maleate (Avil, Sandoz, Turkey) for anaphylaxis prophylaxis. A diagnostic bronchoscopy was performed on the patient, and the cyst content was aspirated. The surgery was postponed to be performed under elective conditions. The case was brought to the intensive care unit in intubation. The case received a mechanical ventilation support for 24 hours as well as an inotropic support treatment for 48 hours since the course of the process was hypotensive. He was then referred to the 3rd day-service department after his clinical picture and hemodynamics recovered.

Discussion

Cyst hydatid is a parasitosis capable of arresting all the organs, notably the liver most frequently. It may occur in any organ, such as the lungs, kidneys, bile ducts, mesentery, brain and the soft tissue (5). It is a health issue still seen in Turkey. The incidence of cyst hydatid in the Turkish society is reported as 1/2000 (6). People contract this disease primarily by getting in contact with the dogs carrying the disease or by consuming contaminated foods. The most affected organs are the liver and the lungs (7).

While the cyst hydatid of the lungs is often seen as solitary, the perforation rate occurring spontaneously in these cases was reported as 0.36%. The iatrogenic perforation is quite rare, like 1% in the studies (4,8).

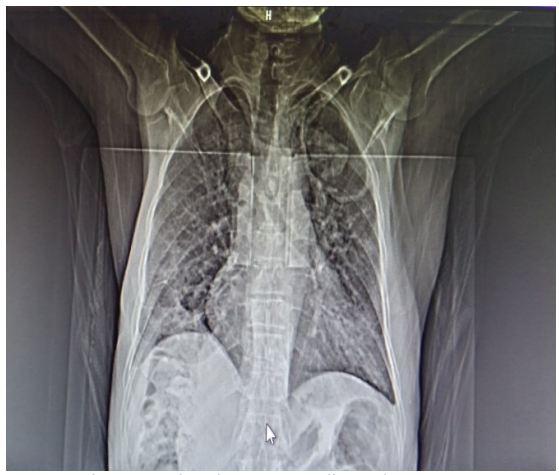

Figure 2: intraoperative chest X-ray radiography

Gunay et al. (9) report that only one out of 16 cyst hydatid cases they treated due to a traumatic rupture in 12 years was settled in the lungs. Şahin et al. (10), on the other hand, stated that in only one case out of 80 cyst hydatid cases had a rupture due to a blunt trauma been determined.

The case we have presented was taken under operation due to diaphragmatic hernia, and right after the intubation was the cyst in the left lung perforated. No surgery had been performed on the case, nor was an interventional action except for the intubation done. For this reason, we are of the opinion that the cyst was spontaneously perforated.

In the literature, perforated cyst hydatid cases seen under anesthesia were reported (7). Yet, no spontaneous perforation associated with intubation was encountered. Apart from this, the point to be taken into consideration in the first place in the cases in which the cyst is perforated is the possibility of the development of anaphylaxis.

When the cyst is perforated, the cyst fluid of high antigenic characteristic permeates into the blood circulation, and anaphylaxis may occur as the result of histamine release (7). In perforated cases, it is advised that anaphylaxis prophylaxis be performed, and measures be taken to protect hemodynamics (1).

In our case, following the consideration on perforation, the anaphylaxis prophylaxis was practised, and a fluid treatment for protecting the blood pressure was performed. However, a hypotension developed in the case in question, and thus, an inotropic support was given in the intensive care unit.

Conclusion

In conclusion, cyst hydatid may be spontaneously perforated in the patients in intubation during unexpected moments. Therefore, we wished to emphasize the fact that cyst hydatid is a serious parasitosis likely to cause difficult airways and anaphylaxis

Conflict of Interest

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article. This study was accepted as a poster presentation in 20th International Intensive Care Symposium - ICISTANBUL 2015, May 8-9, 2015, Istanbul, Turkey.

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