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WHICH HEALTH? : A CONTENT ANALYSIS EVALUATION ON THE SYRIA AND YEMEN CİVİL WARS

İzzet Erdem[1], Ayşe İspirli [2], Fatma Taş[3]

Abstract

Civil war is at the forefront of non-human atrocities that have destroyed societies and individuals in both physcially and spritually. Particularly in Syria, one of the parties that have exposed the people to violence and massacre makes the issue of the government of the country an even more graver and tragic. Assad Regime is used for all types of heavy weapons as well as chemical attacks against civilians. Organ losses, injuries and irreparable physical damage have begun to appear to be almost normal in areas of war. In Yemen, starvation, thirst, absence of medical supplies caused epidemics such as cholera.

The method of study consists of a qualitative research method of document review. TRT's news site www.trthaber.com between September 1, 2017 and December 31, 2017 subject to content analysis on Syria and Yemen. The meaning of health in the domestic warfare is critically questioned. The relationship between war and health is tried to be put forward.

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Keywords:
Civil war, Syria, Yemen, health, massacre

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PURPOSE

The aim of this study; The massacre in Syria and Yemen is the critical question of what health means sociologically for the atrocities and oppression.

METHOD

The method of study consists of a qualitative research method of document review. A document review refers to an analysis of sources containing information about the subject being searched (Yıldırım & Şimşek, 2008). Document analysis has been preferred because it provides enough information and time saving about the research topic. Thus, TRT's news site www.trthaber.com between September 1, 2017 and December 31, 2017 subject to content analysis on Syria and Yemen. The reason why the news is examined for four consecutive months is that it is a process of war, which is the subject of investigationIn this way the process is considered to be better understood.

DATA ANALYSIS

In total, 122 new documents which were published in the last 4 months of 2017, were subjected to categorised analyze. The categorised analyze means the division of a message into units and to classify these units due to certain criteria. (Bilgin, 2014)

INTRODUCTION

War has become a comprehensive and dynamic concept, which has been exist with the humanity, has changed throughout the history and has been different in terms of method and practice. (Eker, 2015) The wars cause many destruction that cannot be compensated. The impact of this destruction is more evident in children who need adults for their needs. Injuries and deaths as a result of conflicts can be defined as the direct impact of the war. This effect is felt more intensely near the war zone. Other problems arise for civilians who may move away from the war zone. (Oğuz et al., 2016) Children are most affected ones by the results of armed conflicts. The environment of war and violence affects even unborn children (Çelik & Özpınar, 2017).

THE SITUATION SYRIA AND YEMEN

In the Middle East in December 2010, popular uprisings in Tunisia began to be known as the Arab Spring. While the governments in Tunisia, Egypt, Libya and Yemen changed, armed non-state actors in the Middle East brought regional instability and chaos (Semin, 2015: 1). Syria is another country where this uncertainty continued since 2011. In Yemen, the severity of violence and war has increased gradually with Ali Abdullah Salih leaving the seat.

The efforts of international organizations, especially the United Nations, the European Union and the Arab League, as well as the global powers, have failed to solve the Syrian crisis (Göker & Keskin, 2015), which started with public demonstrations in March 2011 and became a civil war (Semin, 2015: 1). Thus, the last stop of the revolt in the Middle East was Syria (Orhan, 2011). Terrorist organizations have been produced in the region by the authority gap and the arming of the great states. It is known that one of

these organizations, Deas, has captured a large number of women in northern Syria and Iraq, sold most of them or forced them to marry, and these women and their little girls were raped (Puttick, 2015).

Since the beginning of the war in Syria, where torture and ill-treatment in prisons has been out of control, more than 120,000 people have been imprisoned or lost, and at least 12,000 people have been killed in prison. More than 20,000 children have lost their lives in the country where chemical weapons, marble and barrel bombs are used. One third of the houses and the half of the hospitals and educational institutions were destroyed in Syria, where a great deal of destruction and victimization were experienced under the conflict of interests of global powers (IHH Syria Annual Report, 2017).

In March 2015, Saudi Arabia and members of a coalition it established (hereinafter referred to as the Saudi-led coalition) launched a military operation aimed at restoring the rule of Yemen's internationally recognized President Abdu Rabbu Mansour Hadi (Sharp, 2017). There is a power struggle in Yemen due to regional interests between Saudi Arabia and Iran. Ülke'de İran destekli hükümet karşıtı Husiler ile Suudi Arabistan'ın desteklediği hükümet güçleri arasında savaş devam etmektedir. Yemen people pay the price of this war Because of the embargo of Saudi Arabia in the country, millions have been left with hundreds of hunger, thirst and illness (Salisbury, 2015).

CIVIL WAR AND HEALTH

One of the most well-known and popular definitions of health is the definition of the World Health Organization. Health) A state of complete physical, mental and social well-being and not merely the absence of disease or infirmity state (WHO, 2014). According to the Biomedical Model; biological self-health is evaluated as healthy state and disruption of this balance is considered as a disease or medical condition (Pearson et al., 2005: 44). According to Bircher (2005: 336) the health; Age is a dynamic well-being characterized by a physical, mental and social potential that meets the demands of life in proportion to culture and personal responsibility. It is a condition where the potential is not sufficient to meet these demands. Baudrillard (2010: 177) emphasizes the social determinants of health and defines the healthİ "Health is a social command based on status rather than a biological command that is bound to survival today. Health is more of a burden than a basic value."

It seems rather vicious and meaningless to draw the concept of health for the people who resist to death in the geographies where war and brutality prevail. What does health mean for a helpless Syrian woman who has no home or her goods, who has lost her children and husband and has been raped, and starving Yemeni child? The explanation of the meaning of health for the people of these two countries, who are living their lives biologically, with pain, trauma and meaningless, do not seem possible.

FINDINGS

The distribution of the news examined between 1 September 2017 and 31 December 2017 is given in Table 1.

Table 1: *Distrubition of News by Months*

Months	**News Numbers**	**%**
September	17	13,9
October	18	14,8
November	30	24,6
December	57	46,7
Total	122	100

As seen in Table 1, the number of news stories in Syria and Yemen increased towards the end of the year. It can be concluded that more real events (explosion, conflict, negotiation, attack, explanation, etc.) related to civil war have taken place as of 2018.

In the study, basically 4 basic dimensions were obtained.

Table 2: *Main Dimensions*

Dimensions
1. Efforts
2. Problems
3. Attacks
4. Massacres

1. Efforts

Efforts; It consists of all kinds of actual or verbal attempts made or planned for Syria and Yemen. This dimension consists of 3 categories:

1.Turkey's efforts

2.International efforts

3. Local efforts in Syria and Yemen

2. Problems

The problems point tothe war and any material and spiritual problems that come with war. The problems were categorized under 4 headings. These are:

1. Economıc problems
2. Social problems
3. Pshchological problems
4. Child problems

3. Attacks

Attacks: Express the attacks against the civilian and vulnerable people made by the coalition forces, government forces, terrorist groups and the countries that support them with all kinds of weapons and war vehicles.

The attackers are also classified under 4 headings.

1. Attacks on health ınstitutions
2. Attacks on public spaces
3. Attacks on ivil defence team
4. Attacks on religious minorities

4. Massacres

Massacres: It means the collective death of a group of civilians at the same time in result of any kind of attack. These massacres are carried out especially with bombs and chemical weapons throwed out from planes. The UN has not had any sanctions against the regime for the use of chemical weapons. Types of massacres are listed below:

1. Chemical weapons
2. Heavy weapons
3. Torture
4. Suicide

CONCLUSION

Since the last century in the history of the Middle East, drama, savagery and massacre social traumas have never ended. Still, it does not seem to end. The biggest indescribable pain is suffered by innocent civilians. The fact that the permanent members of the United Nations Security Council (USA, France, Britain, China and Russia) did not take concrete steps to solve the Syrian crisis allowed the Assad regime to carry out major massacres in the civil war in the country (Semin, 2015: 2). Hundreds of health centers and hospitals have been destroyed due to bombings, and doctors have died. Because of non-medication, operations have been performed without sedation (IHH Syria Annual Report, 2017: 27). Hundreds of thousands of people who are unable to meet basic requirements such as food, water, electricity, fuel and medical supplies in Yemen and Syria due to the war; struggles for survival in hunger, disease and poverty

(Çevik, 2016: 82). In Syria, the women captured by the ISIS terrorist organization are raped and sold. It is reported that there are people who died from torture in the regime's prisons. Chemical attacks were carried out hundreds of times by the regime forces. In Yemen, starving babies and children die before the world. Nearly 8 million people are deprived of basic foodstuffs. Although there is limited international assistance, it meets the needs of very few people. Sometimes these aids cannot reach those in need.

Various definitions have been made by the world health organization and different authors about the concept of health. However, it is thought that these definitions in the war environment could not reveal a descriptive and diagnostic situation for oppressed and victimized civilians in the disease-health axis. Due to the fact that many traumas and pain cannot be described and explained, it is not possible to limit the health-disease severity of these people. How the health-disease definition can be explain in the condition of people whose wife, mother, child and brother have been killed, who were wounded by the bombs and bullets that they dont know where it comes from, who were starved, raped, tortured, abducted, and enslaved?

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Narcotic Analgesics: OPIOIDS

Hülya Erbaba[1]

Abstract

Opioids are morphine-like analgesics used for the management of severe pain, such as acute pain and cancer pain. IASP considers the relief of pain in acute or terminal illnesses as a human right, supporting opioid use in patients of all ages. IASP signed the Declaration of Montreal with other parties in 2010, reflecting its point of view. The aim of this study was to describe opioid analgesics and their adverse effects. Outcomes of a current review of the literature were used in this study. Like all analgesics, opioids should be used at the right time, for the right patient, for the right indication, at the right dose, and with the appropriate mode of administration. The acknowledgment of every healthcare worker seeing patients in all branches in medicine will allow for patient access to analgesics via the appropriate approaches.

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Keywords:

Narcotic analgesic, Opioid, Adverse Effects

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INTRODUCTION

McCaffery described pain in 1968 as “whatever the experiencing person says it is, existing whenever and wherever the person says it does”. This definition highlights that pain is a subjective experience (McCaffery, M, 1968). The most reliable indicator of pain is considered to be the feedback given by the pain sufferer (Herr, KA, & Mobily, PR, 1998). Opioids are indispensable treatment agents used in pain centers today (90%) and they are modified morphine derivatives (Yildirim, D, Gulbeyaz, C, 2019). These agents are named as opioids since their effects occur because of their binding to the opioid receptors. They act as agonists at the opioid receptors. The mu1, kappa, sigma and orphanin-nociceptin OFQ/N receptors are the major receptors, to which opioids bind some groups of opioids bind to delta and epsilon receptors, too (Azzam AAH, Mcdonald J, Lambert, DG, 2019). Selecting the type of analgesic medication depends on the severity of the pain. Once the appropriate drug is selected, the route and frequency of administration are determined for treatment. The oral route should always be the first choice. These agents may also be administered intravenously, subcutaneously or transdermally when required (The American Pain Society 2001, Kabalak, A, Ayla O, 2013). Pharmacological approaches are the mainstay of treatment for severe pain affecting the patient's quality of life. Almost half of the individuals having pain-associated impaired quality of lives prefer nonprescription analgesics as the first choice for pain relief. The most preferred analgesics for this type of pain are the opioids (The American Pain Society 2001).

Properties of Opioids and Adverse Effects

Sydenham argued in 1682 that none of the available remedies is as universal and effective as opium to relieve the suffering of man, highlighting the opioid miracle (Andre, J, Karen, O, 1999). The Angelic face of Opium is dazzlingly seductive, but if you look on the other side of it, it will appear altogether a Devil. (*Thomas Willis "Medicine in Man's Body" VII i 128 1848*) (Cyril R, Ballantyne J. 2016).

Opioids have been used since the 1980s. Opioids are chemical agents acting by binding to the opioid receptors, which are mainly located in the central nervous system and the gastrointestinal tract. These receptors mediate both the beneficial and adverse effects of opioids in both organ systems (Katzung, BG, 2004, Berry, PH, 2001).

According to the National Drug Threat Assessment Report (2010), opioids are the most common drugs prescribed incorrectly. Studies demonstrate that opioid-associated deaths have increased by 98% in the period from the year 2001 to 2006. The rate of prescribing opioids for chronic pain relief is reported to be 28% in Europe (Robertson, JA, Purple, RJ, 2016). In a study, mortality and severe adverse effects caused by commonly prescribed opioids were compared according to seven types of opioids. In a 7-year period, 19.480 cases of serious adverse events were identified and it was found that hydrocodone and oxycodone opioids were responsible for 77% of the cases (Murphy, DL, Lebin, JA, Severtson, SG, Olsen, et al., 2018). In recent years, the use of prescription opioid drugs has increased dramatically in the United States, with only 16,651 opioid-related deaths occurring in 2010 (Dart, RC, Surratt, HL, Cicero, TJ, Parrino, MW, et al., 2015). Opioid treatment is mainly applied in pain of severe diseases such as acute pain, cancer pain and AIDS. Denizbasi et al. defined the population of patients, in whom opioid use

should be avoided, as opioid-dependent newborns, cocaine addicts, and poisoned patients with an unidentified stimulant (Altınok, A, Denizbaşı, ÇÖ, Özge O, 2019).

Opioids are classified as below (Erden, ÖF, 2018):

a) Natural opioids

Phenanthrenes (Morphine and Codeine)

Benzyl Quinolines (Papaverine)

b) Synthetic Opioids

Morphine derivatives

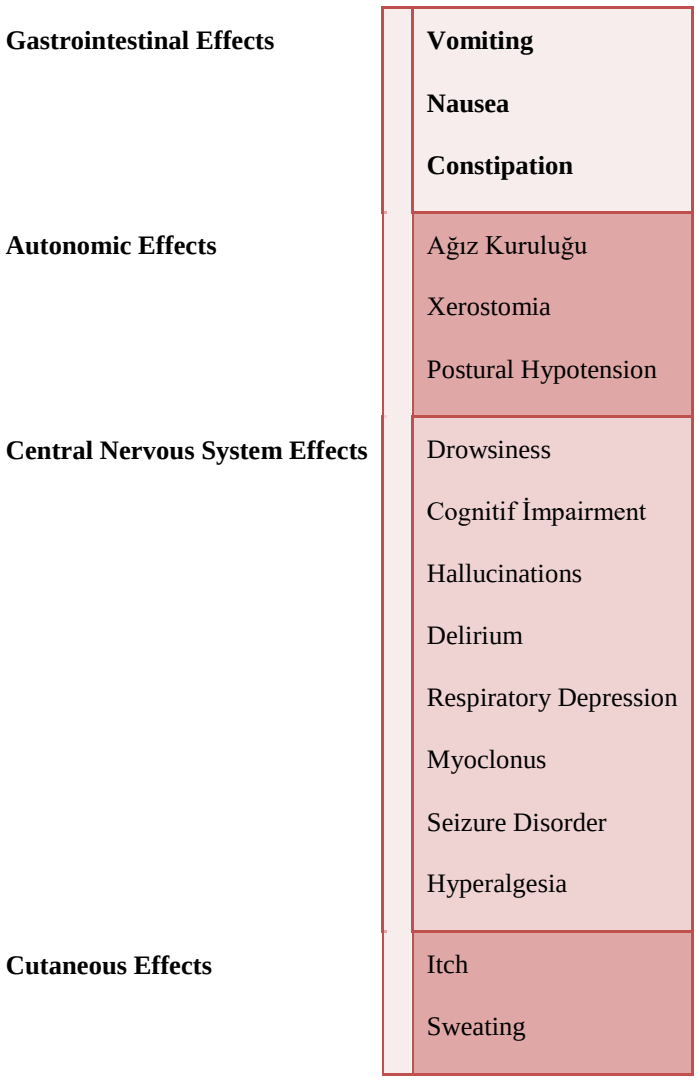
Diphenyl or methadone derivatives

Benzomorphans and phenylpiperidine derivatives.

c) Semisynthetic Opioids

Examples of opioid drugs include codeine, fentanyl morphine, hydromorphine, oxycodone, methadone, meperidine, and hydrocodone. The most commonly prescribed drugs at health care centers are the opioids. The psychological and physical side effects of opioid drugs are considerable. Doctors do profit and lost analysis according to the patient's priorities and the prognosis of the disease. Therefore, they may sometimes ignore, possible adverse effects when giving prescribe (Pathan, H, Williams, J. 2012).

Figure 1. The Common Effects of Opioids (Swegle, JM, Logemann, C. 2006).



Selected side effects of opioids are described below:

Psychological and Physical Side Effects of Opioids: Opioids taken before and after surgery may affect recovery and outcomes. Patients receiving opioids prior to back surgery have been shown to have unfavorable outcomes including pain, impaired functioning, and depression (Dambisya, YM. and Lee, TI, 1995). Patients receiving opioids before knee replacement surgery gave negative feedback about pain (Pivec R, 2014).

Opioid use in the postoperative period is known to delay the recovery. Modern surgical and postoperative procedures are designed to reduce the use of opioids besides other factors in order to accelerate the recovery. However, excessive pain has a negative effect on the recovery processes. Therefore, it is imperative to use a multimodal approach to alleviate the pain and to minimize the use of oral and long-acting opioids (Varadhan, K.K, Lobo, DN., 2010).

Cognitive impairment: The effect of opioid drugs on cognition is still a complex issue.

As it is known, the use of larger doses of opioids can cause drowsiness, lethargy, and even death. Study results about the effects of doses commonly used in the outpatient treatment of pain are more complex because the pain itself may compromise the cognitive functions. A prospective study, evaluating the effects of opioids on cognitive functions, has shown that opioid treatment in patients with chronic pain caused a reduction in the spatial memory capacity and resulted in impairments in the working memory (Schiltenwolf, M, Akbar, M, Hug, A, Pfuller, U, et al. 2014). In another study, urine and hair samples were collected and analyzed from 23 individuals who applied to a trauma center and who were using non-prescription opioids. Neuropsychological tests were also applied to these individuals. As a result of this study, chronic opioid users showed poor performance in recognizing emotions primarily from faces (gesture and facial expression), prosody and complex scenes (Kroll, SL, Nikolic, E, Bieri, F, Soyka, M, et al., 2018). Marco et al. conducted a study of 64 patients who admitted to the emergency department with severe pain and agreed to receive opioid treatment. In this study, the patients who had a mean age of 36 were evaluated with mini mental examination before and after the examination with montreal cognitive assessment scale. At the end of the study, mini mental examination scale scores revealed a relationship between opioid use and decrease in cognitive performance (Marco, CA, Mann, D, Rasp, J, Ballester, M, et al. 2018).

Respiratory depression: Opioids adversely affect the respiratory system. Carbon dioxide (CO2) levels in the blood affect breathing negatively. When the respiratory rate slows down, the levels of CO2 increase. Opioids affect the CO2 and O2 feedback loop (Shenoy, SS, Lui, F, 2018). When the patient receives a high dose of an opioid, wakefulness will be decreased due to the high levels of the opioid. In particularly, mu (m) -opioid peptide agonists with high affinity and good selectivity are obviously excellent analgesics, but in general cause ventilator depression (Azzam AAH, Mcdonald J, Lambert, DG, 2019).

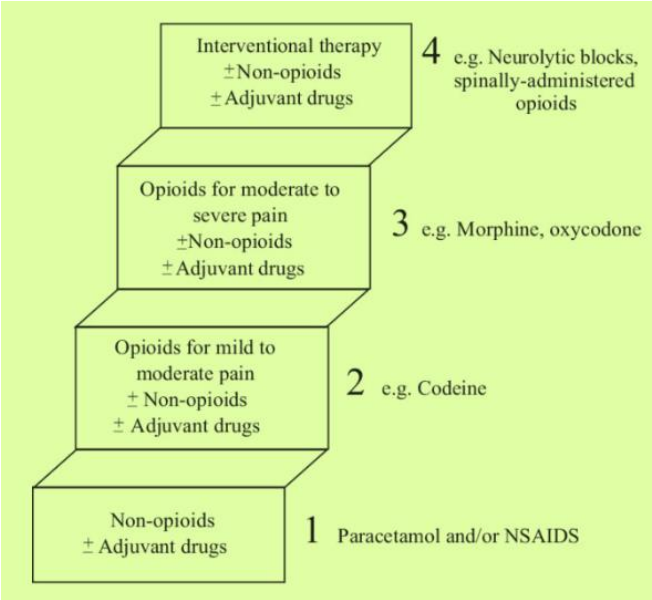
Endocrine-hypogonadism: Chronic use of opioid drugs can cause many endocrine problems. The most obvious problem is the decrease in the released levels of gonadotropin-releasing hormone (GnRH), which promotes the synthesis of sexual hormones (estrogen and testosterone) by our bodies. These low hormone levels can be seen in 50% of individuals receiving chronic opioid treatment (Reddy, RG., 2010).

Constipation: Constipation usually occurs with opioid medication use. Opioids inhibit gastrointestinal peristalsis and slow gastric emptying. They also increase the tone of the anal sphincter, disrupting the defecation reflex and making defecation difficult (Sizar O, Gupta M, 2019). In the other resource the incidence of constipation due to reported opioids is highly variable between 15% and 81% (Tafelski S, Beutlhauser T, Bellin F, Reuter E, et al., 2016). Constipation due to opioids may occur as soon as opioid use begins or in any of the use processes. Problems such as nausea, vomiting, abdominal tension in this type of constipation may not heal despite the use of laxatives. In this case, most patients may discontinue opioid use (Sizar O, Gupta M, 2019).

Nausea and vomiting: Nausea and vomiting are common side effects of opioid drugs and they, too, occur due to the reduced peristaltic activity of the stomach and small intestine (Swegle, JM, Logemann, C. 2006). İncidence of nausea and vomiting between 10% and 50%. Opioids have an emetogenic effect

with many mechanisms. These are; direct stimulation of the chemoreceptor-triggering zone, prevention of peristaltism, mechanisms related to vestibulum. It is very difficult to control these prblems (Porreca, F, Ossipov, MH, 2009).

Figure 2. The "Analgesic Ladder" of the World Health Organization for analgesic use (Kabalak, A, Ayla O, 2013).



Conclusion

The recommendations of the World Health Organization on the following analgesic use principles (Figure 2) need to be considered when using opioids (The American Pain Society, 2001).

Principles of analgesic use

a) Selection of the analgesic should be based on the pain-analgesic ladder principle according to the severity of the pain.

b) The cause and the nature of the pain should be taken into consideration when selecting analgesics.

c) The oral route should be the first choice for the mode of analgesic administration.

d) The dose of a particular analgesic medication should be determined individually for each patient.

e) Analgesics should be given at regular intervals before the onset of pain.

f) Prophylaxis and treatment for side effects should be provided.

g) Ungrounded concerns of patients and their relatives should be ruled out.

h) Adjuvant drugs should not be used unless necessary (WHO 1996, Colleau SM, 2006, Aydınlı, I, 2002, Royal College of Anaesthetists, 1998).

It is considered vital that health professionals follow guidelines on opioids in line with the principle of "Don't give harm firstly".

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IN THE LIGHT OF NUTRI-OMIC SCIENCES "ARE WE REALLY WHAT WE EAT?"

Esra ŞIK[1]

Abstract

Using high quality genomic tools and bioinformatics techniques has increased after the Human Genome Project (HGP) is completed. As a result of this great step taken to carry out comprehensive analyzes of biological systems, the word –omik was added to the end of the already known sciences names and new techniques with a holistic approach began to be used. These techniques called "omik" includes determination and definition of whether of molecules in a particular biological sample is derived from cells, tissue samples, an organ, or an entire organism. The main purpose of omic studies that have been increasing in recent years is to identify genes (genomics), messenger RNA (transcriptomics), proteins (proteomics) and metabolites (metabolomics) in a sample.

Apart from these technologies, nutri-genomic also known as nutritional - omic techniques, nutri-transcriptomic, nutri-proteomic, nutri-metabolomic subunits are the methods that aim to reveal the relationship between genes and diet more clearly and studies are progressing rapidly. In particular, nutrigenomic research includes high throughput analysis using all sub-sciences of system biology to optimize health through personalization of the diet, clarify the complex relationship between nutrients and genetic polymorphisms.

In this review, both understanding the molecular mechanism of the interaction between the human body and nutrition at all regulation levels (genes, gene expression, proteins, metabolites) in addition to the superiority of nutri - omic techniques over traditional approaches and intending the ability of human health to be optimized by food intervention, evaluation of prevention and treatment potential of diseases with nutrition is aimed.

Keywords:

Nutrigenomic, nutrigenetic, metabolomic, nutrition-gene interaction

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INTRODUCTION

In the last quarter century, nutrition research has undergone a significant development, focusing on molecular biology and genetics as well as epidemiology and physiology. It is not possible to understand the relationship between nutrition and health without clearly determining the effect of nutrients at the molecular level. There are some factors that cause this to be noticed [1]. The first is the important evidence about personalized nutrition that genetic variation analyzes performed after the conclusion of the human genome project and the results of studies linking gene variation with disease markers or other phenotypic changes [2, 3]. Second, there are serious diagnoses that micro- and macro-nutrients can be powerful dietary signals that affect cell metabolic programming and play an important role in the control of homeostasis [4]. At the same time, nutritional researchers have begun to accept that genetic predisposition may be associated with diet, such as cardiovascular disease, type II diabetes and cancer [5]. Nutrigenomics (gene - nutrient interaction) studies have gained speed in order to understand both nutrients and genes or their interaction due to the idea that different individuals cannot give exactly the same response to similar diets. Nutrigenomics called nutritional genomics promises to optimize human health and to prevent the disease by determining the most relevant personal nutrition [3, 6].

Genomic science, which is the fundamental omics technique that directs the researches, investigates in an in-depth and holistic approach the structural and functional properties of the DNA where genetic information is stored. These sciences, led by genomics, later formed nutrigenomics and nutrigenetics together with transcriptomic (examines transcriptomes), proteomics (examines proteomes), metabolomics (examines metabolomes) and epigenetics [7]. Even though these two notions are closely related, they show a different approach to understanding the relationship between genes and diet [8]. Nutrigenomics investigate the effects of nutrients on gene expression, while nutrigenetics study the effect of genetic variations caused by nutrients. Unlike nutrigenomics, nutrigenetics deals with how an individual's genetic structure influences the response to diet and thus explores in detail the underlying causes of genetic polymorphisms [9].

Every food taken into the body is converted into many new substances with different biological effects after being metabolized. It is known that environmental factors such as diet type and frequency and quality of diet have the ability to change gene expression [3, 10, 11]. Even in individuals living in the same geography, exposed to the same environmental conditions and belonging to the same culture, the difference in the response to diet is due to genetic variation [12, 13]. Investigating the potential of food intake to alter gene expression is essential to elucidate the effects of nutrition on health.

Biomic techniques provide the basis for the equipment and methods required for nutrigenomic studies used to explain nutrition-gene interactions. Today, it is possible to come across many studies in which system biology subunits (genomic, transcriptomic, proteomic, and metabolomics) and bioinformatics technologies are used effectively for this purpose [14]. In these studies, unlike traditional methods, biomic instruments used in high volume and efficiency at one time: microarrays, PCR, electrophoretic techniques, chromatographic methods, advanced devices such as mass spectroscopy and

higher statistical methods used to perform data analysis. In this study, after the general information about nutri-omic techniques is mentioned, it is aimed to reveal the relationship between nutrition and health through current studies.

2. TERMS

2.1. Genomics

Genomics is a DNA analysis technique that focuses on the cause of genome diversity among individuals. Small changes such as translocation and inversion during the synthesis of DNA do not lead to phenotypic changes that can lead to gene diversity, and cannot yet be analyzed at the genome level. Changes in expression at the nucleotide level (deletions, insertions, duplications) that are important factors that cause polymorphism can directly create variants [15].

Genomics is divided into two groups as structural and functional genomics. Structural genomics provides access to hereditary information by analyzing DNA expressions. Functional genomics, also known as transcriptomic, is the simultaneous examination of messenger RNAs (mRNAs) obtained by transcription from the cell genome. So, intended that to examine the expression of genes at the genome level in terms of form, quantity and time, as well as to learn the functions of the genes and to understand the importance for the organism [16]. Thus, by examining the changes in the nucleotide sequences, it becomes clear how genetic information is affected by nutrition. As a result, the idea of genetically appropriate individual nutrition recommendations is further approached. At the same time, gene expressions of microorganisms carrying the potential health risk for a food can be identified and stored in the database.

2.2. Proteomics

Proteomic studies focus on proteomes and protein-protein interactions. The most important handicap in these studies is the high dynamics of the potential proteins that can be revealed at the amino acid level. The analysis of many different proteins at proteome level with very different chemical character is quite difficult. However, these difficulties have been minimized largely with the techniques used today. Proteomic analysis process is the separation, visualization and separation of proteins as in the traditional methods. Some of the techniques used are advanced techniques such as two-dimensional gel electrophoresis and advanced mass spectroscopy [15, 17, 18].

2.3. Metabolomics

By defining the genes, the unknowns caused by the genetic differences of organisms have not been completely resolved and transcriptomic and proteomic studies have been carried out to clarify. However, the results of these studies were not sufficient to elucidate the phenotypes. The place where the phenotype information is stored in the cell is metabolites, and all metabolites present in a tissue or physiological fluids at a given moment are called metabolome [19]. Metabolomics technology is based on extensive analysis of metabolites and includes quantitative analysis of chemical molecules obtained by biological processes other than substances such as DNA, RNA or protein in the sample [15, 20]. Nuclear magnetic resonance (NMR) and mass spectrometers are the best equipment used today for metabolomics research [15].

3. USE OF OMIC TECHNIQUES IN NUTRITIONAL SCIENCES

In the science of nutrition, the use of omic techniques such as transcriptomic and proteomics has been increased in determining the mechanisms of action of dietary factors and metabolites. These techniques are used to understand both the positive and negative effects of dietary elements on human health and molecular incidents in nutritional diseases such as obesity, diabetes, cardiovascular diseases and colon cancer [11].

To analyze complex and crowded data sets obtained from nutri-omic studies bioinformatics techniques are used. For instance, there is potential interaction of a particular food with 30000 genes or 100000 different proteins in the human genome. The integration of statistics and bioinformatics with biology is essential for analyzing and interpreting the data from these interactions.

In a study, butyrate treatment of colorectal cancer cells was found to cause cell deaths and it was found that growth was inhibited within 48 hours after application. In order to elucidate this mechanism, gene expression sequences were determined by using HT29 colorectal cancer cells as a model and proteomic techniques were applied. As a result of proteomic applications (2D-DIGE electrophoresis and mass spectroscopy), 1347 proteins (including all isoforms and modifications) were detected and 139 of these butyrate treatments were found to play a role in cancer cell death [21, 22]. In the gene expression part of the study, microarray was performed to HT29 cells. As a result of statistical analysis, it was determined that 2550 genes of human genome were changed by butyrate. These genes have been found to be involved in biological events such as DNA repair and transcription, as well as cell metabolism. However, the correlation between gene expression modulation and protein expression has been reported to be poor [21, 24].

Fenech et al. (2011) mentioned how to use omics techniques to better understand the potential effects of nutrition on gene and protein expression. For this purpose reviewed the changes in the gene and protein expression of colon colorectal cancer cells by butyrate, a metabolite produced by bacterial fermentation of dietary fiber or resistant starch in the colon [22]. Dietary fibrous foods and resistant starch are known to promote intestinal health and protect against colorectal cancer [23]. Butyrate, a metabolite formed by the use of resistant starch by microorganisms in the intestine, has been reported to improve intestinal health [24].

The results of studies on nutrition-gene interaction in the literature should be able to guide the consumer and should be practically applicable in the field of dietetics. Cahill et al. concluded that adequate doses of vitamin C are mandatory in individuals with GSTM1 or GSTT1 (glutathione S-transferase) genotype, as inadequate vitamin C induction causes ascorbic acid deficiency in these individuals [25]. In a case-control study conducted by the Singapore Chinese Health Study Cohort on women, a significant correlation was found between the level of green tea drinking and the activity of angiotensin converting enzyme (ACE). According to this result, the risk of breast cancer due to ACE gene polymorphism decreases with consumption of green tea [26].

One of the most important genes associated with obesity is the FTO gene located on chromosome 16 is associated with fat mass. Duicu et al. (2016) in a study, analyzed FTO gene variants (rs9939609 and rs17817449) and some metabolic biomarkers (fasting blood sugar, total cholesterol, HDL and LDL cholesterol, triglycerides) and leptin levels in a 357 Roman obese children group and their

relationship. FTO rs9939609 SNP (single nucleotide polymorphism) carriers have been found to be more than twice the risk of obesity. Carriers of FTO rs17817449 SNP were found to have higher weight, BMI (body mass index), waist and hip circumference, total cholesterol, triglyceride, fasting blood sugar and adiponectin values [27]. Another important gene associated with obesity is the INSIG2 (insulin-induced gene 2) gene on the chromosome 2. In a study, three INSIG2 polymorphisms (rs12464355, rs17047757, rs7566605) related to dyslipidemia were found in 1058 students who had 85% higher BMI (overweight). The relationship between INSIG2 rs12464355 SNP and high LDL-cholesterol, rs17047757 SNP and excess weight, and rs7566605 SNP and high lipid levels were found to be significant [28].

Estruch et al. (2013) carried out their studies with the prediction of "primary prevention of cardiovascular diseases by the Mediterranean diet". They found that when they enriched the diet with especially in extra virgin olive oil, they reduced the incidence of some chronic diseases in subjects at high cardiovascular risk [29]. The same team presented a more comprehensive result of their work in 2018 (the 2013 study is an interim report). This study was conducted with 7447 participants, 57% of whom were women at the age of 55-80 years, who were at risk of cardiovascular disease (but without any disease at the beginning of the study). Three randomly selected groups were assigned one of three diets: the Mediterranean Diet group enriched with extra virgin olive oil, the Mediterranean Diet group enriched with mixed nuts, and the control group in which it was recommended to reduce the amount of fat in the diet. At the end of the 4.8-year tracing period; on extra virgin olive oil and nuts supplemented diet groups, cardiovascular diseases were found to be lower than the control group. The findings of the study support the beneficial effect of the Mediterranean diet on the prevention of cardiovascular diseases [30].

Kashani et al. (2019) investigated whether the microRNAs of the plants constituting an important part of the diet match the human genes that have potential regulatory function. As a result, they found that 4 common plant microRNAs provide excellent matching with 22 human transcripts (CCNC - cell cycle, GIPR - digestion, MYLK - muscle contraction), which exhibit a wide range of body functions from muscle contraction to suppression of tumor formation. According to these findings, regularly consumed foods have great potential to affect our genome and alter body functions [31].

Konstantinidou et al. (2010), in their study examined the in vivo nutrigenomic effects of extra virgin olive oil consumption within the framework of the Mediterranean Diet. In the study conducted with 90 healthy volunteers aged 20 to 50 years, volunteers were randomly divided into 3 groups, and oil source is extra virgin olive oil in the diet of the first intervention group, washed (removed polyphenols) olive oil in the diet of the second intervention group, while the diet of the control group was not intervened. According to the findings; expression of genes related to inflammatory processes (IFN, ARHGAP15 and IL7R), oxidative stress (ADRB2) and DNA damage (POLK) in peripheral blood mononuclear cells decreased. The reduction in expression of genes related to inflammatory processes showed the protective effect of Mediterranean diet and olive oil phenolic compounds on inflammation. The anti-inflammatory and antioxidant effects of important phenolic compounds (tyrosol and hydroxytyrosol) in olive oil have been proven. Additionally, the data obtained provide further evidence that the Mediterranean diet and rich polyphenol-containing olive oils, such as extra virgin olive oil, can be recommended as a useful tool for the prevention of atherosclerosis [32].

4. CONCLUSION

Nutritional genomics is a powerful tool that can be used to provide individual-specific nutrition. Nutri - omics serve to studies which using of advanced technology tools that investigate the relationship between nutrition - gene from basic biology to clinical practice. The human genome's response to nutrition is a science that will help us understand how defective genes are affected by nutrition. There are many studies suggesting that we can optimize nutrition by defining the genotype of an individual. Though it is not possible to change our genetics, in the near future, we will be able to improve the effects of hereditary defects through nutrition, and select the right foods to support our genetic predisposition. However, researches on nutrition - omics applications, which have a history of about twenty years, is still insufficient to be reflected in practice today. Disease-specific biomarkers should continue to be identified. Thus, it will be possible to improve the quality of life through individual-specific nutrition by moving away from the “one size fits all” approach.

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A SYSTEMATIC STUDY OF B -LACTAM ANTIBIOTIC

Rihab Fouzy Alfalah[1]

ABSTRACT

Beta-lactam antibiotics were the first and most common therapy in the treatment of bacterial infections. Multiple resistance emerged and became a major public health problem. To overcome this problem there are several techniques. The main objective of this research is to systematically review and evaluate of b-lactam antibiotic. In this paper, will try to answer the question: what are the techniques and modification that use to enhance drug activity and prevent bacterial resistance. Will start by explaining the meaning of β-lactam antibiotic, then followed by reviewing a type of technique found to decrease bacterial resistance, in the literature review part. It is not in detail, but covers some about b-lactam antibiotic and techniques that overcome the problem of bacterial resistance. Finally, a discussion and the result will be presented to answer the asked question and the conclusion summarizes the reasons why antibiotic resistance is very critical.

Keywords:

β-lactam antibiotic.

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INTRODUCTION

Types of antibiotics and its mechanism: Antibodies are divided into three groups according to their mechanism of action on the bacteria as shown in Fig (1) there are three attack sites for antibiotic: a) Biosynthesis of protein, b) Cell wall synthesis and c) DNA replication (1).

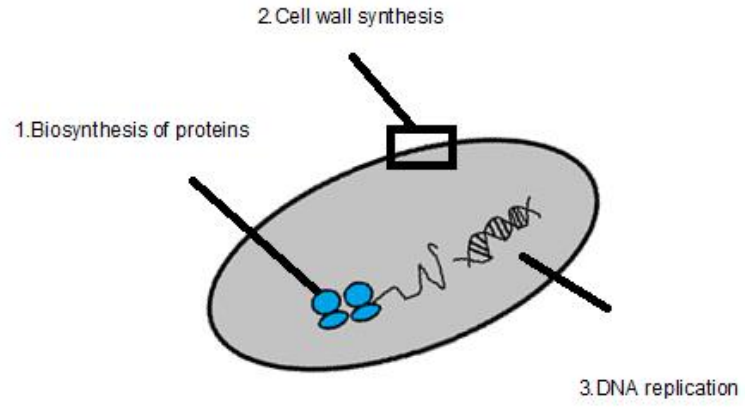


Figure (1):show the mechanism of action of antibiotic class.

β-lactam antibiotic and the bacterial resistance: β-lactam antibiotic means all antibiotic that contains β-lactam in its structure, mechanism of action of these antibiotics by inhibiting cell wall synthesis of the bacterial organism. By permanently bind between the bacterial cell wall and a b-lactam ring of antibiotic, These types of antibiotics the most widely used for all groups of antibiotics (2-6). This group includes penicillin, penicillin combination (penicillin with inhibitors) and cephalosporin and its generation. The bacteria quickly develop resistance to Antibiotics As soon as they are released and started to use. In fact, rapid clinical resistance usually occurs in months to several years after the release of the antibiotic (7). The resistance against this group emerges when continuously used. Bacterial enzymes called β-lactamase that inhibit the therapeutic effect of the β-lactam antibiotic. β-lactamase attacks the lactam loop and prevent the therapeutic action of an antibiotic, the increase of this clinical problem led to discovering β-lactamase inhibitor that used to restore antibiotic action (8-9).

II. Research Question: The aim of this research paper is to get the answer to this question: **Q1** what are the techniques and modification that use to enhance drug activity and prevent bacterial resistance?

III. Research methodology: My research methodology by following a systematic mapping of the published article and researches related to my topic. And to discover the technique use to prevent bacterial resistance. I reviewed the set of paper in the literature part and analyze it. All the paper that I reviewed was published from 2010 to 2019, and collected from the Science Direct library. My research methodology steps are summarized in table 1,2 and 3. After the exclusion criteria 37 papers remain, when just focus on techniques used to prevent the resistance become 10 papers.

Search strategy	
Academic database searched:	Science direct.
Other data sources:	Google scholar.
Target item:	Journal papers & conferences.
Search applied to:	Title, abstract, and key word.
Language:	Papers written in English.
Publication years:	2010-2019

Table1: search strategy

Major term	Alternative term
B-lactam antibiotic.	----

Table2: search string.

Inclusion & exclusion criteria	
Inclusion criteria:	Publication date : 2010-2019 Journal paper& conferences related with research term. Publication title: advanced drug delivery review.
exclusion criteria:	Papers don't focus on b-lactam antibiotic and techniques used to overcome the problem of bacterial resistance.

Table3: selection strategy.

IV. The techniques that are used to enhance drug activity and overcome the problem of bacterial resistance are:

1. Drug combination:β-lactamase inhibitor:

Majority study in bacterial resistance at today is on the b-lactamase field in gram positive and gram negative bacteria (10). B-lactamase inhibitors, non therapeutic agent, but when combined with antibiotic, act to restore the activity of antibiotic by preventing bacterial resistance (11). Up to now, just three b-lactamase (b-lactam class) discovered (Tazobactam, Clavulanic acid, and Sulbactam). Also, a new inhibitor that discovered lately (Avibactam) as a b-lactamase inhibitor (non-b-lactam class) (12). For now only four β-lactamase inhibitors approved by FDA, and more than fifty β-lactam Class antibiotics approved, this is encouraging the discovery of other b-lactamase inhibitors (13,14).

2. Antimicrobial delivery system:

2.1. Antimicrobial polymers: In contrast to conventional antibiotics, antimicrobial polymers were designed to treat surface-related bacteria (15,16,17). Active polymers significantly reduced the burden on systemic antibiotics and also contributed to prolonging the life of traditional antibiotics and inhibiting the development of resistant microbes. In the past, amino acids were the preferred fraction To develop antibiotic polymers, research has recently expanded to include polymers with chemical modifications, polymers with organic or inorganic compounds against bacteria (18,19,20). The combination of an antibiotic with polymers leads to the stability of antibiotics and reduce their toxicity and increase the half-life of the antibody and its effectiveness.

A type of polymer delivery:

2.1.1 Polymers with chemical anti-bacterial modifications: Polymers were modified from 1965 to provide antibacterial and bacterial resistance (21). These modifications are divided into three sections: 1) Very small particles connected to the polymer backbone (22.23). 2) A peptide with antibiotic activity related to biological inactive polymers (24.25). 3) Antimicrobial polymers with biologically inactive polymers (26.27).

2.1.2. Polymers that contain antimicrobial organic compounds: This is the most widely used methods for the manufacture of antimicrobial polymers. However, this method is complex and may enhance bacterial resistance unintentionally. (28)(29.30).

2.1.3. Polymers that contain inorganic compounds antimicrobial: Inorganic compounds such as minerals and mineral oxides. Silver is one of the oldest anti-bacterial polymers in its various forms (ions, salts, Nanoparticles.....), There are many studies related to these polymers (31). There are also other successful strategies such as zinc oxide (32), gold and titanium oxide (33). All these techniques Used in the nano-barticles form (34).

2.1.4. Intrinsic antimicrobial activity polymer: Some of the polymers have antibacterial properties in their composition, often chemical or other structural elements. The most commonly studied types are polymers with a natural -peptides (e.g. Oligo-n-substitutes glycines,(35) and halogen polymers (Containing fluorine or chlorine), polyphenyl ethynylenes (36), polymeric N-halamines (37), and organometallic polymers, and the group may also contain cationic polymers (eg, quarternary pyridinium -salts, quaternary ammonium salts, biguanide, and phosphonium salts) (38,39), or cationic conjugates (e.g. polyoxazolines , polysiloxanes, polyelectrolytes, polyionenes,…etc).

2.2. Nanoparticle /liposome delivery system:

2.2.1 Nanoparticle: Drug delivery system in the nanopartical form it is the approach to improve 1) the therapeutic index, 2) dose administration, 3) bacterial resistance(40), 4) organ targeting to decrease side effects (41,42)**.** Metal nanoparticles like a silver compound used in pharmaceutics and medicine as a carrier of the antibiotic agent(43,44) this is in past .put recently the researchers try to mixed the gold nanoparticles with different species of antibiotic for example :(ciprofloxacillin, and another fluoroquinolone antibiotic)(45), gentamicin (46), vancomycin (47)....etc but the result it is not equal, the researchers found that when decorating the surface of gentamicin with golden nanoparticle enhance the activity against gentamicin resistance (47), but other researchers showed no enhancement in gentamicin resistance (46). This variation may be because of some affect efficacy parameter: for example 1) the characterization of antibiotic. 2) nanoparticle size, 3) experimental condition. Relatively, there are a few drugs in nanoparticle form (48), this is maybe because of complexation of nanoparticle technology(49).

2.2.2. Liposome: The most route of administration of liposome by Intravenous injection the advantage of this technique. 1) Used in biological and hydrophilic compound, 2) antibiotic stability, 3) increase therapeutic index and decrease toxicity.4) targeting of organ (50,51). The advantage of this technique his similarity of membrane structure that leads to easier to fuse in cellular membranes, then delivers a drug directly to inside cytoplasm and prevents bacterial resistance (52). Unfortunately, lipid-based drug delivery has limited efficiency (42), the short half-life of the drug due to the instability of lipid bonds, a fusion of liposomes and aggregation, sensitivity to temperature (49), these reasons can lead to not enough delivery of the drug. The liposome stability can improve by different modification (e.g. Act on a long chain of polymer in hydrophilic part or in charge chain....etc.)**.**

V. Discussion and result:
distribution of papers by years as shown in figure 2

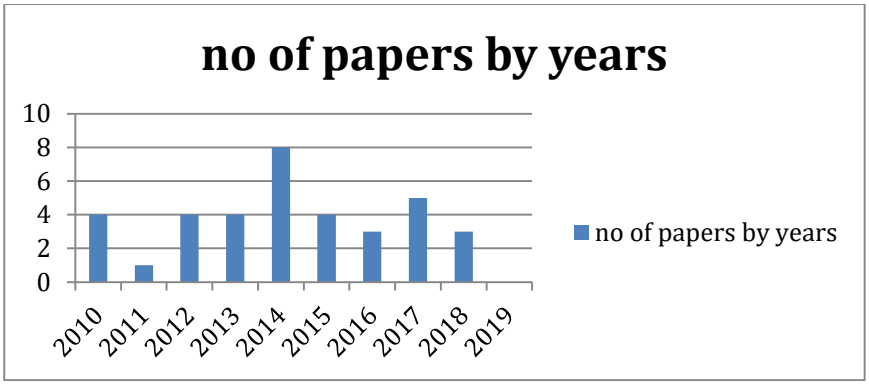


Figure 2: distribution of papers by publication date

Also the type of paper that review show in figure 3

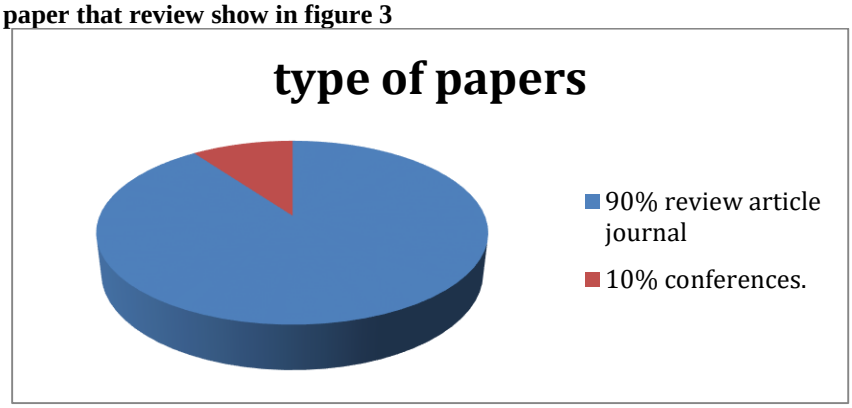


Figure3: distribution of papers by type

Result in techniques thous used to overcome the problem of resistance that collect from reviewing papers {(53), (54), (55), (56), (57), (58), (59), (60).}:

Drug combination: (b-lactamase inhibitor): the Beta-lactamase inhibitors were shown effective as a treatment of bacterial infections in infants, children, and adults. The safety and efficacy of Beta-lactamase inhibitors were evaluated in six prophylaxis studies and 39 therapeutic studies in both pediatric patients and adult.36 shown in both excellent safety and efficacy, with little adverse reported around 10% of patients in most studies. Type of side effect different according to the administration route of the combination drug. Gastrointestinal disturbances and diarrhea are the side-effects that most frequently reported with the orally taken antibiotic, this is due to the antibiotic effect on the normal bacteria in intestinal flora. In the studies show, side effect rarely leads to incomplete treatment and always the problem resolve during therapy or after the end of therapy. It is interesting to note that in the reviewed paper reported a reduction in diarrhea side effect in patients taken the antibiotic in the parenteral route.in Journal of International Medical Research 2002 (45) show the clinical and biological response of infection treated with drug combinations. The result indicates on greater effective of drug combination against bacterial resistance (60).

Clinical and bacteriological response in various infections treated by b-lactamase inhibitor combination as mentioned in the papers reviewed (60).

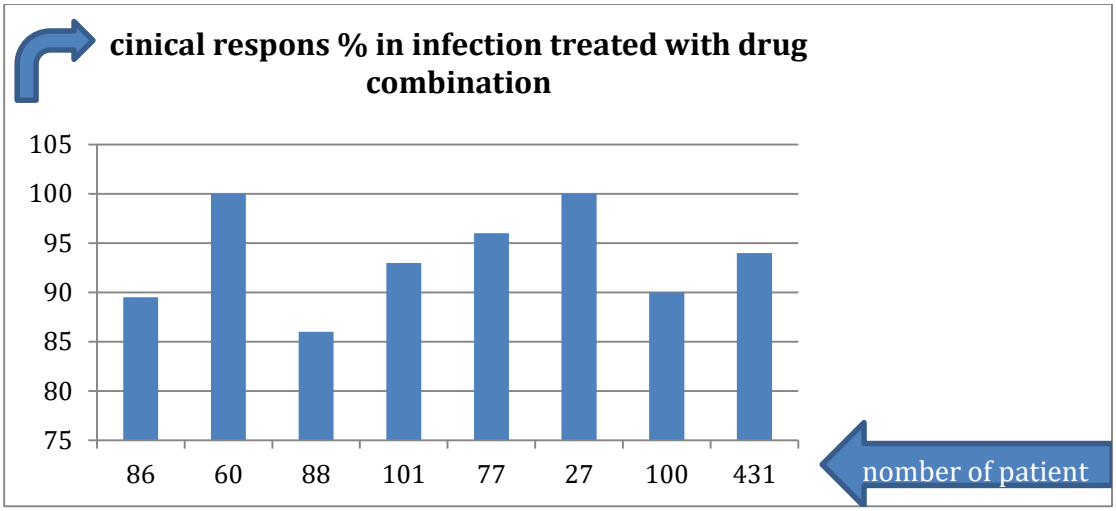


Figure 4: clinical response in infection treated by drug combination technique

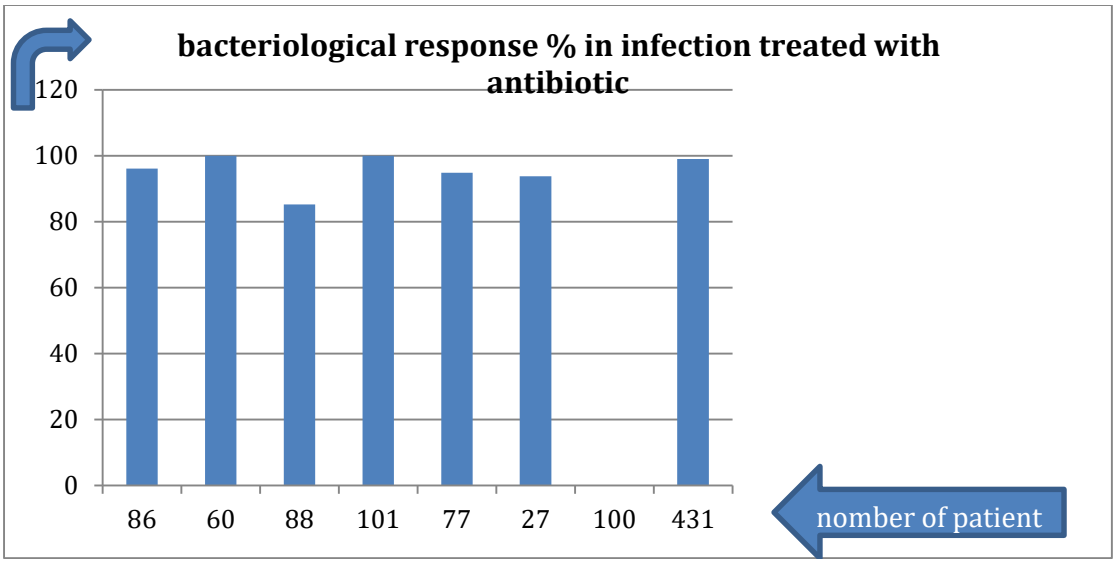


Figure 5: bacteriological response in infection treated with drug combination techniques

Drug delivery system:

Polymer: Advantages and disadvantages of polymer as mentioned in the papers reviewed (57,58) summarized in table 4**:**

Advantages	Disadvantages
Local delivery of drug. Increase sustained drug. Stability. Decrease frequents taken drugs. Decrease side effect. Patient compliance improved.	Some substance may cause the issue to body after degradation (toxic) High drug release after administration of drug.

Table 4: advantage and disadvantage of polymer

Nano-particle and liposome:

Nano-particle: Advantages and disadvantages of different type of nano-particles as mentioned in the papers reviewed (53,54,55,56) summarized in table 5:

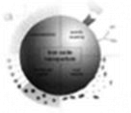
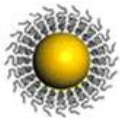
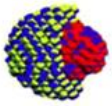
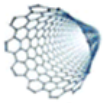
Type of nano-particle	Advantage	Disadvantage
Metal oxide 	_Aproved by FDA for clinical use. _intrinsic magnetic properties. _flexible surface modification with different coating.	_toxicity and bio-compatibility concerns. _inflammation to respiratory system.
Gold nano-particle 	_able to absorb light. _flexible surface modification.	_toxicity. _expensive.
Quantum dots 	_narrow wavelength emission. _high fluorescence efficiency and Photostability.	_Toxicity and bio-compatibility , especially the heavy metals.
Carbon nanotube 	_Intrinsic properties, enabling imaging modalities. _ultra high surface area with inside hollow space for drug efficient and bio-conjugation.	_ Toxicity and bio-compatibility
Radio and fluorescent molecule 	_the highest flexible. _Ability to perform as non invasive real time treatment monitoring.	_short half life. _ Toxicity and bio-compatibility

Table5: advantages & disadvantages of nano-particle type

Distribution of nanoparticle type used in drug delivery system show in figure 6:

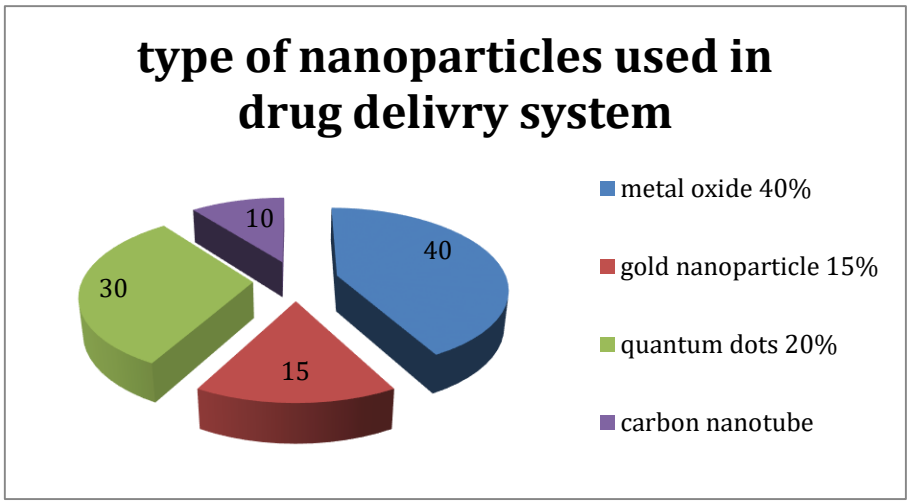


Figure 6: distribution of nano-particle type used as an antibiotic drug form.

Liposome: Advantages of Use Liposomes form was mention in papers reviewed(53,54) can be summarized as: reduced toxicity, increase the time of drug retention, enhance the efficacy of the drug, targeted of specific site delivery (only the infected cells affected by the drug), reduce adverse side effects, and finally, Liposomes have shown to significantly reduce the toxicity of the drug in the free form. The advantages and disadvantages of liposome should be balanced to achieve the desirable results.

In the diagram (figure 7) show the distribution of drug delivery system that used in antibiotic to prevent bacterial resistance, this according to papers reviewed (59).

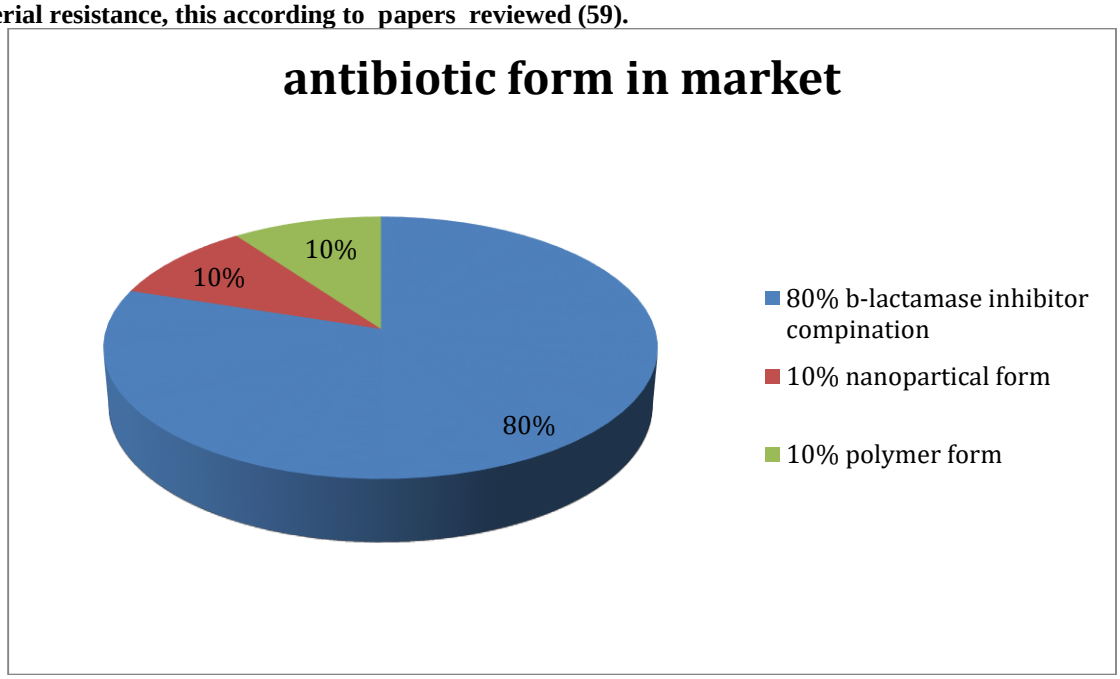


Figure 7: distribution of antibiotic form found in the market.

VI.CONCLUSION

Beta-lactam antibiotics the first and most common therapy in the treatment of bacterial infections. Multiple resistance with b-lactamas emerged and became a major public health problem. To overcome this problem, Antibiotics are given with a combination with a β-lactamase inhibitor. The b-lactam antibiotic combination is an ideal therapy for infections, in adult and pediatric patients, it is safe and has a broad spectrum of activity, and it is available in a variety of formulations that are suitable for sequential therapy, thus ensuring a smooth transition into community management of the hospital. Moreover, a short course of therapy and, simple treatment regimens, that lead to patient compliance with this combination. The b-lactam combination becomes increasingly important for the pediatric and adult infections, especially if there is no bacterial resistance.

Nano-particles drug is designed to improve the therapeutic and pharmacological properties of drugs, by protecting a drug from degradation and enhance the targeting and controlled release. Due to the small diameters, nano-particles are able to cross the blood-brain barrier and act on a cellular level. In comparison with the classical form of drugs, nano-particles drugs are more effective and selective. They can reduce the toxicity and side effects in normal tissues.

In the development of drug delivery technology Polymer play a vital role by offering a release of both type of drugs (hydrophobic & hydrophilic), repeated dosage, and constant release of the drug over extended periods**.**

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INVESTIGATION OF PHYSICAL ACTIVITY AND HEALTHY LIFESTYLE BEHAVIOURS OF INDIVIDUALS APPLIED TO HOSPITAL FOR RESPIRATORY DISTRESS - PİLOT STUDY

Ebru Şeker Abanoz[1], Fahri Köroğlu [2], Özge Tahran [3], Tuğba Çivi Karaaslan [4], Gökşen Kuran Aslan[5], Özge Ünal Bayraktar[6], Esen Kıyan[7]

Abstract

OBJECTIVE: To investigate the demographic characteristics, exercise habits and healthy lifestyle behaviors of patients applied to hospital for respiratory distress.

METHODS: The demographic and clinical data of 26 patients applied to Istanbul University, Istanbul Medical Faculty, Department of Chest Diseases and Yalova State Hospital with respiratory distress were recorded. Physical activities of the subjects were evaluated with "International Physical Activity Questionnaire (IPAQ) and healthy lifestyle behaviors with" Healthy Lifestyle Behavior Scale II (HLBS-II).

RESULTS: Four women (%15.4) and 22 men (%84.6) with a mean age of 65.85±9.72 years were included in the study. Average body mass index was 26.85 ± 4.06 kg/m^2. Cigarette use rates; %19.2(5) were smokers, and %73.1(19) had stopped smoking. The mean cigarette use was 36.15±20.47 pack years. Modified Medical Research Council Dyspnea Scale values of the subjects varied; 0(n = 1), 1(n = 14), 2(n = 4), 3(n = 6), 4(n = 1). In the last year, the number of attacks with respiratory problems was 1.04±1.68, the number of unplanned admissions to hospital was 3.77±7.01, and the number of hospitalizations was 0.46±1:10. FEV1/FVC ratio was %.76.15±8.48 The rate of regular exercise was %15.4(4), IPAQ average total score was 1597.42±1893.56 and HLBS-II average score was 130.58±21.37.

DISCUSSION: %92.3 of the patients with respiratory distress had a history of smoking, exercise habits were very low, physical activity and healthy lifestyle behaviors were moderate.
We think that giving education about smoking cessation and exercise to individuals, will improve their physical activity levels and healthy lifestyle behaviors and reduce the respiratory problems they will encounter.

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KEYWORDS
Exercise, Respiration, Health Behavior, Healthy Lifestyle, Smoking

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INTRODUCTION

According to World Health Organization statistics, 70-80% of deaths in developed countries and 40-50% of underdeveloped countries are caused by diseases caused by lifestyle. According to the National Burden of Disease and Cost Effectiveness Project data, ischemic heart disease are the main causes of death in both sexes in Turkey, cerebrovascular disease and is reported to have COPD. In the formation of these noncommunicable diseases, one's own attitude and behavior, in other words, the way of life, play a big role. Healthy lifestyle is defined as the control of all behaviors that can affect the health of the individual and the selection of the behaviors that are appropriate to his / her health status in the regulation of daily activities. Individuals who adopt a healthy lifestyle behave in a conscious manner about healthy eating, increasing intellectual capacity, prevention of cardiovascular diseases, increasing immunity level, maintaining normal body weight and coping with stress appropriately. As a result of this, individuals feel better and gain a more positive perspective, work effectively and act, and lead a longer and better quality life (1).

Smoking cessation is a necessary treatment for people who suffer from respiratory distress and reduces the prevalence of respiratory symptoms, the number of hospitalizations, the frequency of exacerbations, and overall mortality (2). In addition to quit smoking, appropriate physical activity and high-quality nutrition also play an important role in delaying the disease process and reducing the outcomes associated with respiratory distress (3,4). Therefore, it is recommended to adopt healthy lifestyle behaviors such as smoking cessation, regular exercise and healthy nutrition for self-management of respiratory distress and prevention of secondary pathologies (5).

The most information available on lifestyle management of respiratory distress is limited to high-income countries; data for middle and low income countries are insufficient (6). Our aim in this study was to investigate the demographic characteristics, exercise habits and healthy lifestyle behaviors of patients applied to hospital for respiratory distress.

METHODS

The demographic and clinical data of 26 patients with respiratory distress were collected in Istanbul University, Istanbul Medical Faculty, Department of Chest Diseases and Yalova State Hospital from January to March 2019. The demographic data of the patients were collected with the information

form created by the researchers. The information form included the personal and clinical characteristics of the patients.

The inclusion and exclusion criteria are listed below:

Criteria for inclusion in the study

- Being 40-65 years old
- Applying with respiratory distress
- Not participating in pulmonary rehabilitation or any exercise program for the last 6 months
- To be able to read, write and understand Turkish language

Criteria for exclusion in the study

- Having cooperation problems
- Diagnosed psychiatric disease
- Having had respiratory tract infection in the last 1 month
- Any disease affecting the musculoskeletal system.

Healthy Lifestyle Behaviors Scale II (HLBS-II) developed by Walker et al. in 1996 was used to determine healthy lifestyle behaviors. In 2008, it was translated into Turkish and validity-reliability was made by Bahar et al. (7). This scale consisted of 6 sub-factors consisting of spiritual development, health responsibility, physical activity, nutrition, interpersonal relationships and stress management. The minimum score of the 52 items was 52 and the maximum score was 208. The higher the scores, the higher the individual's stated health behaviors.

Physical activities of the subjects were evaluated with "International Physical Activity Questionnaire (IPAQ). It was developed with the support of the World Health Organization (WHO) and the American Center for Disease Control and Prevention (CDC). It was translated into Turkish and validity-reliability was made by Saglam et al. (8). It provides information about the time and residence time spent by individuals in mild, moderate and severe activities. When evaluating the activities, it is accepted that each activity should be performed for at least 10 minutes at a time. For each activity level, the MET value (metabolic equivalent) is multiplied by day and minute to obtain the "MET-min / week" score (9). The score obtained is classified as having no physical activity (MET = <600 energy level), insufficient activity level (MET = 600-3000 energy level) and sufficient activity level (MET => 3000 energy level).

IBM SPSS statistics for windows, version 20.0 was used for the analysis of the study data. Descriptive and frequency determination methods were used for analysis.

RESULTS

Four women (15.4%) and 22 men (84.6%) with a mean age of 65.85±9.72 years were included in the study. Average body mass index was 26.85±4.06 kg/m^2. Cigarette usage rates; 19.2% (n=5) were smokers, and 73.1% (n=19) had stopped smoking. The mean cigarette usage was 36.15±20.47 pack years. Modified Medical Research Council Dyspnea Scale values of the subjects varied; 0 (n=1), 1 (n=14), 2

(n=4), 3 (n=6), 4 (n=1). For the last year, the mean number of attacks with respiratory problems was 1.04±1.68, the mean number of unplanned admissions to hospital was 3.77±7.01, and the mean number of hospitalizations was 0.46±1.10. FEV1/FVC ratio was 76.15±8.48%. The rate of regular exercise was 15.4% (n=4), IPAQ average total score was 1597.42±1893.56 and HLBS-II average score was 130.58±21.37. Descriptive statistics are shown in table 1 and frequencies are shown in table 2.

Tablo 1. Descriptive statistics

	Mean	Std. Deviation
Age	65.85 years	9.723
Body Mass Index	26.85 kg/m^2	4.066
Smoking Pack Years	36.15 pack years	20.47
Attacks in the Last Year	1.04	1.68
Unplanned Admissions to Hospital	3.77	7.01
Hospitalization	0.46	1.10
FEV1/FVC	76.15 %	8.487
HLBS-II	130.58	21.377
IPAQ	1597.42	1893.567

Tablo 2. Frequencies

		Percentile (%)	Frequency (n)
Gender	Woman	15.4	4
	Man	84.6	22
MMRC	0	3.8	1
	1	53.8	14
	2	15.4	4
	3	23.1	6
	4	3.8	1
Regular exercise	Yes	15.4	4
	No	84.6	22
Smoking	Yes	19.2	5
	No	7.7	2
	Quit	73.1	19

DISCUSSION

Most of the patients with respiratory distress had a history of smoking. Their exercise habits were very low and their physical activity level and healthy lifestyle behaviors were moderate. We think that giving education about smoking cessation and individual exercises will improve their physical activity levels and healthy lifestyle behaviors and reduce the respiratory problems they will encounter.

Epidemiological studies have investigated the long-term effects of regular physical activity on the decline of lung function. Studies show that lung function improves as physical activity levels increase (10,11). In addition, regular physical activity in active smokers shows beneficial effects on lung function (12-14). The prevalence of low physical activity is higher in patients with FEV1 <80% (15). In our study, we found that the level of physical activity was low in patients with respiratory distress. From this point of view, we think that it is important to improve physical activity in patients with respiratory distress.

According to a study in the literature; being a man, being 49-60 years old, being married, having a bachelor's degree and above, having a good socio-economic status, being working, having no additional disease, getting education about their illnesses increased healthy lifestyle behaviors and quality of life. Healthy lifestyle behaviors of patients with heart failure were lower than healthy individuals (16). In a study with prostate cancer patients, it was found that healthy lifestyle behaviors of the patients were affected by the treatment of the patient. On the other hand, a moderate positive correlation was found between healthy lifestyle behaviors and quality of life in patients with prostate cancer. It has been mentioned that the increase in the quality of life in patients with healthy lifestyle behaviors is beneficial in coping with the disease and developing positive health behaviors in patients (17). In our study, we found that healthy lifestyle behaviors of patients with respiratory distress were moderate. We think that awareness raising activities, trainings and rehabilitation programs aimed at improving healthy lifestyle behaviors of patients will be beneficial in coping with respiratory distress as well as improving the quality of life.

Knowing the physical activity level and the effects of healthy lifestyle behaviors on the individuals with respiratory failure, revealing the physical activity, anxiety, depression and healthy lifestyle behaviors of the individuals in the health studies conducted for these individuals will increase the awareness on these issues.

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A COMPARISON BETWEEN DIAGNOSIS-RELATED GROUPS AND COMMUNIQUÉ ON HEALTHCARE PRACTICES IN HEALTH FINANCING: A CASE OF CARDIOVASCULAR DISEASES

Zehra Antep[1]

Abstract

The gradual increase in health expenditure each year highlights the importance of cost-controlled inpatient prospective payment systems in health financing in Turkey and around the world. Being in current use in many developed countries, the Diagnosis-related Groups (DRG) model is an effective inpatient prospective payment systemused in healthcare institutions with a high case mix index. The present study aims to determine the efficacy of the DRG inpatient prospective payment system model in the funding of cardiovascular diseases, and to reveal the differences between the CHP-basedand DRG-based pricing models. Findings of the present study reveal that DRG pricing changes while CHP pricing remains constant in terms of certain parameters such as emergency or elective surgery, accompanying diseases, newborn birth weight, and length of stay in cases involving procedures and operations used in the diagnosis and treatment of cardiovascular diseases.

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Keywords:

Diagnosis-related Groups, Financing, Inpatient Prospective Payment Systems

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INTRODUCTION

Health policies have recently become the focus of public policies. Today health expenditure has exceeded government expenditure on education inthe total general government expenditure in developed countries and countries like ours which are undergoing demographic transformation. World Health Organization (WHO) data shows that total expenditure on health as % of Gross Domestic Product (GDP) in Turkey was 2.5 in 1995, 5 in 2000, and 5.4 in 2014. Total expenditure on health as % of GDP in the USA, however, was 13.1 in 1995 and 2000, and 17.1 in 2014 (https://www.who.int/gho/en/)The gradual increase in health expenditure each year highlights the importance of cost-controlled inpatient prospective payment systems (IPPS) in health financing both in Turkey and around the world.

In our country, approximately 20% of more than 350 million casesin private and public hospitals collectively are treated by tertiary referral hospitals, and a great majority of these are complicated cases. The structure, scope, service distribution, transaction volume, and thus transaction cost, of tertiary referral hospitals differ from others, and may also be specialized accordingly. In addition, as a duty, tertiary referral hospitals intrinsically have to continue their teaching and research activities, employ more qualified specialists, and maintain a better technical infrastructure and equipment. This in turn increases the operating costs. Furthermore, since the patients referred to these hospitals are more complicated cases, this affects the diagnosis, treatment and monitoring costs negatively.

Communiqué on Healthcare Practices (CHP) is a communiqué which sets out the terms and conditions to receive the SSI-funded health services for people whose health benefits are funded by the Social Security Institution (SSI), as well as the considerations which are determined by the Health Services Pricing Commission and payable by SSI in relation to the said services (http://www.resmigazete.gov.tr/eskiler/2013/03/20130324-3.pdf). The CHP-based inpatient prospective payment system (IPPS) fails to meet the cost of the cases especially in tertiary referral hospitals. Being in current use in many developed countries, however, the Diagnosis-related Groups (DRG) model is an effective IPPS model used in tertiary referral hospitals with a high case mix index DRGmodel is anIPPS system using certain parameters, in addition to the main diagnosis, such as severity of the disease, demographics of the patients, accompanying diseases, length of stay, and complications during the procedures in pricing the treatment procedures.

According to DRG approach, if we can categorize the patients into groups with similar healthcare needs, we can compare the healthcare given to any patient with the healthcare given to all other patients in the group (i.e. average healthcare). Each patient is unique and each patient has a number of different diagnoses, risk factors, family dynamics, and environments. Variety at the patient level is virtually endless. In order to understand this variety, one needs to classify the cases into groups with similar needs. The main starting point is the main diagnosis. Grouping the patients according to their main diagnoses, followed by subgrouping based on the presence or absence of other conditions, is the most important

classification approach used in DRG model.Even though diagnosis-based classification is carried out in this way, procedures and patient demographics contribute to the determination of the groups as well.Assignment of relative values to each group based on the average cost of these patients falling into the groups determined explains the use of this system as an IPPS method. Each hospital receives a share from the budget depending on the DRG codes itcreates for its inpatients and on the relative values corresponding to these codes.

Diagnosis-related Groups (DRG)

DRG is an inpatient prospective payment system where cases are classified into groups based on clinical and cost data and comparable diseases are put into similar groups (Akdağet al., 2011).DRG was first developed by the researcher Robert Fetter, of the Yale University,and his friends in 1970s, and its main purpose is to identify the hospital products and measure what hospitals actually do. It is a system which essentially aims for patient classification and inpatient prospective payment for hospitals (Ünalet al., 2014). It was first implemented in 1980 in New Jersey. After a 3-year pilot period, it was put into use in 1983 around the world, and particularly in the USA. It is an actively used system in Australia, the USA, Canada, New Zealand, Singapore, Thailand, Malaysia, Korea, Taiwan, China, Costa Rica, Romania, the Czech Republic, Ireland, Hungary, Slovenia, Bulgaria, and many others. Across Europe, it has been adopted by Austria, Belgium, Denmark, the Netherlands, the UK, Finland, France, Germany, Italy, Portugal, Spain, Sweden, Switzerland, and the Wales within the scope of Euro-DRGproject (Quentin et al., 2013).

DRG data input began in Turkey in 2005 – 2006 with 7 pilot hospitals within the scope of Infrastructure Development for Improving and Reforming the Health Services Financing Management Project carried out by Hacettepe University, and the pilot study continued in 2008 with the participation of 48 hospitals by the end of the year and finished in November 2009, also marking the end of the project ("HÜAP Report D.B.3.1", 2006). The Turkish Ministry of Health took initiative in 2009 and created an institutional body within the Ministry to maintain and establish this system, and gave more weight to creating a national DRG system. First, 50 pilot hospitals were included in the DRG system in 2009. In 2010, 260 hospitals became integrated into the system and this number reached 550 by 2011 (Ünal et al., 2014).

Basic Concepts Concerning DRG

DRGclassifies the diseases based on the main diagnosis first, and then on the procedures. It estimates the treatment costs in relative value rather than in monetary value. Basic concepts concerning DRG, namely *main diagnosis, secondary diagnosis, procedures (ACHI), relative value,* and *case mix index (CMI)* are defined in detail below:

Main diagnosis

It is the diagnosis which, upon analysis, constitutes the main reason for inpatient treatment (or admission to the healthcare institution)(Şencan et al., 2013).

Secondary Diagnosis

It is the diagnosis of a condition or complaint accompanying the main diagnosis or manifesting during inpatient stay or outpatient treatment(Şencan et al., 2013).

Procedures (ACHI)

Procedures are an ACHI (Australian Classification of Health Interventions) classification and grouped as surgical, diagnostic and investigative procedures. The surgical procedures as a whole encompass diagnostic procedures, allied health interventions, and dental procedures. ACHI classification is structured by the anatomical site. ACHI coding is a numerical coding system. The first 5 digits represent the general features and the definition of that particular intervention while the remaining 6^{th} and 7^{th} digits provide information about the specific interventions included (Akdağ et al., 2011).

Relative Value

Relative value is the ratio of the average cost of a single DRG to the average cost of all DRGs. Cost data is required in order to calculate the relative value (Akdağ et al., 2011).

$$\text{Relative Value} = \frac{\text{Average Cost of 1(One) DRG}}{\text{Average Cost of All DRGs}}$$

If a DRG's relative value is greater than that of any other DRG, this means that it requires more resources for treatment. In order to create a relative values list, the above calculation should be repeated for each DRG individually. After normalizing the calculated values, the relative values list is created with 1.0 being the limit (values above and below the limit). The 2012 cost analysis performed by the Turkish Ministry of Health estimated the average case cost per relative value to be TL 1,531.56 (Öztürk, 2014). Since the case mix index of the health services created by hospitals vary from month to month, cost per relative value varies each month as well. Thus, the present study takes the cost per relative value as TL 1,500.

Case Mix Index (CMI)

CMI is the ratio enabling us to compare a particular hospital's case production to that of another hospital. It is a value used to measure the complexity (comorbidity) of the diseases treated by a hospital (Kurşun &Yümsel, 2017). Following are the uses of CMI method:

- Measuring the clinical activities,
- Evaluating the inter-hospital performance,
- Financing,
- Intra-hospital management tool,
- A tool to begin quality assessment with,
- Making clinical and financial decisions in the hospital,
- Comparison statistics between physicians and determination of healthcare giver profiles,
- Intra- and inter-hospital healthcare quality comparison,
- Supporting the clinical guidelines, protocols and sustainable quality projects, and
- Creating data and identification standards.

CMI Calculation

The following formula is used for CMI calculation(Kurşun &Yümsel, 2017):

$$\frac{\sum (\textit{DRG Relative Value X Number of Cases})}{\textit{Total Number of Patients for Hospital A}}$$

Therefore, a hospital's having a higher CMI compared to another hospital suggests that it has treated cases with higher relative values (complicated cases).

AIM AND METHOD

The present study aims to find out the quality and efficacy of the DRG inpatient prospective payment system model for cardiovascular diseases, which is an inpatient classification method involving classification of diseases based on clinical and cost data, and to present recommendations based on the results of the evaluations of financial differences between CHP and DRG.

This study analyses the case simulations where cardiovascular disease diagnoses and procedures were performed since these case simulations have a high case mix index. Of the procedures used in diagnosis and treatment of cardiovascular diseases, this study includes case simulations of coronary angiography, coronary artery bypass graft, surgeries for aneurysm and dissection, and congenital heart surgery. The study compares the DRG and CHP pricings for these cases based on certain parameters such as main diagnosis, secondary diagnosis, age, birth weight (if a newborn), personal history of other diseases, type of hospitalization (emergency/elective), and length of stay.

The present study hypothesizes that DRG-based IPPS system involves, based on objective and measurable data,a higher paymentto the hospitals treating complicated cases, a lower payment to the hospitals treating less complicated and more costly cases, and allocating budget to each hospital based on the relative values they create for their inpatients. Based on this hypothesis, the present study is restricted to the field of cardiovascular diseases with a high case mix index.

FINDINGS

This part of the study includes the analyses of case simulations comprising of procedures performed in diagnosis and treatment of the cardiovascular diseases.

Table 1. DRG and CHP Pricing Comparison for Coronary Artery Bypass Graft (CABG) Cases

	Diagnosis	Procedure	Relative Value	DRG Pricing	CHP Pricing
Case 1	Coronary artery disease	Coronary Artery Bypass Graft	5.33	TL 7,995	TL 7,428
Case 2	Coronary artery disease Congestive Heart Failure	Coronary Artery Bypass Graft	7.18	TL 10,770	TL 7,428

As can be seen in Table 1, both cases underwent coronary artery bypass graft, and since Congestive Heart Failure (CHF) accompanying the second case's main diagnosis Coronary Artery Disease would change the episode of care, the pricing (financial cost) of the second case increased by 35%. The DRG-basedIPPS model priced the procedures at TL 7,995 Case 1, whereas the pricing for Case 2 was TL 10,770 because the cost of healthcare would be increased by the changes in length of stay, treatment type, and healthcare services due to CHF, which was the secondary diagnosis. On the other hand, the CHP system priced both procedures at the same amount, i.e. TL 7,428, for both cases.

Table 2. DRG and CHP Pricing Comparison for Coronary Angiography Cases

	Diagnosis	Procedure	Relative Value	DRG Pricing	CHP Pricing
Case 1	Coronary Artery Disease	Coronary Angiography	0.92	TL 1,380	TL 415
Case 2	Myocardial Infarction (MI)Coronary Artery Disease	Coronary Angiography	1.46	TL 2,190	TL 415
Case 3	Coronary Artery DiseaseCongestive Heart Failure	Coronary Angiography	1.7	TL 2,550	TL 415
Case 4	Myocardial Infarction Coronary Artery DiseaseCongestive Heart Failure	Coronary Angiography	2.53	TL 3,795	TL 415

Table 2 shows that all of the four cases underwent Coronary Angiography.The DRG-based IPPS model priced the elective coronary angiography at TL 1,380 for Case 1, the emergency coronary angiography due to MI at TL 2,190 for Case 2, the elective coronary angiography at TL 2,550 for Case 3 since the cost of healthcare increased due to CHF-induced changes in length of stay and healthcare services, and the coronary angiography at TL 3,795 for Case 4 since both the emergency procedure and the secondary diagnosis, CHF, increased the cost of healthcare. On the other hand, the CHP system priced the procedures at the same amount, i.e. TL 415, for all of the four cases.

Table 3. DRG and CHP Pricing Comparison for Aneurysm and Dissection Cases

	Diagnosis	Procedure	Relative Value	DRG Pricing	CHP Pricing
Case 1	Thoracic Aortic Aneurysm	Ascending Aorta Graft+ Replacement of the Aortic Valve	6.55	TL 9,825	TL 14,323
Case 2	Thoracic Aortic Aneurysm, Ruptured	Ascending Aorta Graft+ Replacement of the Aortic Valve	12.57	TL 18,855	TL 14,323
Case 3	Thoracic Aortic Dissection	Ascending Aorta Graft+ Replacement of the Aortic Valve	27.19	TL 40,785	TL 14,323

Table 3 shows that all three cases underwent the same procedure. The DRG-based IPPS model priced the elective surgery for aneurysm atTL 9,825 for Case 1, the emergency surgery for aneurysm due to rupture at TL 18,855 for Case 2, and the emergency and high-risk dissection surgery at TL 14,323 for Case 3. On the other hand, the CHP system, which priced all the procedures at TL 14,323 for all of the three case simulations, did not take the changes in episode of care and healthcare costs into consideration in the pricing process.

Table 4. DRG and CHP Pricing Comparison for Congenital Heart Surgery

	Diagnosis	Procedure	Birth Weight	Relative Value	DRG Cost	CHP Cost
Case 1	Patent Ductus Arteriosus (PDA)	PDA Division	3,000 gr	4.92	TL 7,380	TL 4,747
Case 2	Patent Ductus Arteriosus (PDA)	PDA Division	750 gr	28.61	TL 42.915	TL 4,747

As shown in Table 4, both case simulations underwent PDA ligation. The DRG-basedIPPSmodel priced the PDA ligation at TL 7,380 for the 3,000 gram newborn in Case 1, and the PDA ligation at TL 42,915 for the 750 gram newborn in Case 2 since the low birth weight increased the length of stay, episode of care, and cost of healthcare.

DISCUSSION

Findings of the present study show that DRG-based pricing changes while CHP-based pricing remains constant in terms of certain parameters such as emergency or elective surgery, accompanying diseases, newborn birth weight, and length of stay in cases involving procedures and operations used in the

diagnosis and treatment of cardiovascular diseases. Based on the results of this study, especially the tertiary referral hospitals treating more complicated cases such as cardiovascular diseases and maintaining their teaching hospital status have higher case pricings since they employ more qualified and professional specialists, and have better medical materials and equipment. Therefore, the present study concludes that case pricing process would be more just and fair if the differences between the types of hospitals were taken into consideration in the inpatient prospective payment process.

Just like all the other businesses in the service industry, healthcare institutions meet their costs by selling services and receiving a certain amount of payment in return for these services. Currently, healthcare institutions are refunded for their services based on the amounts determined by CHP pricing. The results of the present study, however, show that the healthcare services provided by healthcare institutions do not meet the costs within the CHP pricing system. It can always be argued that each payment system has its own weaknesses and strengths compared to others. What is important here is to find and implement a system with maximum benefit by properly analyzing these weaknesses and strengths.At this point, the DRGsystem stands out from the other inpatient prospective payment systems. Since some current payment systems do not take the severity and type of disease into consideration, they have caused great losses of right and suffering in terms of inpatient prospective payment. As with any other business, this hinders the proper operation of the healthcare institutions and affect their financial capabilities negatively. The DRG system, on the other hand, bases the case pricing for the patients treated by healthcare institutions and the inpatient prospective payment these institutions will receive on the severity of disease, and it also involves paying different amounts depending on the type of disease. From this perspective, it can be said that the DRG system's most important strength compared to other systems is this fundamental feature.

In conclusion, a DRG-based pricing model creates its pricing schemes upon extensive analysis of the demographic, clinical, and cost data. The present study recommends the use of the DRGinpatient prospective payment system not only as a financial instrument but also as an effective tool in research, planning, process and output evaluation in health services, quality assessment, and institutional and clinical performance assessment to support administrative and clinical decisions.

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INNOVATION IN NURSING AND INNOVATIVE ATTITUDES OF NURSES

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Abstract

In today's world, where scientific studies are increasing and new scientific knowledge is produced almost every day, innovation activities have become extremely important. Adopting, developing and implementing the innovation process and innovative practices will increase the quality of patient care, improve the quality of life and contribute positively to the national economy. As a professional health discipline, it should develop innovative thinking skills in order to keep up with the rapidly changing and developing science in nursing, to manage global competition well, and to benefit from innovative methods especially in health care practices. Compared to other health care professionals, nurses who spend the most time with patients are more likely to recognize inadequacies and deficiencies in patient care and are more likely to develop innovative practices for them. In literature, it is stated that nurses should have creative, equipped, leadership role and risk-taking personality traits in order to produce innovative solutions. In addition, it has been determined that manager support has great importance in the development of innovation culture. It was emphasized that nurses supported and guided by managers were more successful in innovation. Increased workload is one of the leading factors that negatively affect the nurses' innovative attitudes. Although in recent years innovative ideas and innovation studies in Turkey has increased, a limited number of studies were found for the nursing profession. In this review, it is aimed to draw attention to the importance of nursing innovation and nurses' innovative attitudes.

Keywords:
Nursing, Innovation, Innovative Attitudes

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INTRODUCTION

The word, innovation, means ‘’making a change’’ in Latin. According to Turkish Language Association (TLA), innovation is expressed as ‘’yenileşim (renovation)’’. This means that there is still no meaningful translation in Turkish. Today, innovation has become an important factor in handling competitive advantage and modernization (Kartal, 2018;TLA, 2019)

Innovation has social and economic benefits. A promising, useful, high quality and innovative product; occurs at the end of a complex path that demands such difficult and serious education as marketing, international market strategy and innovation (Sengun, 2016).

Nowadays, with the development of medicine; nursing practices and care have become more complex. In order to keep up with the rapidly developing knowledge and scientific era and to manage global competition well, innovation in nursing has become compulsory (Kartal, 2018). In addition, Investments in innovation and R & D activities have been increased as a result of the development of technology and the expectations of individuals receiving health services (Ozbey, 2018). In addition to innovation, it is essential to produce inexpensive, accessible and useful solutions developed with advanced technology and education for health services with limited resources. The growing population is getting older and the number of people with chronic diseases is increasing. Besides, the given care and needs are also changing. Not only the income level and the degree of disease change, but the demands and expectations of health care also change. It is thought that the innovative products and programs to be developed in health services will increase the quality of care and reduce the costs as well as provide socioeconomic contribution to the country (Arslanhan, 2012; Sengun, 2016).

According to Drucker, the factors that drive people and institutions to innovation are:

* Unexpected situations: In routine, situations faced by individuals and groups may differ in sudden and unexpected levels. In such cases, the creative thinking of people comes into play and leads to newness and innovation in order to keep up with these new problems.

* Mismatch between expectation and outcome: If a product, program or service falls below social expectations and is no longer useful, this feature comes into play and directs the individual (s) to innovation and restructuring.

* Process needs: The works carried out in the process of creating innovation and the order and policies applied to these works can lead people to design new products by pushing them to new ideas.

* Demographic changes: Individuals' perceptions, tolerance situations against uncertainties, risk-taking behaviors can lead people to innovation.

* New informations: With the development of technology and science, new products or programs can be developed in line with new needs (Drucker, 2007; Sarioglu, 2014).

INNOVATION IN NURSING

In an article published in 2009, ICN described the innovative nurse as a salaried health professional who produces, develops and markets innovative programs / projects in the field of health care (ICN, 2004). In order for health organizations to act and to be modernized in accordance with the age, it is important to increase the culture of innovation and their innovative development (Yilmaz, 2014). ICN (International Council of Nurses) advocated that nurses should be pioneers in emerging care practices in order to provide qualified services to individuals, families and society. Thus, it stated that innovation and development in nursing is still on the agenda and should be (Herdman, 2009). In a globalizing world, qualified nurses should be educated to meet the deficiencies and needs (Dil, 2012).

Florence Nightingale, the founder of modern nursing, said in the 19th century, "A more livable world; such a world will not be granted us, so let's work without hesitation to create this world. We should change it instead of conforming life.'' Saying that she emphasized the importance of innovation and modernization (Kartal, 2018).

Innovation is extremely important for the improvement of nursing profession and nursing care quality (Herdman, 2009). Determining the needs and searching for the answers in the providing of health care is possible with the strong use of the profession and professionalization. Professional development is sustained by encouraging nurses who follow scientific developments and innovations and perform innovative activities (Arslan, 2012). In addition, nurses should have an innovative culture of thought, risk-taking, and be aware of opportunities and deficiencies (Yilmaz, 2014). In the health sector, innovation is experienced intensively.

In order to be caregivers, decision makers and managers, nurses who are professional in health care, need to develop innovative products and practices and deliver them to society and the health of society (Atasoy, 2014). Because nurses spend more time with patients and healthy individuals compared to other health care professional groups and they are primarily responsible for health care. Innovative ideas, together with holistic care given to patients, have been asked and emerged from nurses. Especially in the 21st Century, There is a significant progress in nurse's development of innovative values and designing innovative products / programs. (Karagozlu, 2008; Merih, 2018).

INNOVATIVE ACHIEVEMENTS OF NURSES

Nurses, in recent years, have made many innovations both in Turkey and worldwide (Merih, 2018). Innovative studies in Turkish nursing were first performed by Perihan Velioğlu, a doyenne of the nursing profession. She has made many innovations from the use of green dressing in the operating rooms to university education. Nurse Ozlem Oktay's 'Stomakit' is the first product developed in nursing (Merih, 2018; Ozbey, 2018).

In our country, there is the Innovative Nursing Association (INA) which supports and guides innovative activities in nursing. Many innovative achievements have been achieved within this association (INA, 2019). Some of the innovative achievements of our country; Meltem Kaya and Nursen Ulke's 'Portlet' (2012), which rescues chemotherapy patients from infusion devices, Uterus Massage Belt (UMKEM) (2015), designed by Ikbal Engin and Meltem Soydan, which can detect uterine atony early, Arzu Erkuc

Hut's medical ampoule opener (2018), Esra Sen's 'Patient Washing System' (2014) and Yeliz Dogan Merih's 'Wearable Serum Hanger' (Merih, 2018; Ozbey, 2018).

In 2009, while Jamie Rutherford was responsible nurse of the renal transplantation unit, she developed a filtration plasma exchange device for dialysis patients, which is accelerating more the dialysis process (Herdman, 2009). Designed and programmed in collaboration with the Boston Medical School and Northeastern University in the United States, the virtual clinical nurse has been very successful in collecting and providing information to patients (Abbott, 2016). Again, In the United States, the academic nurse of Philadelphia Pennsylvania University Assoc. Dr. Martha A. Curley has developed the 'Intensive Care Synergy Model with a donation of $ 15 million and with the support of the American Society of Intensive Care Nurses. This model is being used in many magnet hospitals and school curricula throughout the country (Herdman, 2009). Another non-technological innovative achievement is the Program Orientation Program developed by Chan and colleagues with a multidisciplinary structure (nurse, psychologist, social worker, other support specialists). This 90-minute program facilitates compliance and participation in patients (Herdman, 2009). Ruggiero and colleagues who realized that the return to hospitals increased due to incorrect or incomplete medical treatment of patients after discharge, developed a protocol in 2015 that reduced the use of wrong medication and regulated the medical follow-up of patients after discharge. Thanks to this protocol, they have managed to avoid the problem (Kartal, 2018). A high level of urinary infection can be seen in patients with a permanent catheter, which increases the length of hospital stay. In 2012, Adams and her colleagues developed a protocol called HOUDINI. HOUDINI is named after the initials of health problems such as hemarturia, stenosis, urinary surgery, decubitus ulcer, end-of-life care, and immobility where the catheter is indicated. With this protocol, only cases where the permanent catheter is indicated are identified and thus, the situations in which the urinary catheter is inserted are reduced and the urinary infection problems caused by this condition are prevented (Kartal, 2018). Another problem with the permanent catheter is that the patients get away from people and socially isolate themselves because of this catheter. Ya-Lie Ku and colleagues from Fooyin University in Taiwan, looking for a solution to this problem, have developed a specially designed trouser with legs. The leg area of the trousers can be opened with a zipper and a permanent catheter can be fixed in it. In this way, the permanent catheters of the patients do not appear from the outside and shame is tried to be prevented. At the same time, thanks to the product design, patients cannot raise the catheter above the bladder level. Thus, reflux was prevented (Ku et al, 2017).

FACTORS AFFECTING THE INNOVATIVE ATTITUDES OF NURSES

Nowadays, health care nurses are expected to be intertwined with technology, think critically, identify problems and become leaders. It is necessary for the nurses to recognize the points that are missing or need to be developed in the system for care applications and to approach these points in an innovative way and to develop individual innovation features (Erol, 2018). Yuan and Woodman described individual innovation as the development and implementation of an existing innovation (Yuan, 2010). According to Kilicer; It is defined as an individual should be willing to innovation, adopt and have a

positive perspective towards innovation and be able to use and benefit from it (Kilicer, 2010; Ozpulat, 2018).

In a study conducted by Ozpulat and Karakuzu in 2018 with 200 health workers, the factors affecting the innovative behaviors of hospital employees were examined. According to this study, 30.1% of the participants answered yes to the question 'Is there an innovation in your professional practices?' and this innovation was found to be mostly technological innovations. In the same study, 58.5% of the respondents stated that management support is very important when it is considered that the effective factors in developing the innovative behaviors determined. According to the participants, workload was found to be very important in innovation and innovative thinking (Ozpulat, 2018).

It has been stated that reducing the feeling of burnout in hospitals and other healthcare institutions, directing and supporting managers to innovation, increasing personal development programs, equipping employees with up-to-date information, and providing more innovative activities both within and outside the organization (Derin, 2012). According to a survey conducted by Iscan and Karacabey in 2007 with other occupational groups, increasing workload has been found to reduce innovation support (Iscan, 2007). In Akkoc and colleagues' study, conducted with 426 people in 2011, it was found that the support of a manager is very important in innovation and innovative thinking and gained a significant positivity. According to a study conducted by Sonmez and Yildirim in 2014 with nurses, autonomy was found to be an important factor in innovative thinking and orientation towards innovation. In the same study, other factors affecting the innovative behaviors of nurses were; it has been found that the high quality of education increases individual behaviors in individual factors and the freedom to make individual decisions in professional factors (Yildirim, 2014). When the researches are examined, it is determined that the most important factors affecting innovative attitudes are executive support and increased workload (Derin, 2012; Yildirim, 2014).

There is an opinion in the literature that nurses are successful in diagnosing problems and being creative (Gillmartin, 1999). In a study conducted by Kerler-Baumann on the creativity scale in 2011, it was found that nurses scored higher and were more prone to innovation (Kerler Baumann, 2011).

In order to follow innovations, identify changing or differentiating needs and initiate changes, executive nurses need to have innovative thinking skills, risk taking, perceiving problems, creative and entrepreneurial characteristics (Kalkan, 2010). In a study conducted by Yilmaz and colleagues, in 2014, risk taking and innovative behaviors of executive nurses were studied. According to the results of the research, it is determined that health care managers are innovative and risk-taking individuals; risk taking capacity increased with the age. In a similar study by Dobre and colleagues, a significant relationship was found between innovation and educational level and professional position (Dobre, 2009). According to a study conducted by Basim and Sesen in 2009, nurses' risk taking and innovation levels were also good (Basim, 2009;Yilmaz, 2014). Health care managers, who play a major role in shaping nurses' innovative attitudes, should be innovative and able to take risks. These skills are important in terms of increasing their personal and professional competencies and professional strength (Yilmaz, 2014).

CONCLUSION

Innovation and innovative achievements are the dynamic processes that contribute to increasing the quality of patient care to the national economy. Innovative initiatives to increase productivity and reduce costs in healthcare institutions have increased in recent years. It was found that nurses who spend more time with patients in health sciences are more susceptible to innovation. The adaptation of nurses to the innovation process and their attitudes towards this adaptation is very important for the development of an innovative culture whether their attitudes are motivated or not. In our study, it was emphasized that nurses with an innovation culture should have a risk-taking and entrepreneurial structure.

The increase in the number of individuals receiving health care in recent years, global competition, the development of technology and science and the expectations of patients or individuals who apply to institutions for health services as a result of the increase in hospitals and health institutions paves the way for innovation. It was determined that nurses' innovative attitudes should be supported by managers in order to meet patient needs and increase the quality of care. It was emphasized that nurses supported and guided by managers were more successful in innovation. The lack of executive support and increasing workload are the factors that negatively affect the nurses' innovative attitudes.

As a result, nurses' participation in innovation and their innovative attitudes; is dependent on the features such as; manager's attitude, workload, quality of education and risk taking, entrepreneurship. In order to direct nurses to innovation and to develop their innovative attitudes positively, nurses should be supported in terms of increasing in-association education, reducing the workload, having administrative support and supporting the transformation of the innovative element to commercial products. The rewarding of the products / projects by the managers will be an incentive. In our study, it is recommended that more research can be made on the factors that affect the nurses' innovative attitudes.

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WHY RATIONAL DRUG MANAGEMENT IN AN ELDERLY INDIVIDUAL?

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Abstract

Health requirements of the aging population, the importance of which is increasing with each passing day due to the changing population structure in the world and Turkey, has gained a place as the most important health policy today. In elderliness when several diseases can coexist simultaneously, it is very important to properly select among an increasing number of drugs and to use them in safe dose ranges. In elderly individuals, drug side effects, overutilization of drug, and cognitive problems such as forgetting and comprehension are common. It is therefore difficult to distinguish whether the symptoms observed in an elderly individual are drug side effects or the interaction between drug and disease. Rational drug management in the elderly includes starting treatments at a low dose and increasing the dose slowly, that is "start low, go slow", and continuing with as low dose as possible to avoid unnecessary drug doses. In this context, clinical staff should be able to closely monitor the effects and side effects of drgus administered to elderly individuals, provide the required training to the patient and family, and be able to recognize cognitive changes early.

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Keywords:

Aging, drug, pharmacodynamic and pharmacokinetic effect, rational drug use.

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INTRODUCTION

Today, the world population is getting older in parallel with the factors such as benefiting from the opportunities of modern medicine more, developing economic and sociocultural conditions, and declining birth rate. According to the United Nations Population Fund (UNFPA) 2019 data, it is estimated that the population aged 60 years and older is over 900 million in the world and this number will reach 2.1 billion by 2050. In other words, it is reported that one in very five people in the world will be 60 years old and over in 2050. According to the Turkey 2019 data, the proportion of elderly population is 8.8%, and this rate is expected to increase to 10.8 per cent in 2023 and to 23.8 percent in 2050 (Kutsal,2019; Oztop et al., 2018; Turkish Council on Ageing 2019). These demographic changes in the elderly population affect health systems both socially and financially. In the most general sense, polypharmacy can be defined as the simultaneous use of one or multiple drugs. In terms of clinical significance, the use of 5 or more drugs can be considered as polypharmacy (Oztop et al., 2018; Turgeon et al., 2019). In a study conducted in Europe, it was found that 37.9% of individuals aged over 65 years had 4 or more chronic diseases and 50% of the patients were using 6 or more drugs a day, and one out of every two people were on psychotropic drugs with a high risk of side effects in the elderly (Oztop et al., 2018). In a 2008 study, the risk of developing drug side effects with the use of two drugs is 15% and this rate increases to 58% with the use of five drugs, and up to 82% with the use of seven or more drugs (Masodi, 2008; Yildirim and Kilic, 2017)

The most common used drugs in the elderly are central nervous system (CNS), cardiovascular system and gastrointestinal system drugs. The drugs that frequently cause side effects include those causing CNS depression, antibiotics, analgesics, anticoagulants, antihypertensives, bronchodilators, diuretics and oral hypoglycemics (Bahat et al., 2012; Oztop et al., 2018;). In the meta-analyses, it has been found that hospitalization and mortality rates due to predictable and preventable drug side effects are significantly increased in the elderly than in young adults. Moreover, the incidence of problems such as weight loss, fall, functional and cognitive decline, hip fracture, urinary incontinence has also been shown to increase (Beijer &Blaey, 2002).

PURPOSE

In this review, the importance of safe drug use in elderly individuals and the correct selection of drugs increasing with aging is emphasized.

WHY RATIONAL DRUG MANAGEMENT IN AN ELDERLY INDIVIDUAL?

There are age-related differences in the treatment of each disease or medical problem. Aging is a natural but risky life period that includes various disciplines. The increase in chronic diseases with aging causes excessive drug use. Pharmacokinetic and pharmacodynamic properties of drugs change with age. Therefore, rational drug management in an elderly individual will have a significant place in the preventive health services for elderly population both in the near and far future.

Therefore, the physiological and functional changes in the organism during the aging process should be known first.

What is Aging?

Aging is a physiological process occurring over time at the level of cells, tissues and systems in the organism and comprising irreversible functional and structural alterations (Aslan and Hocaoglu, 2017; Turnheim, 2003). Aging begins with birth and continues by undergoing many changes until the death of each different organism (Aslan and Hocaoglu, 2017). It is not a stable period and shows differences between individuals. During this period, a decline in body functions, a decrease in organ reserves, difficulty in adapting to the environment and stressors, and a period vulnerable to diseases and injuries are experienced (Turnheim, 2003). The changes in the structure and functions of the human body are called biological aging and the changes in the organs are called physiological aging, while the change in lifestyle due to the individual's feeling himself or herself old is called social aging (Akın, 2006; Turnheim, 2003).

Physiological Changes and Disability in Aging

Cardiovascular system

Although aging itself directly affects the cardiovascular system, the occurrence of cardiovascular diseases may vary depending on age-related structural changes, presence of risk factors and concomitant diseases. The most common cardiovascular diseases in the elderly period are hypertension, heart failure, coronary artery diseases, atrial alibrillation, acute myocardial infarction, valve diseases and venous thrombosis. Therefore, the majority of cardiovascular deaths occur in the elderly population (Tiftik et al., 2012). Thickening and calcification of the heart valves, increase in the left ventricular thickness and left atrial size occur. On chest x-ray, the cardiac shadow appears slightly enlarged. The muscle structure undergoes atrophy and the cardiac output decreases due to the reduced volume of blood pumped at each contraction. The amount of adipose tissue around the heart increases and the pumping ability of the heart decreases by 1%. Heart rate and filling volume decrease and a fibrous tissue is formed in the sinoatrial node. The diameters of the lower extremity veins begin to expand and the activity of the baroreceptors decreases. During this period, the probability of arrhythmia increases and the circulation decreases due to the decrease in blood flow to all organs (Dedeli, &Karadakovan, 2011; Karadakovan & Arslan, 2011; Nalbant, 2008; Tiftik et al., 2012). Although the regeneration of the heart muscle and coronary arteries seems possible in the stem cell study, cardiovascular diseases continue to be an important health problem for both young people and the elderly (Nalbant, 2008).

Pulmonary System

Pulmonary functions and vital capacity are reduced in the elderly due to decreased elasticity of lung, increased stiffness of chest wall and weakening of respiratory muscles. Very few changes occur in the bronchioles. The degeneration of the alveolar walls results in a reduction in the surface area for gaseous exchange. Acid base balance is disrupted. Posture change develops as a result of decreased rib cage flexibility. Alveolar membrane thickens, the cilia movements slow down and cough reflex decreases. The respiratory center slows down and the peripheral perfusion decreases. Oxygen saturation and

respond to hypoxia are reduced. The efficiency of the respiratory system lowers and chest breathing is replaced by diaphragmatic breathing. While expiratory flow rate decreases, residual lung volume increases (Pehlivan and Karadakovan, 2012, Yildirim et al., 2013).

Neurological System

Brain weight and blood flow decrease with normal aging process. Nervous loss occurs in the Central Nervous System. As the blood circulation decreases, neuronal loss is more common in certain parts of the brain, while some parts are preserved. Sympathetic and parasympathetic system function losses. Concomitant reduction in various neurotransmitters and dendritic connections. Loss of sensitivity occurs in receptors. In addition to dementia, there is no decrease in cognitive functions despite the loss of advanced neurons in many regions. Many neurofunctional abilities decrease with age. A decrease in intellectual capacity is observed. Although within normal limits, most of the functions related to learning and memory may decelerate. With the delay of reflexes, the patient cannot protect himself against traumas, and intracranial hemorrhage is more common in motor vehicle accidents and other traumas. As mental disorders can be seen as agitation and laterji without trauma, caregivers can easily bypass the trauma (Pehlivan and Karadakovan, 2012; Ozkayar and Ariogul, 2007).

Musculo-Skeletal System

Aging decreases muscle mass and strength. Bone mineral loss increases and joint mobility decreases. As the body fat mass increases, the spine becomes round. In the musculo-skeletal system with aging; osteoporosis, osteoarthritis, degenerative joint diseases, rheumatoid arthritis, pelvic fractures and falls fractures. Studies have shown that the most common osteoporosis, lumbar, knee and cervical region degenerative diseases are seen (Pehlivan and Karadakovan, 2012). The muscle mass and strength are reduced. Decrease in muscle mass makes it difficult to perform daily activities and lowers the level of physical activity. Bone density and mineral losses occur in women between the ages of 30-35 and in men between the ages of 50-55 and 0.75-1%. The number and size of muscle fibers are reduced. An increase in the amount of intercellular fat is observed in muscle fibers. After 30 years, muscle strength decreases by 10-15% every 10 years and accelerates after 50 years. Therefore, the bones weaken and break easily. Degeneration of the intervertebral discs and calcification of cartilage and ligaments occur. Loss of elasticity in the joint and deterioration of cartilage occurs. Elderly, both in the posture and walking problems are experienced balance (Karadakovan and Arslan, 2011; Nalbant, 2008; Tiftik et all., 2012).

Digestive System

With aging, tooth loss is experienced and the sensitivity of taste and smell receptors is reduced. Absorption in the digestive system slows down and blood flow to the liver decreases. Chewing power is reduced, all secretions and enzymes are reduced. Pancreatic response decreases and sphincter tone decreases and metabolism slows down. Approximately 40% of healthy elderly patients complain of dry mouth. Basal salivary secretion probably decreases with age. Stimulated salivation is unchanged. Fecal incontinence can be seen due to loss of control of the anal sphincter. Elderly individuals due to changes in the digestive system; problems such as loss of appetite, indigestion, diarrhea, constipation, cachexia and obesity can also be seen. Appearance of foods should be made attractive, meals should be presented frequently and gradually, balanced and adequate nutrition should be provided. Since the inability to taste can cause excessive salt and sugar use, the family should be warned and controls should be performed.

Decreased sensitivity at the receiving nerve endings negatively affects appetite. If the use of prosthetics is added to this, nutritional problems may arise. In order to solve this problem, it is necessary to cooperate with the elderly and their families to prepare their favorite foods and to learn about their hot or cold eating habits and to consume foods that contain fiber, vitamins and minerals and prevent constipation. (Karadakovan and Arslan, 2011; Nalbant, 2008; Tiftik et all., 2011, Yildirim et all., 2012).

Physiological Changes That May Affect Drug Pharmacology In The Elderly

Pharmacokinetic Effect in the Elderly

Cognitive problems such as drug side effects, intoxications, drug-drug interaction, excessive drug use, forgetting and comprehension are common in elderly individuals. Polypharmacy causes drug side effects, drug interactions, nonadherence to treatment, increase in cost, hip fracture, weight loss, fall, cognitive impairment, prolonged length of hospital stay and death. Therefore, it is very difficult to distinguish whether the symptoms observed in the elderly are drug side effects or the interaction between drug and disease (Guc, 1997; Gulhan, 2013). Side effect refers to a possible expected event, while adverse effect refers to unexpected events (Yesil et al, 2012). Drug pharmacokinetic and pharmacodynamic change as a result of systemic and functional transformations in aging.

In the elderly period, the absorption of drugs, their distribution in the body, metabolism, excretion and response to drugs, which are pharmacokinetic properties, vary as a result of changes at the receptor level (Guc, 1997).

1-Absorption: Salivary secretion is reduced, which may affect the dissolution of drugs. With aging, the secretion of hydrochloric acid in the stomach is reduced. Although changes such as decrease in pepsin, pancreatic lipase and trypsin secretion, splanchnic blood flow and gastric motility occur, no significant change occurs in the absorption of drugs. Absorption may be affected due to the simultaneous use of multiple drugs. For example, congestive heart failure, one of the most common diseases in the age group of 65 and over, affects the absorption negatively by decreasing the splanchnic blood flow. However, active transport of vitamin B12, iron and calcium decreases, while the absorption of levodopa may increase as a result of decreased dopa decarboxylase enzyme activity in the gastric mucosa. As a general rule, it is stated that the amount of absorption does not change but the rate of absorption slows down. On the other hand, changes in nutritional habits in the elderly people and drugs used (such as antacids, anticholinergics, some herbal products) may change the rate of absorption (Aslan et al., 2017; Erenmeyenoglu, 2006)

2-Distribution: In aging, water and lean body mass decreases, while body fat percentage increases. This increases the plasma concentrations of water-soluble drugs such as gentamicin, digoxin, theophylline, lithium, ethanol. If this process cannot be compensated by excretion from the kidneys, it poses a risk especially for drugs with a narrow therapeutic index and leads to drug toxicity. Moreover, loading doses of drugs such as digoxin should therefore be reduced. Since the baroreceptor sensitivity decreases with the amount of body water in the elderly, orthostatic hypotension may develop as a result of using diuretic and vasodilator drugs. The distribution of water-soluble substances such as vitamin B is low. (Aydos, 2011; Erenmemisoglu,2006; Ozer & Ozdemir, 2009). Albumin is a plasma protein that is actively

involved in the transport of drugs. In the elderly, the levels of albumin decrease and free (unbound) forms of drugs increase due to liver dysfunctions and malnutrition. The dose of free drug in circulation creates drug side effects and toxicity. When warfarin, sodium and oral hypoglycemic drugs, the drugs that bind to protein with albumin decrease, are used in combination, severe bleeding and hypoglycemia may develop, which are the side effects of the drugs (Ozer and Ozdemir, 2009).

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3-Metabolism (Biotransformation): With aging, a decrease in liver mass, a 12-40% decrease in liver blood flow and a decrease in enzyme activity occur. The liver is an organ that has high blood flow due to its vital functions, where the toxic substances and drugs in the organism are metabolized and made harmless. As the age progresses, the removal of toxic substances consequently decreases. In the elderly group, with the change in liver, a slowing in the elimination and metabolism of drugs such as barbiturates, warfarin sodium, diazepam, an increase in the plasma levels, and an increase in the incidence of side effects are observed (Erenmemişoğlu, 2006; Ozer and Ozdemir, 2009). The synthesis of vitamin K-dependent coagulation factors decreases and the sensitivity to anticoagulant drugs increases. Therefore, hemorrhage due to degenerative vascular diseases and anticoagulant therapy, may occur in elderly people (Ozer and Ozdemir, 2009).

4-Excretion The most important clinical factor that changes the drug's effect in the aging process is the kidneys. Renal blood flow may decrease by 30-40% (1% per year after age 50). With advanced age, nephron loss occurs and kidney mass decreases. Along with nephron loss, glomerular filtration rate and tubular secretion decrease up to 50%. Therefore, the elimination of water-soluble antibiotics, aminoglycosides, diuretics, digoxin, and lithium slows down, their half-lives prolong and the risk of toxicity increases. Creatininclirence should be taken into consideration in the calculation of drug dose in the elderly (Erenmemişoğlu, 2006; Özer & Ozdemir, 2009).

5-Receptor sensitivity: It is the change in receptor number, change in receptor affinity, change in secondary messenger function, change in cellular response. In elderly people, sensitivity to drugs affecting the central nervous system has also increased. Therefore, drugs with sedative effect (eg diazepam) should be used in low doses in the elderly group. In addition, an increase in the undesired adverse effects of anticholinergic drugs such as confusion is seen with the decrease in cholinergic neurons and receptors in the elderly (Gelal, 2006; Kaya et al., 2017; Ozer and Ozdemir, 2009).

Pharmacodynamic Effect in Elderly Individuals

Although pharmacokinetic changes are easily recognizable in the elderly, pharmacodynamic changes are more difficult to detect (Kaya et al., 2018) Pharmacodynamics is classically defined as 'dealing with what drugs do on the human body and how they do it'. More generally, pharmacodynamics is a branch of pharmacology that deals with the effects of drugs on physiological, biochemical and pathological events in humans and can be defined as the effect of drugs on the body. (Gelal, 2006; Kaya et al., 2018) Even if the drug level in the target tissue is the same, the effects of drugs may be increased or decreased in old age. Changes in tissue receptor sensitivity and/or homeostatic control mechanisms as a result of aging may change the effects of drugs (Gülhan, 2013). .Pharmacodynamic changes are primarily seen in drugs affecting the cardiovascular system and central nervous system. Drugs with aging-dependent increased sensitivity (warfarin, diazepam, morphine, etc.) should be chosen carefully as they can cause significant side effects. In cases where receptor sensitivity is decreased, higher doses of the drug may be needed for the drug to show its efficacy (Gelal, 2006). At the same time, in elderly individuals, some drugs produce different responses than expected, and sensitivity to drugs develops. For example, there is a decrease in sensitivity to beta receptors in the cardiovascular and respiratory system in the elderly, whereas there is a sensitivity increase to sedative-hypnotics, benzodiazepines, analgesics, opioids and neuroleptics in the central nervous system. Especially benzodiazepines, even at low doses, can cause significant sedation. Side effects of neuroleptics such as delirium, extra-pyramidal side effects, arrhythmia and postural hypotension are more common in the elderly. It has been found that anticholinergic side effects of tricyclic antidepressants, antihistamines, and antispasmodics such as dryness of the mouth, visual impairment, constipation, urinary retention, delirium are increased. While there may be severe hypotension at the beginning of the treatment with angiotensin converting enzyme inhibitors, long-term antihypertensive efficacy may not be successful. Decrease of the synthesis of vitamin K-dependent coagulation factors may also lead to increased sensitivity to warfarin and risk of hemorrhage. Therefore, it should be used at a lower dose (Gülhan, 2013).

Basic Rules For Rational Drug Use In The Old Age

In 1985, the World Health Organization (WHO) defined rational drug use as "getting the most appropriate drug according to the clinical findings and individual characteristics of the patients, in the most appropriate doses that meet their individual needs, at a reasonable time, at the lowest cost for themselves and the community, and their easy access". When deciding the patient's treatment plan, targeted drug options should be evaluated in terms of effectiveness, safety, suitability, and cost (WHO, 1985; Gülhan, 2013; Kaya et al., 2018). When treating the elderly patients safely, using appropriate and reliable dosages of drugs is essential in terms of Rational Drug Management. Apart from the pharmacokinetic and pharmacodynamic changes caused by aging, the most common problems encountered in this group of patients are multiple drug use, namely polypharmacy, drug overdose, drug-drug interactions and difficulty in compliance and continuation of treatment (Gülhan, 2013; Gökçe, 2006; Kaya et al., 2018). Polypharmacy in the elderly increases the incidence of side effects of drugs, leads to the deterioration of compliance due to use, causes a decrease in quality of life and an increase in cost. In

the studies carried out in order to determine the drug-related financial burden, drug expenditures have an important place in the general health expenses of the countries (Top & Tarcan, 2004; Ozer & Ozdemir, 2009).In the UK, although the elderly population aged 60 years and over constitutes only 1/5 of the total population, it is observed that 59% of the prescribed drugs are used by this population, and 20% of those over 70 years of age use 5 or more drugs (Milton, 2008). In randomized controlled studies with elderly individuals, generally, diseases such as hypertension and osteoporosis are focused on. However, there are more than one disease and drugs used that can interact with each other in the elderly. In the United States between 2002 and 2011, efficacy and safety data for the elderly patient group have been found to be sufficient in only 74 of the 214 drugs that can be used by the elderly patient group (Gülhan, 2013).

When the elderly people live holistically, physicians, nurses, pharmacists and all health workers have important roles and responsibilities in drug management. Especially doctors and nurses have ethical and legal responsibilities in drug administration. Elderly and his family need information and help to use therapeutic drugs safely and effectively. and notes. For elderly individuals with swallowing difficulties, solid form tablets should be used instead of liquid form or powder form. Rational drug management of the elderly; start-up and slow increase of treatment (startlow, goslow) ", continue as low as possible and avoid unnecessary use (Turkey aging workshop, 2015; Güç, 1997)Tablets can be crushed or liquid and so on. It should be questioned whether mixing with food makes any change in the effectiveness of the drug. The nurse should assess not only the disability and needs of the elderly individual, but also the resources and self-management strategy (Kaya et all., 2018; Pehlivan & Karadakovan, 2012; Ozer and Ozdemir, 2009).

Elderly people with visual problems should be informed about how to prepare and take their medicines in an illuminated environment. Medicine boxes and boxes of these elderly people should be written and labeled with big and colored pencils according to the requirement. Elderly individuals and their relatives should be informed about the storage of the drugs in suitable environments in terms of heat, light and humidity. Problems caused by drug use other than prescribed drugs should be explained to the elderly individual and family (Ozer and Ozdemir, 2009).

Basic Principles of Drug Use in Elderly

1. When offering medication to the elderly patient, treatment should be individualized; o the most appropriate drug should be selected for the patient.
2. A diagnosis must be made before starting treatment; medication should not be recommended only for signs of disease.
3. Medical problems should be treated without medication as much as possible.
4. Other doctors should be asked if they have prescribed medication.
5. The drug should be started at the lowest possible dose.
6. If necessary, the dose of the drug should be increased in a controlled manner.
7. Sedation, sedative drugs should be recommended and used with caution as they may affect the person's daily activities.

8. Dose adjustment should be done carefully.
9. Drugs that may have side effects should be used and discontinued as soon as possible.
10. Drugs should be started after laboratory tests such as blood-urine examinations are necessary.
11. Drug treatment should be simplified.
12. In order to increase the patient's compliance with the treatment schedule, the usage schedule should be prepared and the medicine boxes should be clearly labeled.
13. Treatment should be reviewed regularly and unnecessary drugs should be removed
14. The treatment plan should be simplified as much as possible. (İskit, 2006; Ministry of elderly health diagnosis and treatment guide, 2010).

Considerations For The Elderly

1. The drug should not be taken immediately for each symptom or complaint.
2. He should bring all medicines used on his way to the hospital.
3. Always show your medication to your doctor.
4. Tell your doctor if you are smoking, drinking alcohol or drinking caffeinated beverages.
5. Use less medication as far as possible.
6. Take your medicine at the dose recommended by your doctor and try to comply with the treatment schedule.
7. If you have any problems or questions, always ask your doctor.
8. Always tell your doctor about any side effects related to the medications you use.
9. Tell your doctor if you have any difficulty using medication (for example, difficulty opening the lid of the medicine boxes, difficulty swallowing the drug, mixing tablets of the same color).
10. Make a mark on your calendar to remember details about drug use.
11. If you are going to use substances that are defined as if medicinal plants arasında among the people, be careful and think with your doctor that you may affect your current diseases or the dosage and efficacy of the drugs you are presently using. (Kutsal, 2019, İskit,2006; Ministry of elderly health diagnosis and treatment guide, 2010).

CONCLUSION AND SUGGESTION

As a result; the problems related to drug use in the elderly cause an increase in mortality and morbidity. It should be kept in mind that aging has its own characteristics and that every medical condition and application has important differences with respect to the elderly. The most important responsibility of the health care team and the nurse regarding drug treatments is that they have knowledge about pharmacodynamic and pharmacokinetic changes that develop with aging. In this period in which several chains of disease are seen together, every disability of the patient should be considered and the elderly

individual should be evaluated as a whole. Rational drug management of the elderly; start-up and slow increase of treatment (startlow, goslow) ", continue as low as possible, prevent unnecessary drug use. In this context, the nurse should monitor the effects and side effects of the drugs, provide education to the patient and the family, and closely monitor the mental state of the patient for cognitive changes.

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