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Review

Anesthesia Management in transvaginal ultrasound guided oocyte retrieval procedure: A mini review

Transvajinal ultrason eşliğinde oosit toplama işleminde anestezi yönetimi: Mini derleme

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ABSTRACT

Anesthesia/analgesia management in oocyte retrieval procedures plays a pivotal role in ensuring patient comfort, safety, and procedural success in in vitro fertilization treatment. This mini review addresses pre-/periprocedural considerations, choice of anesthesia techniques and anesthetic drugs to provide adequate pain relief and comfort tailored to individual patient needs, through conscious sedation, regional anesthesia, or general anesthesia in patients scheduled for transvaginal ultrasound guided oocyte retrieval. Clinicians must consider patient comorbidities, medication history, and procedural requirements when selecting anesthesia techniques.

Keywords: oocyte retrieval; anesthesia; analgesia; sedation; in vitro fertilization

ÖZ

Oosit toplama işlemlerinde anestezi/analjezi yönetimi, in vitro fertilizasyon tedavisinde hasta konforunun, güvenliğinin ve prosedürel başarının sağlanmasında çok önemli bir rol oynamaktadır. Bu mini derleme, transvajinal ultrason eşliğinde oosit toplanması planlanan hastalarda bilinçli sedasyon, rejyonal anestezi veya genel anestezi yoluyla bireysel hasta ihtiyaçlarına göre yeterli analjezi ve konfor sağlamak için işlem öncesi/işlem sırasındaki hususları, anestezi tekniklerinin ve anestezik ilaçların seçimini ele almaktadır. Klinisyenler anestezi tekniklerini seçerken hastanın komorbiditelerini, ilaç kullanımlarını ve prosedürel gereklilikleri göz önünde bulundurmalıdır.

Anahtar Kelimeler: oosit toplama; anestezi; analjezi; sedasyon; in vitro fertilizasyon

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Introduction

In recent years, reduced maternal morbidity and mortality have resulted in a paradigm shift toward addressing infertility as a new challenge. In vitro fertilization (IVF) has emerged as a promising treatment option that requires ovarian stimulation, transvaginal ultrasound-guided oocyte retrieval (TUGOR) procedure, laboratory fertilization, and embryo transfer [1]. Retrieving oocytes from the ovary via the transvaginal route is a vital and pivotal process in IVF treatment, offering a more conservative and expeditious option than laparoscopic retrieval [2]. Although this procedure offers numerous advantages, it has challenging issues, including pain relief, patient comorbidities, and anxiety during oocyte retrieval procedures, which are exacerbated by hormonal manipulations that are necessary for the procedure [3].

As a result, anesthesia technique plays a crucial role in ensuring patient comfort, safety, and effective procedural outcomes. The severity of pain and level of comfort experienced by the patient are linked to the quantity of follicles that need to be collected and the duration of the procedure [4]. A shorter technique would have less impact on the quality of the oocytes and embryos [5]. To prevent medication accumulation in the follicular fluid, anesthetic approaches for oocyte retrieval should utilize agents with rapid onset and recovery features, which are typically performed on day case basis [4].

Pre/peri-procedural Considerations

Regardless of the anesthetic technique used, routine preoperative examinations should be performed. The cause of subfertility can alter anesthetic management. For example, a high body mass index is a common cause of subfertility, and obese patients may have an increased risk of regurgitation, difficult airway, increased opioid sensitivity, and frequent desaturation during the procedure [6]. Before initiating IVF therapy, it is important to address any existing conditions, such as anemia, any infections, or hypo/hyperthyroidism, and seek medical consultation. Additionally, severe endometriosis can cause persistent pelvic pain, requiring more effective pain management strategies [7].

Anesthesia techniques for transvaginal ultrasound guided oocyte retrieval (TUGOR)

Anesthetic choices include sedation under monitored anesthesia care (MAC), general anesthesia, and regional/local anesthesia. Effective pain relief is necessary for the immobilization and prevention of vascular puncture as well as for patient comfort. The most suitable approach should be customized to meet the preferences of both patients and clinicians. In the most recent Cochrane Review, Kwan et al., examined 24 randomized controlled trials (RCT) involving 3160 patients in five comparisons, no particular method or technique was found to be superior in providing effective conscious sedation and analgesia for pain management during and after TUGOR. However, the combined use of sedation and analgesia, including opioids, along with supplementary approaches such as paracervical block (PCB) or acupuncture, resulted in superior pain relief compared with using any single approach alone [8].

Monitored Anesthesia Care and Moderate Sedation

Monitored anesthesia care is a type of anesthesia provided by an experienced anesthesia provider during diagnostic or therapeutic treatment. In moderate sedation, a qualified physician guides or primarily administers sedative and/or analgesic drugs to ensure that the patient responds intentionally to verbal commands, either alone or with gentle tactile stimulation [9]. Various approaches for MAC and moderate sedation combined with analgesia used for TUGOR appear to result in improved pain relief compared to using a single modality alone [8]. Monitored anesthesia care and moderate sedation are generally simple to administer, and medications are well-tolerated and ideally suited for ambulatory settings. The challenge lies in anticipating periods of increased surgical stimulation to adjust drug doses while maintaining spontaneous ventilation [7]. The use of entropy monitors can significantly reduce the amount of anesthetics used and the need for postoperative analgesia for TUGOR [10]. Target-controlled infusion (TCI) is a widely used system designed to maintain a specific target plasma drug concentration through the application of standard pharmacokinetic equations. The TCI has been employed during TUGOR becoming a commonly utilized method in contemporary practice [11-13]. Coskun et al. demonstrated that TCI of remifentanil at 1.5 or 2 ng/mL could provide early recovery [11]. The optimal approach should be tailored to the specific needs of patients, anesthesia providers, and available resources.

General Anesthesia

Most anesthetics used in general anesthesia are found in follicular fluid, and volatile halogenated agents and nitrous oxide interfere with reproductive physiology in vitro [14]. However, according to a few studies, it may be a safer option for anesthesiologists to maintain the airway and prevent movement [4, 15]. As the uterus becomes more relaxed after general anesthesia, the clinician can more easily aspirate a large number of ovarian follicles, unlike during moderate sedation, when ovarian extraction may be hampered by a constricted myometrium [4]. General anesthesia may be recommended for highly anxious patients or in scenarios where an extended procedure duration is expected, particularly for the retrieval of a substantial number of oocytes. A laryngeal mask airway or mask anesthesia may generally be preferred in such situations. Various techniques for the maintenance of anesthesia,

including volatile anesthetics and total intravenous anesthesia, may be utilized and supplemented with opioids for pain relief. However, in women with active gastroesophageal reflux disease, securing the airway through endotracheal intubation, which is facilitated by the administration of muscle relaxants, is necessary [6]. Despite the benefits of general anesthesia, it is crucial to recognize its drawbacks, including prolonged recovery time and a higher risk of postoperative nausea and vomiting, which may delay the patient's discharge [15]. In addition, to prevent potential harm of general anesthesia medications, the duration of general anesthesia should be minimized [16].

Regional/Local Anesthesia

• Paracervical and preovarian blocks

Preovarian and paracervical blocks provide local anesthesia around the vaginal cervix and fornicular areas. Thus, pain during needle insertion and even the postoperative period is minimized. These blocks are frequently used with conscious sedation [8]. However, the optimal medication or technique combination remains controversial. According to Gunaydin et al.'s study comparing remifentanil infusion alone with remifentanil infusion plus PCB resulted in higher plasma remifentanil concentrations without PCB [17]. In a previous similar study, the addition of PCB to IV remifentanil infusion demonstrated superior pain relief and diminished the incidence of nausea compared with IV remifentanil infusion alone [18]. Patients should be informed that using these techniques neither increases nor decreases the pregnancy success rate.

• Neuraxial blocks

Neuraxial blocks, either spinal or epidural, should encompass at least the upper section of the vaginal wall and pelvic viscera [19]. Spinal anesthesia provides excellent surgical conditions by inducing sensory and motor blocks. A Cochrane review showed higher pregnancy rates in spinal anesthesia than in conscious sedation with PCB [8]. A study comparing spinal anesthesia and general anesthesia found higher pregnancy rates in the spinal anesthesia group [20]. Administering a segmental block with epidural anesthesia, blocking the lower abdominal region while sparing the lower extremities, enables the patient to maintain comfort and analgesia while retaining the ability to move the lower extremities and walk [19]. The advantages of neuraxial block, including limited systemic absorption and minimal impact on oocytes, must be considered alongside potential adverse effects such as headache, back pain, urinary retention, hypotension, epidural/spinal hematoma, abscess, or nerve injury [5]. Spinal and epidural anesthesia may be advantageous when general anesthesia is avoided, in patients with morbid obesity, moderate-to-severe obstructive sleep apnea, gastroesophageal reflux disease, or inadequate fasting time.

Acupuncture

Acupuncture activates the body's endogenous opioid system, which can result in an increase in β-endorphin levels. This can provide antidepressant, anxiolytic, and sympatho-inhibitory effects, and it has been used in combination with various conscious sedation techniques and paracervical/preovarian block to enhance pain relief during TUGOR [8]. Compared to sedation, patients in the electroacupuncture group tolerated procedures well. However, higher pain scores were reported in this group [21]. In Gejervall et al.'s randomized study including 160 women, electroacupuncture could not be routinely recommended, but it may be a viable non-pharmacological option for women seeking alternative methods [22].

Anesthetic Agents for Transvaginal Ultrasound Guided Oocyte Retrieval

Propofol, thiopentone, etomidate

Propofol displayed no detrimental effects on oocyte and embryo quality, fertilization, pregnancy, and live birth rates, making it an adequate anesthetic for oocyte retrieval with quick onset and recovery compared to thiopentone [23, 24]. Although one RCT showed no substantial differences in fertilization rates between high- and low-dose propofol, the clinical pregnancy rate in the high-dose group was significantly lower [16, 25].

Etomidate, at a dose of 0.25 mg/kg, has been reported to impair ovarian endocrine function within 10 minutes of administration and, thus it is not recommended for oocyte retrieval procedures [26].

Opioids

Analgesia can be provided for oocyte retrieval using morphine, meperidine, fentanyl, remifentanil, and alfentanil. Even at high doses, none of these compounds demonstrated toxicity or negative effects on oocyte retrieval. In recent years, remifentanil has shown great promise because of its short half-life and rapid onset of action [11, 17]. In a retrospective cohort study involving 2127 oocyte retrieval procedures, intramuscular administration of alfentanil achieved the lowest pain scores, followed by intravenous fentanyl and non-sedative oral analgesics [27].

Benzodiazepines

Benzodiazepines have sedative, anxiolytic, and amnesic effects. Midazolam is the most widely used benzodiazepine for TUGOR. A trace amount of benzodiazepine was detected in the follicular fluid sample, but no harmful consequences were observed [28]. Their synergistic effect with opioids enables the use of reduced doses of both drugs. However, the risk of apnea and respiratory depression may increase with co-administration of opioids and benzodiazepines. Physicians must recognize the potential risk of depression in the

respiratory center, which may result in respiratory depression or arrest, especially after the painful stimulus has ceased [29]. Women with high levels of anxiety, low perceived control, or negative prior gynecological encounters tended to report higher pain scores [30]. Therefore, the administration of an anxiolytic to relieve pain during oocyte retrieval can lower the required analgesic dose.

Dexmedetomidine

The presence of any drugs in the cumulus cells of the ovary might have a critical effect on oocyte maturation and fertilization by releasing and/or mediating signals to oocytes when used during TUGOR. There has been an experimental study demonstrating the dexmedetomidine's less apoptotic effects in terms of caspase-3 activity in oocyte cumulus cells than that of propofol in a rat ovulation induction model [31].

Therefore, dexmedetomidine, a highly selective α-2 adrenoreceptor agonist, having dose-dependent sedative, hypnotic, analgesic, and sympathetic-blocking properties and lacking respiratory inhibiting effects have been also used with propofol and midazolam for TUGOR [32, 33].

Nitrous Oxide

Nitrous oxide impairs methionine synthetase, which in turn limits the amount of thymidine available for DNA synthesis in dividing cells such as embryos and oocytes [34]. However, during oocyte retrieval, oocytes are not exposed to N2O for a prolonged duration because of their low solubility and slow deactivation of methionine in the liver. Some studies have demonstrated that nitrous oxide increases the success rate of IVF by lowering the concentration of other potentially harmful and less diffusible anesthetic drugs [35]. However, the introduction of propofol and remifentanil in subsequent years, known for their patient- and embryo-friendly profiles, has reduced the appeal of nitrous oxide. Hence, the effects of N2O on IVF outcomes remain unclear.

Volatile halogenated agents

The use of volatile halogenated compounds has been demonstrated to hinder DNA synthesis and mitosis in cell cultures, leading to the absence of proper cytoplasmic separation during mitosis and a subsequent increase in irregular mitotic figures [36]. Deleterious effects (embryo development, blastocyte formation, genotoxic effects, and low pregnancy and delivery rates) of halogenated fluorocarbons on IVF outcomes have been demonstrated by most studies, despite the use of volatile anesthetics for both general anesthesia and MAC [4]. Isoflurane, in particular, has been found to have adverse effects on in vitro embryonic development [37]. Sevoflurane has been linked to the induction of genotoxic effects in ovarian cells, although its influence on reproductive outcomes remains undetermined [38]. Additionally, these volatile agents may influence IVF outcomes by elevating prolactin levels, which are associated with impaired oocyte development and uterine receptivity [39].

Side Effects, Complications, and Postoperative Management

Ovarian hyperstimulation syndrome

Ovarian hyperstimulation syndrome (OHSS) is a condition characterized by an excessive response that results in enlargement of ovarian cysts, abdominal distention, and fluid shifting from the intravascular space to the peritoneum. This can lead to the development of ascites, pericardial and pleural effusions, and generalized edema. Some complications associated with OHSS include thromboembolism, adnexial torsion, lobar pneumonia, acute respiratory distress syndrome, and pulmonary embolism [40]. The incidence is 0.2-2% per cycle [41]. The OHSS is an important complication of IVF because of its hemodynamic effects. Upon diagnosis, prioritizing the treatment of OHSS is advisable, as elevated intra-abdominal pressure and loss of intravascular volume can alter the hemodynamic response to anesthesia.

Fever may be attributed to ovarian stimulation, which is commonly observed in IVF patients. It typically resolves with acetaminophen. However, if the temperature remains persistently high after the procedure, the patient may require hospitalization for further examination and treatment.

Postoperative Pain

Postoperative pain, if present, can typically be alleviated with simple analgesics such as acetaminophen or nonsteroidal anti-inflammatory drugs. However, opioid use may be necessary for severe pain. Pain may become more pronounced if the procedure is prolonged or if more than six eggs are retrieved. Women with previous negative experiences or longer procedures should be considered at a high risk of perioperative pain [30]. Despite the lack of agreement on the ideal scale for measuring pain, the majority of RCTs have used the visual analogue scale. [42]. Patients receiving diclofenac sodium had significantly reduced pain scores before discharge, which did not compromise the treatment outcomes [43]. However, if the pain persists and the patient develops rebound tenderness, clinicians should suspect major organ or tissue damage, or rupture.

Postoperative Nausea and Vomiting

The use of volatile anesthetics, opioids, and ovarian manipulation leads to peritoneal irritation and contributes to nausea and/or vomiting. After documenting a 34.6% incidence of nausea in the first observational study using remifentanil infusion plus PCB, the 2nd comparative study demonstrated that combined approach reduced the likelihood of nausea and vomiting (42% versus 20% in remifentanil infusion alone versus remifentanil infusion plus PCB, respectively) [18, 44]. The

reason for the higher incidence of nausea and vomiting was explained in a further study comparing plasma remifentanil concentrations of the groups (remifentanil infusion alone versus remifentanil infusion plus PCB) which was significantly higher in the remifentanil infusion group alone with respect to the remifentanil infusion plus PCB (3.1 ng/mL versus 2.6 ng/mL) (17). In order to prevent nausea and vomiting, antiemetic medications such as ondansetron, cyclizine, and metoclopramide are typically used, and in some cases, rescue therapy may be required during the recovery.

Conclusion

The anesthetist's goal is to provide adequate pain relief and comfort tailored to individual patient needs through conscious sedation, regional anesthesia, or general anesthesia in patients scheduled for TUGOR. Despite increase in the ongoing research on the impact of anesthetics on IVF outcomes, further investigations with standard methodologies are required. Clinicians must consider patient comorbidities, medication history, and procedural requirements when selecting anesthesia techniques. Furthermore, anesthesia duration should be fair enough to avoid the anesthesia related risks for best IVF outcome.

Conflict of Interest statement

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