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Research Article

Investigating the Role of Dexmedetomidine and Propofol on Fertility Rate in IVF Candidate Patients

Faranak Behnaz[1]*, Atiyeh Tizghadam[2], Gholamreza Mohseni[2], Leila Nazari[3]

[1]*Department of Anesthesiology, Shohada Tajrish Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran.*

[2]*Anesthesiology Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.*

[3]*Department of Obstetrics and Gynecology, Preventative Gynecology Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.*

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ABSTRACT

Background: One of the most important treatments used in women with infertility is IVF, and improving its results can affect the success of assisted reproductive techniques. It was previously shown that anesthetics can enter the follicular fluid (FF), so there is concern about the accumulation of anesthetics in the FF and their negative effects on fertilization and fetal growth under general anesthesia. The use of drugs that have both analgesic and sedative effects but do not have hemodynamic side effects is of particular importance and dexmedetomidine is one of the drugs introduced in this field. On the other hand, the use of sedatives such as midazolam and propofol may cause hemodynamic disturbances and severe hypotension in these patients, which limits the use of such drugs. Accordingly, and considering the importance of the issue, in this study, we decided to evaluate and compare the effect of propofol and dexmedetomidine on fertility in IVF candidates.

Methods: In this clinical trial study, 78 infertile patients who underwent IVF were randomly examined. After dividing the patients into two groups receiving dexmedetomidine and propofol or standard recording doses, the fertility rate of the patients in the two groups was evaluated using chi-square and Fisher tests at a significance level of 0.05.

Results: The use of dexmedetomidine for (P = 0.0348) Pressure_After_Dia, HR_Before (P = 0.0204), Injection_Time (P =0.000) and Recovery Time (P =0.000) indices caused a significant increase compared to the propofol group.

Conclusion: The results of the present study did not show a significant difference in the use of these two drugs on fertility.

Introduction

Since the birth of the first child by In vitro fertilization (IVF) method in 1978, its use has made significant progress [1-2]. Given that one of the most important therapies used in women with infertility is IVF, improving its results can be effective in the further success of assisted reproductive techniques [3]. IVF victory depends on positive results in a number of IVF stages, counting controlled ovarian incitement (COS), oocyte pick-up (OPU), fertilization, fetus exchange, and implantation. The OPU handle is vital, as oocyte quality impacts fertilization, fetus quality, and implantation. The method includes goal of follicles containing follicular liquid and cumulus-oocyte complexes. Although the OPU prepare may be a negligibly obtrusive strategy, it is difficult. In this manner, it is as a rule performed beneath anesthesia [4].

The foremost commonly utilized anesthetic agent during OPU is intravenous propofol, with premedication

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*Corresponding author.
E-mail address: faranak.behnaz@gmail.com

including an anxiolytic/analgesic combination of midazolam or fentanyl, individually [5]. Propofol could be a short-acting anesthetic agent with brief acceptance and recuperation times as well as great sharpness and minimal nausea within the postoperative stage [6]. Propofol was thought to be a secure medicate for utilize in IVF, since a least measurement is satisfactory to realize anesthesia [7].

Ketamine is additionally used for common anesthesia and manages of pain amid OPU [8]. Drawbacks are visiting queasiness, psychomimetic impacts, tachycardia, and a long recuperation time [9]. A combination of ketamine and propofol (P + K) is considered reasonable for brief procedural sedation and absence of pain [10-11].

It was previously shown that anesthetics can enter the follicular fluid (FF), so there is concern about the accumulation of anesthetics in the FF and their negative effects on fertilization and fetal growth under general anesthesia [12]. Therefore, the drugs used, including the drugs used in sedation during this procedure can be important in this regard.

Dexmedetomidine is a drug from the group of alpha-2 receptor agonists, of course, is a highly selective manner, which, unlike other common drugs such as midazolam, propofol, and fentanyl, has the property of causing sedation without respiratory complications, apnea, and hypoxia [13-14]. The drug was first approved by the US Food and Drug Administration (FDA) in 1999 and later approved by the FDA in 2008 for sedation and analgesia in patients undergoing surgical and non-surgical procedures [15]. Dexmedetomidine is a drug with a relatively short duration of action but has few side effects and can also cause hemodynamic stability in patients and also due to its analgesic effects, reduces the need for opioid analgesics and their complications [16]. Whereas pain relief without hemodynamic effects is important; the use of drugs that have both analgesic and sedative effects but do not have hemodynamic side effects is of particular importance and dexmedetomidine is one of the drugs introduced in this field. On the other hand, the use of sedatives such as midazolam and propofol may cause hemodynamic disturbances and severe hypotension in these patients, which limits the use of such drugs. Therefore, recognizing the effects that these drugs have on a deeper look at the results and fertility rate and comparing them with each other can be effective in improving the final prognosis of IVF treatment.

Accordingly, and considering the importance of this issue, this study examines and compares the effect of propofol and dexmedetomidine on fertility in IVF candidates.

Methods

The present double-blind clinical trial study with registration number: with code (IRCT20190121042444N2) has been approved by the ethics committee in biomedical research of Shahid Beheshti University of Medical Sciences (IR.SBMU.MSP.REC.1398.995). Patients undergoing IVF procedure referred to Shohada Tajrish Hospital for a period of 12 months were included in the study if they met the inclusion criteria (all patients with infertility, being a candidate for IVF treatment and lack of known drug hypersensitivity) and the written consent form was signed by the patients, and full explanations were given to the patients about how to conduct the study and its objectives. Meanwhile, patients who with defects in the file, in addition patients who had drug complications such as patients who need general anesthesia due to decreased oxygen saturation were excluded from the study (Exclusion criteria). The main researcher was not aware of the grouping of the patients and also the patients were blinded to the injected drug (double-blind). In general, 78 patients were included in this study and were randomly by using a table of random numbers divided into two study groups (Figure1).

In this study, patients in the propofol group underwent intervention with the drug propofol at a dose of 10-20 micrograms based on weight per minute during artificial insemination. Then, pregnancy success was checked one week after artificial insemination by blood test in terms of fertility. Meanwhile, in the other group, dexmedetomidine with a dose of 0.4-0.2 micrograms based on weight per minute was placed during artificial insemination. Then, pregnancy success was checked one week after artificial insemination by blood test in terms of fertility.

All quantitative variables were expressed as mean and standard deviation, and qualitative variables were expressed as numbers (percentage). The normality of quantitative variables was checked by Kolmogorov Smirnov test and box plots and the probability of normalization. Non-parametric Mann-Whitney test and Student's t-test were used to compare quantitative variables at a significance level of 5%. All statistical tests in two fields will be performed at a significance level of 5%. SPSS 23 software was used for data analysis.

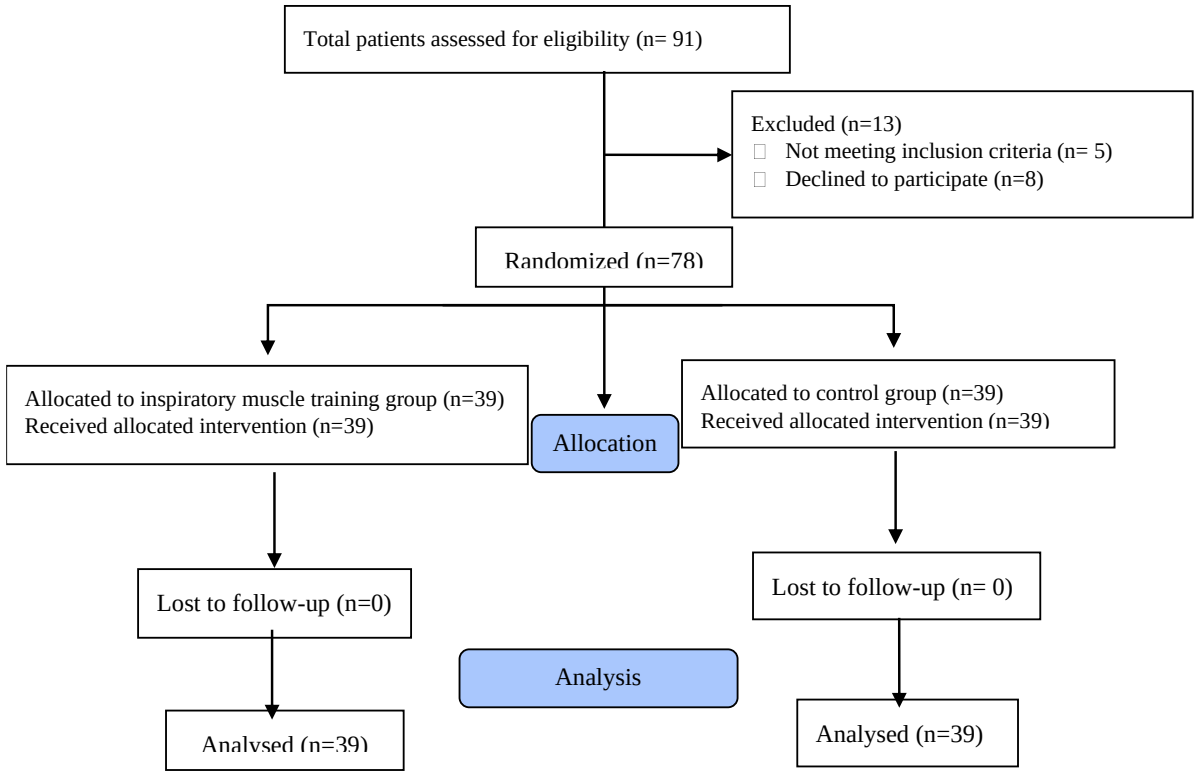

Figure 1- Flow diagram of patients participating and excluded no harmful complication were reported in the two groups

Results

All participants were randomly assigned to two groups of dexmedetomidine (mean age 33.5±6.2 years) and propofol (mean age 35.2 ± 5.7 years). Demographic and baseline information of patients is shown in (Table 1). Quantitative data is represented as SD ± mean and qualitative data is represented as (%).

Based on the results in (Table 2), the indicators of DBP_After (P=0.034), HR_Before (P=0.020), Injection anesthetic drug time (P=0.00) and recovery time (P=0.00) had significant changes between the two groups.

Table 1- Comparison of demographic and baseline information of two groups of patients included in the study based on T-test

	DEX group Mean ± SD	Propofol group Mean ± SD	P value
Age	33.5±6.2	35.2±5.7	0.1928
BMI	71.1±10.8	65.0±15.0	0.5582

Table 2- Evaluation and comparison of patient's status indices in DEX and propofol groups comparison of demographic and baseline information of two groups of patients included in the study using student T-test statistical method

	DEX group Mean ± SD	Propofol group Mean ± SD	P value
Pressure_Before_Sys	121.9±12.0	123.1±11.8	0.6640
Pressure_Before_Dia	78.7±9.4	80.1±9.7	0.4955
Pressure_After_Sys	110.7±11.5	107.5±11.5	0.2236
Pressure_After_Dia	71.1±8.1	67.4±6.7	0.0348
HR_Before	100±13.00	92±14.00	0.0204
HR_After	81±12.00	81±11.00	0.9471

Injection_Time	28±5.00	6±1.00	< 0.0001
Infertility Duration	6±3.00	7±3.00	0.5619
Opration Time	25±4.00	24±3.00	0.6290
Recovery Time	84±11.00	56±9.00	< 0.0001
Number of fetuses	5±5.00	4±3.00	0.3697
Fertility	10	14	0.345

Discussion

The present study was conducted to investigate the role of dexmedetomidine and propofol as two anesthetic drugs on the fertility rate of IVF patients. The results obtained from our study showed that IVF-induced fertility in patients in the dexmedetomidine group was weaker than in the group under anesthesia with propofol. However, no statistically significant difference was observed between the two groups. According to the results of our study, the using of dexmedetomidine had no effect on the quality and number of offspring after the embryo transfer process. In addition, Injection anesthetic drug time and recovery time had significant changes between the two group and in the propofol group, this time was less.

Based on the results obtained from previous studies, propofol has a toxic effect on the egg fertilization rate, which depends on the dose and time of use [17-19]. The researchers found that the use of propofol-based anesthesia technique causes a significant concentration of it to be present in the follicular fluid. The higher the concentration and the longer the duration of use, the more effective it will be [20]. In addition, if the unfertilized egg is exposed to this drug, we will witness a high degree of parthenogenetic activation [19]. Despite these valuable results that determine the effect of anesthetics on oocyte physiology, the quality of embryo growth and the processes after egg fertilization and embryo transfer, the effect of anesthetics on fertility has not been studied much.

In this study, it was observed that postoperative diastolic pressure, preoperative HR, Injection Time, and recovery time in patients receiving dexmedetomidine were significantly higher than patients in the propofol group. Investigating the toxic effect of propofol on the fertility rate of rats has been associated with different result. However, in other studies, the toxic effect of propofol and its side effects have not been confirmed [21-22].

Ben-Shlomo et al. They found that the successful conception of the fetus is not related to the duration of anesthesia and the dose of propofol [23]. Investigating the effectiveness of dexmedetomidine in egg retrieval by Elnabtity et al. It was done and showed that the use of intravenous drugs is a postoperative analgesic method that has fewer side effects than the removal of propofol during surgery [24]. Investigations have shown that Dexmedetomidine can protect against reperfusion and ischemic damage of rat ovarian tissue [23]. Studies indicate that dexmedetomidine can also protect the ovarian tissue in the conditions of oxidative stress caused by pneumoperitoneum [16]. Researchers have associated the protective effect of this drug with α-2 adrenoceptors. Gu et al. Showed that dexmedetomidine can reduce lung damage caused by renal ischemia-reperfusion through independent and α2-adrenergic-related mechanisms [19].

The small statistical population and the single center of this study were some of the limitations of this study. Therefore, using a larger statistical community and implementing the process in a multicenter way can help to provide reliable results.

Conclusion

The use of propofol in patients undergoing IVF improves some parameters compared to patients undergoing dexmedetomidine. However, the use of these two anesthetic agents does not have a significant effect on patients' fertility. Finally, the present study did not show a significant difference in the use of the two evaluated drugs on the fertility of patients undergoing IVF. Therefore, using another study with a larger statistical population and even as a multi-center can provide more reliable and citational results.

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References

[1] Cohen ME. The “brave new baby” and the law: Fashioning remedies for the victims of in vitro fertilization. Am J Law Med. 1978; 4(3):317-36.

[2] Dow K. ‘The men who made the breakthrough’: How the British press represented Patrick Steptoe and Robert Edwards in 1978. Reprod Biomed Soc Online. 2017; 4:59-67.

[3] Van Voorhis BJ. Outcomes from assisted reproductive technology. Obstet Gynecol. 2006; 107(1):183-200.

[4] Goutziomitrou E, Venetis CA, Kolibianakis EM, Bosdou JK, Parlapani A, Grimbizis G, Tarlatzis BC. Propofol versus thiopental sodium as anaesthetic agents for oocyte retrieval: a randomized controlled

trial. Reprod Biomed Online. 2015; 31(6):752-9.
[5] Janssenswillen C, Christiaens F, Camu F, Van Steirteghem A. The effect of propofol on parthenogenetic activation, in vitro fertilization and early development of mouse oocytes. Fertil Steril. 1997; 67(4):769-74.
[6] Sherry E. Admixture of propofol and alfentanil: use for intravenous sedation and analgesia during transvaginal oocyte retrieval. Anaesthesia. 1992; 47(6):477-9.
[7] Ramìrez-Paesano C, Fhima IB, Medina R, Urbina MT, Martínez C, Biber JL. Evaluation of Plasmatic Concentration of Propofol 2.5 μg/ml by TCI using Marsh Modified Model, during oocyte retrieval for IVF in Latin-American women (Venezuelans). JBRA Assist Reprod. 2015; 19(1):2-7.
[8] Majidinejad S, Esmailian M, Emadi M. Comparison of intravenous ketamine with morphine in pain relief of long bones fractures: a double blind randomized clinical trial. Emergency. 2014; 2(2):77.
[9] Krauss B, Green SM. Procedural sedation and analgesia in children. Lancet. 2006; 367(9512):766-80.
[10] Stevic M, Ristic N, Budic I, Ladjevic N, Trifunovic B, Rakic I, et al. Comparison of ketamine and ketofol for deep sedation and analgesia in children undergoing laser procedure. Lasers Med Sci. 2017; 32:1525-33.
[11] Wu J. Deep sedation with intravenous infusion of combined propofol and ketamine during dressing changes and whirlpool bath in patients with severe epidermolysis bullosa. Paediatr Anaesth. 2007; 17(6):592-6.
[12] Christiaens F, Janssenswillen C, Verborgh C, Moerman I, Devroey P, Van Steirteghem A, et al. Propofol concentrations in follicular fluid during general anaesthesia for transvaginal oocyte retrieval. Hum Reprod. 1999; 14(2):345–348.
[13] Arcangeli A, D'Alò C, Gaspari R. Dexmedetomidine use in general anaesthesia. Curr Drug Targets. 2009; 10(8):687-95.
[14] Chrysostomou C, Schmitt CG. Dexmedetomidine: sedation, analgesia and beyond. Expert Opin Drug Metab Toxicol. 2008; 4(5):619-27.
[15] Pasin L, Greco T, Feltracco P, Vittorio A, Neto CN, Cabrini L, et al. Dexmedetomidine as a sedative agent in critically ill patients: a meta-analysis of randomized controlled trials. PLoS One. 2013; 8(12):e82913.
[16] Mato M, Pérez A, Otero J, Torres LM. Dexmedetomidine, a promising drug. Rev Esp Anestesiol Reanim. 2002; 49(8):407-20.
[17] Tola EN. The effect of anesthetic agents for oocyte pick-up on in vitro fertilization outcome: A retrospective study in a tertiary center. Taiwan J Obstet Gynecol. 2019; 58(5):673-679.
[18] Budak Ö, Bostancı MS, Tuna A, Toprak V, Çakiroğlu H, Gök K. The effect of Propofol versus Dexmedetomidine as anesthetic agents for oocyte pick-up on in vitro fertilization (IVF) outcomes. Sci Rep. 2021; 11(1):23922.
[19] Reshan RG, Ameen BG, Hassan AA. Effect of TIVA with Propofol Versus Inhalational Anasthesia Plus Ketamine on Fertilization and Clinical Pregnancy Rate in ICSI. Int J Psychosoc Rehabilitation. 2020; 24(05).
[20] Vlahos NF, Giannakikou I, Vlachos A, Vitoratos N. Analgesia and anesthesia for assisted reproductive technologies. Int J Gynaecol Obstet. 2009; 105(3):201-5.
[21] Janssenswillen C, Christiaens F, Camu F, Van Steirteghem A. The effect of propofol on parthenogenetic activation, in vitro fertilization and early development of mouse oocytes. Fertil Steril. 1997; 67(4):769-74.
[22] Romanski PA, Farland LV, Tsen LC, Ginsburg ES, Lewis EI. Effect of class III and class IV obesity on oocyte retrieval complications and outcomes. Fertil. Steril. 2019; 111(2):294–301.
[23] Ben-Shlomo I, Moskovich R, Golan J, Eyali V, Tabak A, Shalev E. The effect of propofol anaesthesia on oocyte fertilization and early embryo quality. Hum Reprod. 2000; 15(10):2197–2199.
[24] Elnabtity AM, Selim MF. A prospective randomized trial comparing dexmedetomidine and midazolam for conscious sedation during oocyte retrieval in an in vitro fertilization program. Anesth Essays Res. 2017; 11(1):34–39.