

Azoospermia and testicular biopsy before intra-cytoplasmic sperm injection: Does the type of anesthesia make a difference?

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Abstract

Aim: Azoospermia is the most common form of male factor infertility, due to which sperms are retrieved for intra-cytoplasmic sperm injection (ICSI) under general or local anesthesia. The aim of the present study was to compare the efficacy of general and local anesthesia in an attempt to extract a sufficient quality of sperm for men with azoospermia, who intend to undergo ICSI. **Materials and Methods:** A total number of 50 patients with azoospermia, who were within the age range of 20-40, were randomly scheduled for testicular sperm extraction with either general or local anesthesia before ICSI. The hormonal abnormalities and severe varicocele were evaluated and treated before the testicular sperm extraction. The inclusion criteria obliged the researchers to focus on men with azoospermic, those who were diagnosed by two semen analyses after a 3-day abstinence from coitus according to the modified WHO criteria, and 19 < body mass index ≤ 28. The concentration, motility, and morphology of the spermatozoa of the two groups were also compared. **Results:** A total number of 76 men, with a mean age of 35.1 ± 6.0, were selected, 26 were excluded from the study, and the remaining participants were randomly divided into two groups such as general anesthesia and lidocaine group. According to the results, the differences between the values of sperm parameters within various hours after the testicle biopsy were not statistically significant. Also, there was no significant difference between the two groups in terms of sperm motility and sperm morphology during various timing after the processing. **Conclusion:** The present study demonstrated that there was no evidence found for values of sperm parameters between the two groups, undergoing local and general anesthesia, within various hours after the testicular biopsy. Further investigations with more focus on concentration-dependent lidocaine on human sperm parameters need to be carried out.

Key words: Anesthesia, assisted reproductive techniques, male infertility, sperm retrieval

INTRODUCTION

Azoospermia refers to the absence of sperm in ejaculated semen, which has a frequency exceeding 15% in infertile

couples, seeking fertility treatment.^[1] This condition is currently classified as obstructive and nonobstructive.

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Fortunately, some cases of azoospermia are treatable through intra-cytoplasmic sperm injection (ICSI). In many cases of nonobstructive azoospermia, spermatozoa could be obtained from the epididymides and the testes of patients through such various surgical sperm retrieval procedures as testicular biopsy, testicular sperm extraction, and testicular sperm aspiration.^[2-4]

There is no conclusive evidence that one procedure works better than other. All these procedures were performed under general or local anesthesia, leading to mixed results.^[5-8] Local anesthesia has previously proved to be effective and safe for patients.^[9] Given that there is a lack of inadequate facilities and experts for general anesthesia, local anesthesia is performed for surgical sperm retrieval in many assisted reproductive centers in Iran.^[10] Concentration, motility, and morphology also play a central role in ICSI. The current study, however, strove to examine and compare the effect(s) of the two techniques, general and local anesthesia, on extracting a sufficient quality of sperm for men with azoospermia, undergoing ICSI.

MATERIALS AND METHODS

This prospective, single-blind, randomized, clinical trial included 50 men with very low sperm production, who attended Infertility and Reproductive Health Research Center in Babol (North of Iran). The study protocol was approved by the Ethics Committee of Babol University of Medical Science and written informed consents were also obtained from the participants before the implementation of the study. Clinical Trial Registration Number is IRCT201505071760N39. The inclusion criteria were azoospermic men as diagnosed by two semen analyses after 3-day abstinence from coitus, which are compatible with the modified WHO criteria^[11] and 19 <body mass index (BMI) ≤28.

Our exclusion criteria were hypersensitivity to lidocaine, history of particular medicine to induce or suppress spermatogenesis, high temperature, radiotherapy and lower abdomen surgery, current alcohol use and smoking, and any exposure to gonadotoxin for 3 months. Hormonal abnormalities and severe varicocele were also evaluated and treated before testicular sperm biopsy.

A total number of 76 patients with azoospermia, who were between 20 and 40 years of age, were recruited for the purpose of this study. Fifty men meeting the selection criteria were chosen for testicular sperm extraction before ICSI and were randomly scheduled to go through either general or local anesthesia through a computer-generated sequence.

The scrotal area of all patients was prepared with 0.5% sodium chloride which was followed by physiological saline, and then it was draped. The intravascular infusion of ringer solution 37°C (5 ml/kg) began for each patient in general anesthesia group upon their arrival to the operating room. It is worth mentioning that pulse oximetry, noninvasive blood pressure monitoring, pulse rate, and three lead electrocardiograms were also used as monitoring indices until the end of the process. Besides, the clinical monitoring of respiratory status was constantly carried out for all patients throughout the study. Before the induction of anesthesia, the patients in general anesthesia group were intravenously premeditated with fentanyl (1-2 µg/kg) and midazolam (1-2 mg/kg). The induction of general anesthesia was carried out by incremental intravenous doses of propofol (2.5 mg/kg) as a bolus dose. The anesthesia was maintained by propofol (10-20 mg) incrementally until the residual of muscle relaxant was reversed until the end of the procedure. The patients were managed by airway through face masks.

The local anesthesia was, on the other hand, achieved in the operating room with 10 chromic catgut (cc) of 2% plain lidocaine (Sina Daru Ltd., Iran) using a 25-gauge needle. After 5 min, the epididymis was grasped between the thumb and fore-finger of the nondominant hand. A small incision was then made over the same area immediately. The size of the incision was about over 0.5-1 cm. A vascular area close to mid portion of medial, lateral or anterior surface of the testicle was chosen. Then, a tunica albuginea was longitudinally incised with a 15° ultrasharp knife. The testicular parenchyma (approximately 50-750 mg) was excised with sharp, curved scissors, and it was then placed in temperature-adopted Hams F₁₀ culture medium supplemented with 10% of plasmanate. The wet preparations were transferred to the *in vitro* fertilization lab. Individual tubules were isolated by immediate initial dispersal of the specimen with two sterile glass slides. The mincing of the tissue with sterile scissors in the Hams F₁₀ medium additionally allowed for the mechanical dispersal, and prepared the sequential passes of the tissue suspension (detection of fully condensed spermatids) through a 24-gauge angiocatheter. As soon as spermatozoa were identified, no further testicular incisions were made. To prevent the devascularization of the testicles and protect them against any damage threatening the subtunical testicular blood supply, additional biopsies was cautiously performed. The biopsy of the contra lateral testicle is commonly performed if there is no sperm found in the previous side. The incised segment of the tunica albuginea was closed. All patients left the clinic within 2 h after the operation and were highly recommended to go through a posttesticle biopsy.

About 10 cc of 2% lidocaine was injected into a testicular cord, and the incision was 0.5-1 cm on the side of scrotal

skin. The testicle was exposed to subcutaneous tissue and tunica vaginalis after the incisions of the skin. Then, a small piece of the testicular tissue was biopsied and subsequently processed in ART lab. The incisions were repaired with 2-0 cc. It should be noted that the biopsied sample was placed in a dish, in an environment covering 10% of Ham's F₁₀, which was prepared through adding 1 cc of albumin to 9 cc Ham's F₁₀. The tubules within the biopsied sample were totally opened by a special needle. Potentially, any existing sperm cells had to enter the cell culture media when the tissue was broken through this method. Afterward, 10-12 μm of media with sperm cells had to be pulled by a sampler placed onto a microscopic slide, which was subsequently analyzed under a microscope to detect the presence or absence of sperm within the sample. The remnant of the mentioned mixture was centrifuged at 500 rpm, allowing the pieces of tissue to sink to the bottom of the dish. The mixture was then centrifuged again at 3000 rpm for 5 min, and the sperms were then placed in a more transparent environment. The supernatant was then discarded, and 0.5 cc of media was added to the sediments at the bottom of the tube. Then, a uniform sample was obtained through shaking the tube, and a drop of the resultant solution was placed on the slide of microscope. The slides were then analyzed through a microscope, and the concentration, motility, and morphology of the spermatozoa, present in each sample, were evaluated immediately after processing, and 1 or 2 h after processing. The values were compared within and between both groups. The data obtained were statistically analyzed using Statistical Package for Social Sciences (SPSS, Chicago, IL, USA) software version 16.0 for Windows. Chi-square and *t*-test were also used to compare the values within the groups. *P* ≤ 0.05 was considered statistically significant.

RESULTS

A total number of 76 men, with the mean age of 35.1 ± 6.0, were selected for the purpose of this study, of whom twenty-six men were excluded from the study, and the remaining ones were randomly assigned to general anesthesia and the lidocaine group.

The mean age of patients in local anesthesia group was 35.7 ± 6.8, and it was 34 ± 7.8 in the general anesthesia group. The mean duration of infertility was 48.6 ± 46.2 months in the local anesthesia group and 30 ± 27.6 months in the general anesthesia group. In addition, the mean BMI was 23.2 ± 3.2 Kg/m² in the local group and 24.1 ± 2.3 Kg/m² in the general group.

Table 1 shows the nonsignificant differences between the general anesthesia and the lidocaine groups with regard to the categorization of age, duration of infertility, and BMI.

The mean (and standard deviation) sperm concentrations were 9.1 ± 1.0, 9.0 ± 1.1, and 11.3 ± 1.2 immediately after processing, or within 1 or 2 h after processing. The mean sperm motility was 2.8 ± 5.6, 9.3 ± 4.0, and 4.1 ± 9.4, and the sperm morphology (sperm abnormality) was 6.7 ± 19.6, 10.9 ± 26.8, and 4.1 ± 9.4 immediately after processing, or within 1 or 2 h after processing. There were no significant differences found between the values of sperm parameters in various hours after the testicle biopsy. Table 2 shows the nonsignificant values between the two groups in terms of sperm motility and sperm morphology during various timing after processing.

DISCUSSION

Testicular biopsy, done through lidocaine, is the most common surgical sperm retrieval procedure for obtaining sperms from the epididymides and the testes. However, the effects of lidocaine administered during testicular biopsy remain controversial,^[11] and there is also a significant

Table 1: Characteristics of participants undergoing testicular biopsy according to type of anesthesia

Variables	Local anesthesia n (%) (n = 25)	General anesthesia n (%) (n = 25)	P
Age (years)			
<35	13 (52.0)	16 (64.0)	0.390
≥35	12 (48.0)	9 (36.0)	
BMI (kg/m ²)			
<25	15 (60.0)	15 (60.0)	1.00
≥25	10 (40.0)	10 (40.0)	
Duration of infertility			
<5	17 (68.0)	22 (88.0)	0.088
≥5	8 (32.0)	3 (12.0)	

P ≤ 0.05, BMI: Body mass index

Table 2: Sperm parameters in various hours following testicular biopsy in 50 azoospermic men according to type of anesthesia

Sperm parameters	Mean ± SD			P
	Total (n = 50)	Local anesthesia (n = 25)	General anesthesia (n = 25)	
Sperm count (h)				
0	9.1±1.0	9.6±0.9	8.6±0.1	0.752
1	9.0±1.1	10.0±1.1	9.8±1.3	
2	11.3±1.2	12.4±1.2	10.4±1.4	
Sperm motility (h)				
0	2.8±5.6	3.6±6.4	2.0±4.6	0.246
1	4.0±9.3	5.8±11.3	2.2±6.3	
2	4.1±9.4	5.5±11.3	2.8±7.1	
Sperm morphology (h)				
0	6.7±19.6	7.2±19.7	6.3±19.8	0.452
1	10.9±26.8	15.3±32.1	6.4±19.7	
2	4.1±9.4	15.4±32.1	10.3±27.2	

P ≤ 0.05, SD: Standard deviation

question regarding the effect of lidocaine on sperm parameters.

Shirazi *et al.* injected a single dose of papaverine (35 mg/kg), lidocaine (4 mg/kg), and verapamil (0.1 mg/kg) intraperitoneally to three groups of rats, respectively. In animals treated with papaverine, the testis sperms were count, and the motile sperms were increased in comparison with other groups. The sperm morphology in both groups under study was within the normal range.^[12]

Wood *et al.* also evaluated the effect(s) of diltiazem, methylene blue, and lidocaine on the human sperm motility, viability, and cervical mucus penetration. They found that lidocaine had a partial inhibitory activity at similar concentrations.^[13]

Gorgy *et al.* examined 37 patients undergoing percutaneous epididymal sperm aspiration and/or testicular sperm aspiration procedures under local anesthesia (lidocaine 1%). They reported that 24 patients felt relaxed, 9 were mildly anxious, and only four felt extremely anxious during the time the procedure was in progress under lidocaine.^[14]

One limitation of the present study was its failure to assay the various values and concentrations of lidocaine, which could be due to the potential health threats and the ethical concerns. Hence, the present study only examined the sperm parameters in one concentration, but within various hours after biopsy. It is suggested that various concentrations and the time interval could influence the sperm parameters after biopsy. Another limitation of the current study was its failure to thoroughly clarify the possible mechanisms for the effect of lidocaine on sperm parameters. We did not make an attempt to assess the procedure related pain, either.

CONCLUSION

The present study illustrated that there was no evidence of difference found between the two groups, local and general anesthesia, in terms of the values of sperm parameters within various hours after the testicular biopsy. However, further investigations, with more focus on concentration-dependent lidocaine on human sperm parameters, need to be carried out.

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Conflicts of interest

There are no conflicts of interest.

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