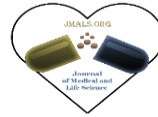




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Journal of Medical and Life Science
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Review of Intrauterine insemination (IUI) treatment factors and influence on the success rates

Samah Amer Hammood¹, Azhar Shyaa Youns¹, Shaymaa Hussein Jaber²,
Zahraa S. M. ALkaabi¹.

¹Department of Laboratory Investigation, Faculty of Science, University of Kufa, Najaf, Iraq

²Biology Department, Faculty of Science, Kufa University – Iraq

Samah.alobaidi@uokufa.edu.iq

Azharsh.alaseese@uokufa.edu.iq

Shaymaa.alasaaedi@uokufa.edu.iq

Zahraas.a@uokufa.edu.iq

DOI: 10.21608/jmls.2023.307223

Abstract

It is generally accepted that intrauterine insemination (IUI) with homologous semen should be preferred as a first choice treatment to more invasive and expensive techniques of assisted reproduction in the case of cervical, unexplained, and moderate male factor subfertility. Scientific validation of this strategy is difficult because the literature is rather confusing and not conclusive.

The rationale for the use of artificial insemination is to increase gamete density at the site of fertilization. Many variables may influence success rates after IUI treatment procedures. Some factors will never be solved by methodological adjustments such as female age, duration of infertility, etc. However, quite some variables can be improved upon using different strategies.

Key Words; intrauterine insemination. (IUI), homologous semen, subfertility

Introduction

1 -Assisted reproduction (ART)

Infertility is currently successfully treated with assisted reproduction (ART) in a variety of clinical circumstances. It encompasses a broad range of methods, the most well-known of which are intracytoplasmic sperm injection (ICSI), in vitro fertilization (IVF), and intrauterine insemination (IUI). In contrast to IVF/ICSI techniques, IUI is simple to carry out, affordable, and has specific advantages including the minimal equipment needed, an easy technique to learn, being less intrusive, and having a lower psychological strain on the couple. In natural cycles, clomiphene citrate, or low-dose HMG (human menopausal gonadotrophins) ovarian stimulation protocols, IUI has a good couple

compliance (low drop-out rate), a low risk for OHSS (ovarian hyperstimulation syndrome), and a low multiple pregnancy rate (1).

Increasing the gamete density at the location of fertilization is the goal of intrauterine insemination (IUI). Despite the wealth of information available on artificial insemination using the husband's sperm, there is still debate concerning its efficacy, particularly in comparison to IVF and ICSI (2).

2: Indications for IUI

2.1. Cervical factor

IUI during natural cycles considerably raises the likelihood of conception in the case of an isolated cervical factor, which is characterized by repeated negative post-coital tests despite normal semen quality and appropriate time (3). Subfertile couples

with an isolated cervical factor were treated for six months with either IUI or expectant management in a prospective, randomized study (3).

2.2. Male factor subfertility

Older evidence, frequently from cross-over trials, revealed a considerable positive effect of IUI. However, a Cochrane review demonstrated that there is inadequate evidence to draw any conclusions about whether IUI is successful or not in cases of moderate and mild male infertility. The practice of reporting findings as live birth rates per couple is now widely recognized (4).

2.3. Type of subfertility

Natural cycle IUI is not significantly superior to expectant care in a meta-analysis of numerous trials for infertility that cannot be explained (5). However, we must take into account that the ovarian stimulation regimen in many of these studies was rather aggressive, resulting in high multiple pregnancy rates. On the other hand, this meta-analysis also demonstrates that the combination of ovarian stimulation and IUI significantly improves live birth rates in couples with unexplained infertility (6). It has not yet been established if moderate ovarian stimulation techniques significantly increase live birth rates.

2.4. Sexual disorders

There is frequently no need for intra-uterine insemination in cases of hypospadias, vaginismus, retrograde ejaculation, and impotence because semen can be implanted intravaginally or intracervical. Semen preparation followed by IUI can be utilized as a first-line treatment when semen parameters are low, as is frequently the case in men with retrograde ejaculation.

2.5. Semen quality and IUI

Despite the lack of level 1 evidence discovered in the literature regarding the link between sperm quality and IUI success, numerous prospective observational studies and meticulously planned retrospective analyses can still be found. The IMC (inseminating motile count after washing), sperm morphology using strict criteria, TMSC (total motile sperm count in the native sperm sample), and TM

(total motility in the native sperm sample) were the four sperm parameters that were most frequently examined.

It has been amply demonstrated that a significantly greater pregnancy rate every cycle requires a score of more than 4% normal morphology when rigorous criteria are used (7, 8). According to Ombelet et al. (10) an IMC of 1 million can be used as a reasonable threshold level above which IUI can be performed with acceptable pregnancy rates, while Van Weert (9) suggested a cut-off value for the IMC between 0.8 and 5 million motile spermatozoa to reach a substantial discriminative performance.

2.6. Prevention of infections in an IUI program

Semen and vaginal secretions can transmit many viral agents, including cytomegalovirus (CMV), hepatitis B, C, and D (HBV, HCV, and HDV), herpes simplex virus type 2 (HSV-2), human T-lymphotropic virus (HTLV), and human immunodeficiency virus (HIV). Before processing or cryopreserving any biological specimen, patients are typically routinely checked for HIV, HBV/HCV, and other commonly prevalent sexually transmitted infections (STIs) (11). The laboratory personnel must be informed of the test results before processing or cryopreserving any biological specimen.

Couples should be aware that sperm preparation techniques do not guarantee that HIV is 100% removed from the post-processed sperm sample of HIV-positive males, even though no seroconversions of female partners were reported in the literature after inseminations with washed sperm from HIV-positive men. Leukocytospermia may signal the presence of an infection in the semen sample and may be linked to poor sperm quality, according to the WHO laboratory manual (12). Discontinuous density gradient centrifugation offers a better method for separating highly mobile spermatozoa from detritus, leukocytes, and other cell types in these circumstances. Gamete survival will undoubtedly suffer from contact with pollutants in the workplace and exposure to infections or other microorganisms from healthcare workers. To advance quality and

safety within the ART unit, strict criteria for acceptable laboratory practices are required (11).

2.7. Semen preparation techniques (SPT)

Density gradient centrifugation (DGC) showed to be superior to the swim-up and simple wash technique: a clear improvement of morphologically normal spermatozoa with grade A motility and normal DNA integrity are obtained in the prepared sample. The DGC selects spermatozoa according to their density and gravity. In a Cochrane Review (13) there was no clear evidence which sperm washing technique is superior when clinical outcomes after IUI are investigated.

2.8. Ovarian stimulation and prevention of multiple pregnancies

In couples with unexplained subfertility, little to mild endometriosis, and mild male subfertility, IUI combined with light ovarian stimulation is beneficial. To prevent high-order multiple pregnancies, one should strive for a maximum of two dominant follicles, per van Rumste et al.'s risk analysis (14).

Although clomiphene citrate (CC, 50–100 mg daily for 5 days) might have a deleterious impact on the endometrium, it is still the treatment of choice for modest ovarian stimulation. In contrast to gonadotrophins, CC is less expensive, easier to utilize, and more widely available. HMG or recombinant FSH in dosages of 50–75 IU per day can be given if necessary. Each stimulated cycle must be strictly monitored using ultrasonography. However, any follicles greater than 10 mm should be assessed and taken into consideration when setting cancellation criteria. One should aim for two dominant follicles larger than 15 mm. Aromatase inhibitors, GnRH agonists, and antagonists appear to have no role in IUI programs, according to the literature and cost-effectiveness analysis (15,16).

2.9. Timing and number of IUIs per cycle, bedrest after IUI

Oocytes and spermatozoa have a finite lifespan, as is common knowledge. Therefore, it appears that timing the insemination properly is crucial. It was widely agreed that insemination should take place as soon as possible before or no later than 10 hours

following ovulation. A larger temporal window, between 12 and 36 hours after HCG injection, can be observed, according to the currently known evidence (17). LH surge detection or HCG injection can be used to time IUI (17).

In most studies, couples with unexplained subfertility are advised to have a single, carefully scheduled IUI (18). Only one study (19) found that double insemination helped couples who were experiencing male subfertility. Since a second IUI will raise the costs and psychological strain, a double IUI should only be advised when it has been demonstrated to be effective. The outcome of urgently required randomized controlled trials will determine whether double insemination should be advised. 15–20 min of immobilization after intrauterine insemination, with or without ovarian stimulation, significantly increases cumulative continuing pregnancy rates and live birth rates, according to two prospective randomized trials (20, 21).

2.10. Fallopian sperm perfusion

In contrast to standard IUI (0.3-0.5 ml), fallopian tube sperm perfusion (FSP) uses a higher volume (4 ml) of inseminate. The goal of FSP is to increase the number of motile spermatozoa that reach the eggs and cause flushing of sperm through the tubes. The ultimate objective is to increase the likelihood that gametes will collide and fertilize (22). The fact that other, perhaps less effective variations of FSP have been created by various research organizations complicates the evaluation of FSP. IUI is preferable to FSP if a Foley catheter is utilized, according to two prospective trials (23,24). In contrast, most other published trials found that the pregnancy rates achieved with FSP were at least on par with those achieved with IUI, if not superior. It is currently uncertain whether this observation justifies a firm recommendation against using the Foley catheter for FSP (25).

3. Laboratory factors

3-1: Sperm washing methods

Prostaglandins and reactive oxygen species (ROS) will be eliminated during preparation and washing. When a raw semen sample is used for IUI, the

prostaglandins must be eliminated because they will induce excruciating uterine pains. For successful IUI, the preparation will concentrate morphologically more normal and motile spermatozoa. The swim-up techniques, density gradient centrifugation, and use of Sephadex columns are the most common. On the advantages of any one preparation procedure in terms of fecundity, conflicting findings have been observed (26).

3-2: Addition of substances in sperm preparation

It is still uncertain and unproven whether adding compounds like pentoxifylline, kallikreins, follicular fluid, etc. would improve the outcomes. While eliminating the scavengers from the seminal plasma and boosting spermatozoa's production of ROS are two ways that sperm preparation techniques can harm spermatozoa, it is crucial to be aware of this possibility. More research is required to determine whether improving PR with IUI in specific situations by treating spermatozoa with antioxidant-containing solutions during sperm preparation. The impact of PAF exposure on sperm during the preparation of semen for IUI was assessed in two double-blind randomized experiments (27).

3-3: The effect of the abstinence period

In prospective research presented by(28) De Jonge et al. (2004), abstinence did not affect sperm morphology, total or grade A motility, or sperm DNA fragmentation. Chromatin quality was impacted negatively by a brief (24 h) abstinence interval. Three days or less between periods of abstinence were linked to greater PR after IUI (29).

3-4: Advantages of IUI:

When a person has a health issue that prohibits them from engaging in sexual activity, such as erectile dysfunction in men, Lack of mucous fluid secretion, which aids in sperm transfer from the cervix to the uterus in females, or because the mucous fluid includes compounds that kill sperm, as well as prior endometriosis infection or mild to moderate endometriosis. One of the proteins in the semen, which is eliminated before artificial insemination, and weak or few sperm in a man cause the woman's allergy(30).

3-5: Disadvantages of IUI:

After the insemination technique, cramps or minor bleeding may occur. pelvic region infection or irritation. Using fertility medications before fertilization increases the likelihood of getting pregnant with twins or triplets, which raises the risk of pregnancy issues like preterm birth. In some rare instances, ovarian hyperstimulation syndrome manifests as nausea, vomiting, and stomach discomfort, and in more severe situations, it can cause dehydration, chest pain, and shortness of breath (30).

Conclusion

In many situations of human subfertility, treatment by artificial insemination using the husband's sperm is still a worthwhile first option treatment before beginning more intrusive and expensive treatments of assisted reproduction, at least if tubal patency is verified. It is an easy and non-intrusive technique that does not require expensive infrastructure to be used. Evidence-based statistics, taken into account in daily practice, show that an IMC above 1 million, a morphology score of more than 4% normal forms, a TMCS of more than 5 million, and an early total motility of more than 30% boost the success rate of IUI. IUI during natural cycles considerably increases the likelihood of conception in couples with cervical factor subfertility, while the combination of ovarian stimulation and IUI is advised in couples with unexplained subfertility. The creation of a should be the aim of ovarian stimulation. Two dominant follicles at most. During an AIH operation, sperm-washing procedures are used to stop partner-to-partner transmission, but they do not ensure that infections are completely removed from the post-processed sperm sample, and no sperm-washing approach is better than another when comparing the success of IUI. In couples with male factor subfertility, double IUI increases pregnancy rates compared to single IUI, but not in cases of unexplained infertility. The best window of time between HCG injection and IUI appears to be between 12 and 36 hours, and every insemination

attempt should be followed by at least 10-15 minutes of immobility.

Conflict of interest

No conflict of interest is to be declared.

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