

Evidence-based IUI in developing countries

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Abstract

Intrauterine inseminations (IUI) are easier to perform, less invasive and less expensive than other methods of assisted reproduction. The rationale for the use of artificial insemination is to increase gamete density at the site of fertilisation. It is generally accepted that IUI with homologous semen should be preferred as a first choice treatment above more invasive and expensive techniques of assisted reproduction in case of cervical, unexplained and moderate male factor subfertility. Scientific validation of this strategy is difficult because the literature is rather confusing.

Effectivity has been documented in controlled studies under the condition that the inseminating motile count exceeds more than 1 million motile spermatozoa. Risks and costs are minimal, provided the multiple gestation incidence can be reduced to an acceptable level and provided at least one tube is patent. Training is easy and severe complications are almost non-existing.

Reasons enough to promote the use of IUI as a valuable first line treatment for most cases of non-tubal infertility in developing countries.

Key words: Artificial insemination, assisted reproduction, human, intrauterine insemination, IUI, semen, semen quality.

Introduction

Contrary to IVF/ICSI methods, IUI is easy to perform, inexpensive and offers particular advantages such as the minimal equipment required, an easy technique to learn, being less invasive with a reduced psychological burden on the couple when compared to IVF/ICSI. Subsequently IUI has a good couple compliancy (low drop-out rate), a low risk for OHSS (ovarian hyperstimulation syndrome) and a low multiple pregnancy rate in natural cycles and clomiphene citrate or low-dose HMG (human menopausal gonadotrophins) ovarian stimulation protocols (Ombelet et al., 2008).

Although there is a lack of good quality studies on IUI performance, we will try to make an overview of the actual evidence-based data on different levels of IUI practice.

Indications for IUI

Cervical factor

In case of an isolated cervical factor, defined as a repeated negative post-coital test despite a normal semen quality and adequate timing, IUI in natural cycles significantly increases the probability of conception (Steures et al., 2007).

Male factor subfertility

In a Cochrane review it was clearly shown that there is insufficient evidence to conclude whether IUI is effective or not in moderate and mild male infertility (Bensdorp et al., 2007). Older evidence, often from cross-over trials, found a significant beneficial effect of IUI.

Unexplained subfertility

It seems that natural cycle IUI has no significant beneficial effect over expectant management in case of unexplained infertility (Verhulst et al., 2006). On the other hand the combination of ovarian stimulation and IUI significantly improves live birth rates in couples with unexplained infertility (Verhulst et al., 2006), but we have to take into account that the ovarian stimulation regimen in a lot of these studies was rather aggressive resulting in high multiple pregnancy rates. In a recent economic analysis it was shown that IUI-ovarian stimulation is the preferred treatment to start with in case of unexplained infertility. When IVF-eSET (elective single embryo transfer) results in a higher ongoing pregnancy rate (> 38%), IVF would be the preferred treatment (Van Rumste et al., 2014).

Semen quality and IUI

The four sperm parameters that are most frequently examined were the following: (a) the IMC (inseminating motile count after washing), (b) sperm morphology using strict criteria, (c) the TMSC (total motile sperm count in the native sperm sample) and (d) the TM (total motility in the native sperm sample).

It was clearly shown that a score of more than 4% normal morphology using strict criteria is needed to result in a significantly higher pregnancy rate per cycle (Van Waart et al., 2001; Ombelet et al., 2003). According to Ombelet et al. (Ombelet et al., 1997; 2014) an IMC of 1 million can be used as a reasonable threshold level above which IUI can be performed with acceptable pregnancy rates. For the TMSC and the TM a cut-off value of 5 to 10 million and 30% was most frequently reported respectively.

Ovarian stimulation and prevention of multiple pregnancies

IUI in combination with mild ovarian stimulation is effective in couples with unexplained subfertility, minimal to mild endometriosis and mild male subfertility. According to a risk analysis by van Rumste et al. (2008) one should aim for a maximum of two dominant follicles in order to avoid high-order multiple pregnancies.

Clomiphene citrate remains the first-choice drug to use although CC might have a negative effect on the endometrium. If needed HMG or recombinant FSH can be used in dosages of 50-75 IU per day. Strict ultrasound monitoring of each stimulated cycle is mandatory. One should strive after two dominant follicles larger than 15 mm but all follicles

larger than 10 mm should be measured and taken into account when defining cancellation criteria.

Timing and number of IUIs per cycle, bedrest after IUI

Adequate timing of the insemination seems to be essential. According to the current available a time frame from 12 to 36 hours after HCG injection can be used (Cantineau et al., 2009).

One study reported a positive effect of double insemination in couples suffering from male subfertility (Liu et al., 2006). Double IUI should only be advised when proven effective, since a second IUI will increase the costs and psychological burden.

According to two prospective randomized trials 10-15 minutes immobilization subsequent to intrauterine insemination significantly improves cumulative ongoing pregnancy rates and live birth rates (Saleh et al., 2000; Custers et al., 2009).

Semen preparation techniques (SPT)

In a Cochrane Review (Boomsma et al., 2012) there was no clear evidence which sperm washing technique is superior when clinical outcomes after IUI are investigated.

Although DGC showed to be superior to swim-up and wash technique concerning laboratory outcomes (e.g. semen parameters) there is insufficient evidence to recommend any specific SPT when speaking about clinical outcome after IUI.

Fallopian sperm perfusion

In fallopian tube sperm perfusion (FSP) a larger volume (4 ml) of inseminate is used when compared to regular IUI (0.3-0.5 ml). The rationale behind FSP is to create a sperm flushing of the tubes and an overflow of motile spermatozoa closer to the eggs (Kahn et al., 1993).

Because of the promising results in many studies I believe that a well-powered multi-centre prospective randomized trial comparing pregnancy outcome of FSP (without Foley catheter) with regular IUI in case of unexplained and moderate male infertility should be performed.

Conclusion

Treatment with artificial insemination with husband's sperm remains a valuable first choice treatment before starting more invasive and more expensive techniques of assisted reproduction in

many cases of human subfertility, at least if tubal patency is proven. It is a simple and non-invasive technique which can be performed without expensive infrastructure in poor-resource countries.

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