

# Efficiency of intrauterine insemination as a method of treating marital infertility

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## Citation

F Fetahovic, Z Popivoda, D Radonjic, D Kljakic, G Vukcevic, S Raicevic. *Efficiency of intrauterine insemination as a method of treating marital infertility*. The Internet Journal of Gynecology and Obstetrics. 2009 Volume 13 Number 2.

## Abstract

**Introduction:** Marital sterility is a special problem that the WHO declared as the disease and it is estimated that 15% of couples have been treated by this disease. The causes of marital infertility are 45-50% of men, 45-50% of women and 5-10% couples of unknown causes. Total fertility rate in Montenegro has been reduced by about 10%. The aim of the study was to make the assessment of successfulness of intrauterine insemination, as one of the methods of treatment of marital infertility. **Material and methods:** We studied 27 infertile married couples, where 52 cycles were stimulated. In 42 (80.7%) of cycles the ovulation was confirmed and made intrauterine insemination (IUI) by husband's sperm, which was prepared by swim-up modified method. In 10 cycles there has been no adequate growth of follicles and the folliculogenesis stimulation was interrupted. The causes of infertility in the study group were: cause of male infertility (n = 11) mild and easy forms of endometriosis (n = 6) cervical factor (n = 4) and polycystic ovarian syndrome (n = 6). **Results:** The pregnancy occurred in 4 female patients. Percentage of pregnancy was 10.8%, compared to cycles in which ovulation was confirmed, after which intrauterine insemination was done. Percentage of pregnancy in married couples, according to the different causes of infertility was: infertility caused by cervical factor of 25%, the causes of male infertility 16.6%, with mild or easy endometriosis 18.2%, polycystic ovarian syndrome 16.6%. **Discussion:** Examination presents prospective study, which included 27 infertile couples, in which ovarian stimulation were performed with Clomifen citrate and made intrauterine insemination. In 18 pairs was about the secondary, and in 9 pairs, the primary infertility. We believe that our results are satisfactorily and consistent with published results in the reference literature. **Conclusion:** Intrauterine insemination is a cheap and minimally invasive method compared to other methods of assisted reproduction. Numerous reports indicate that the pregnancy rate is much higher if the IUI is combined with controlled ovarian stimulation.

## INTRODUCTION

Marital sterility is a special problem that the World Health Organization (WHO) declared as the disease. It is estimated that 15% of couples has been treated by this disease. Infertility should be regarded as a psychophysical problem of couple, but as well as a demographic problem of society. The causes of marital infertility are 45-50% of men, 45-50% of women and 5-10% couples of unknown causes. Total fertility rate in Montenegro has been reduced by about 10% at the last few years. Number of children per a woman in Montenegro, in the generative period, according MONSTAT (national statistical organization of Montenegro) in 2001 was 1.79. If the sterility could be successfully treated; it is primarily to carry out detailed diagnostics, with both partners. There is a defined diagnostic protocol of sterility, which needs to be done in order to ascertain the cause of infertility. In most cases, simple and inexpensive methods are enough, sometimes it is common gynecological

examination and ultrasound to determine the cause.

Treatment of marital infertility is strictly individual and is determined after adequate diagnosis. There are several ways of assisted reproduction. Assisted reproduction procedures are based on improving the natural fertile capacities of a couple. These procedures are directed towards realization of the contact between egg cells and sperm, shortening the way to their merger, or bringing them into direct contact. The essence of all these procedures is inducing of ovulation and delivery of prepared seeds in larger or smaller nearness to egg cell in the body (AIH) or outside the body of woman (IVF). Usually, the first choice in case that sperm gram doesn't deviate much from the normal is intrauterine insemination (IUI). IUI is a procedure which involves placing sperm inside a woman's uterus to facilitate fertilization. This fertility treatment does not involve the manipulation of a woman's eggs and that uses a catheter to place a number of washed sperm directly into the uterus.

The goal of IUI is to increase the number of sperm that reach the fallopian tubes and subsequently increase the chance of fertilization. IUI can be offered on a natural or stimulated cycle.

By the time, a various modifications of insemination, such as cervical, intrauterine, intratubular even intraperitoneal, have been developed. In addition, insemination can be done by clean sperm, after liquefaction or by processed sperm when different laboratory techniques of spin, rinsing and conditioning of spermatozoa are used. Insemination can be a homologous (with husband's sperm) or heterologous, so-called heteroinsemination (usually of unknown sperm donor), which is performed only in state institutions.

Most commonly performed modification of insemination is IUI, by treated or untreated (centrifuging, medium washing, conditioning) sperm. It represents the simplest form of assisted fertilization. It can be done in spontaneous or stimulated cycles. This method is often used before. After the introduction of IVF, insemination is less used, although sometimes it gives good results and because of its simplicity should not be completely forgotten. For its success it is important good preparation of sperm. The price of intervention is much lower compared to other methods of assisted reproduction.

Artificial insemination has mainly been used to treat unexplained infertility (usually combined with superovulation) and male factor infertility<sup>9</sup>. IUI is the best studied and most widely practiced of all the insemination techniques<sup>2</sup>.

The aim of the work:

The aim of this research is that we through the presentation of our results make assessment of successfulness of intrauterine insemination, as one of the methods in the treatment of marital infertility.

**MATERIAL AND METHODS**

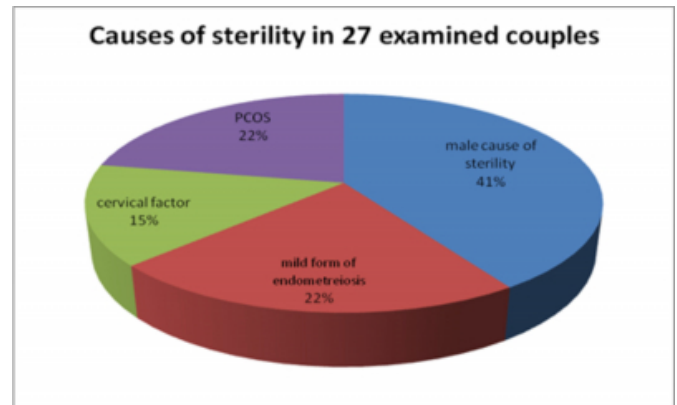
Examination presents prospective study, which included 27 infertile couples, where ovarian stimulation was performed with Clomifen citrate and made intrauterine insemination. In 18 pairs it works about the secondary, and in 9 pairs, the primary infertility.

With above mentioned 27 infertile married couples (Chart 1.), 52 cycles were stimulated. In 42 (80.7%) of cycles the ovulation was confirmed and made intrauterine insemination (IUI) by husband's sperm which was prepared by swim-up

modified method .In 10 cycles there has been no adequate growth of follicles and the folliculogenesis stimulation was interrupted. The causes of infertility in the study group were: cause of male infertility (n = 11), mild and easy forms of endometriosis (n = 6), cervical factor (n = 4) and polycystic ovarian syndrome (n = 6).

**Figure 1**

Chart 1. Causes of sterility in 27 examined couples



Before inclusion in the protocol, married couples were completely clinical and laboratory processed. All of them made: microbiological analysis (CB, VB, sperm culture and urethra swab), hormone analysis, folliculometre, sperm gram, HSG (in 11 women), anti spermatozoid antibodies (in 9 pairs and 6 women). By clinical examination we found the absence of inflammatory processes of the uterus and adnex.

Before starting of folliculogenesis stimulation, all female patients were examined by ultrasound (transvaginal ultrasound on the equipment Aloka SD 1700 color Doppler and Siemens Sonoline Versa Pro) on the second or third day of the menstrual cycle. Clomifen citrate was applied in doses of 50-100 mg / day during 5 consecutive days, starting from the third day of spontaneous or by gestagen caused menstrual bleeding. When at least one leading follicle diameter was 18 mm in diameter, ovulation was induced with 5 000 ij of Human chorionic gonadotropin (Pregnyl). Insemination was done 24-36 hours after of HCG application. Female patients abstained from food and drink at least 4 hours before the intervention. When the parameters of folikulometre became favorable, the intrauterine insemination was done. At the time of planned intervention, for that purpose specific catheter, 1.5 ml of previously prepared husband's seed was taken and brought it in the cavity of the uterus. After the intervention, 200 mgr of Cytotec was applied in the last fornix of vagina . After the insemination, 2 grams of a Longaceph was given,

intravenously, preventively. In 4 cases was given analgesic Novalgetol, from half an hour up to two hours after intervention, because of the pain in the bottom of the stomach and in adnex area.

Samples of sperm for insemination were prepared by “swim-up” technique. The “Sperm Rise” or “Swim-up” technique is one in which two to five cc of medium are carefully layered on top of 0.2-0.5 cc of semen. Motile sperm cells “swim-up” into the culture medium. After some time (30-90 minutes) the medium (containing motile sperm cells) is carefully harvested and centrifuged. If necessary, fresh medium is layered on top of the seminal fluid again to harvest more sperm cells.

Serum beta-hCG was determined 16th.day after insemination, in women who are not given period. Transvaginal ultrasound examination was done from 24 th. to 29 th .day after insemination

**RESULTS**

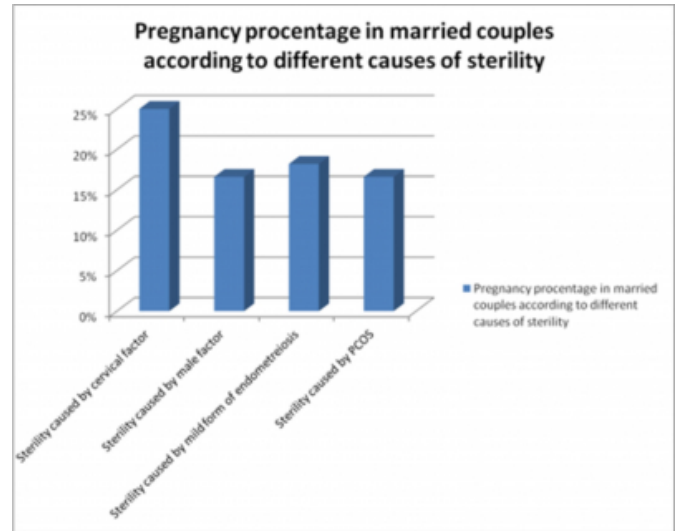
The pregnancy occurred in 4 female patients. Percentage of pregnancy was 10.8%, compared to cycles in which ovulation was confirmed, after which intrauterine insemination was done.

Percentage of pregnancy in married couples (Chart 2.), according to the different causes of infertility was:

- 1. Infertility caused by cervical factor 25%
- 2. Causes of male infertility 16.6%,
- 3. Mild or easy endometriosis 18.2% 4. Polycystic ovarian syndrome (PCOS)16.6%.

**Figure 2**

Chart 2. Pregnancy procentage in married couples according to different causes of sterility



In one female patient there was a miscarriage, after the successful insemination

Side effects of mild intensity that occurred in our female patients:

10 our female patients complained of pain immediately after the intervention, and three hours after the intervention.

4 our female patients required analgesics therapy.

3 female patients had nausea, also immediately after the intervention.

We had no serious complications.

**DISCUSSION**

Artificial insemination encompasses a variety of procedures. All involve the placement of whole semen or processed sperm into the female reproductive tract, which permits sperm–oocyte interaction in the absence of intercourse. The placement of whole semen into the vagina as a mode of fertility treatment is now rarely performed. Insemination is a method with a deep and strong medical logic. Mechanisms that could be included in the explanation of the efficiency of insemination are shortening the time (about 5-8 cm) that spermatozoa must undergo in natural conditions. In the case of a small number of spermatozoa and their poor mobility, this could be indeed a powerful argument in favor of insemination. In addition, the insemination is bypassing the vagina and cervix, whose secretions can be “hostile” oriented towards spermatozoa, whether it is about “acid”

vagina, cervical infection or the presence of antibodies. Manipulation of sperm, such as rinsing and conditioning, can also liberate sperm of poor quality seed liquid, antibodies, bacterial toxins etc.

The success of IUI is variable and depends on several factors: women age, the type of ovarian stimulation that is used, infertility duration, infertility causes, the number and mobility of spermatozoa, and from other factors. The success of IUI for women after 35 years is in significant decline, while in women over 40 years is very small. No pregnancy occurred in women older than 44 years or in cases with a total motile sperm count before semen preparation of  $< 1 \times 10^6$ .<sup>5</sup>

The sperm quality that is necessary for successful IUI is lower than World Health Organization threshold values for normal sperm. Intrauterine insemination is effective therapy for male factor infertility when initial sperm motility is  $> \text{or} = 30\%$  and the total motile sperm count is  $> \text{or} = 5 \times 10^6$ . When initial values are lower, IUI has little chance of success<sup>1</sup>. The number of motile sperm available for insemination and especially their 24-hour survival are highly predictive of IUI success. This advanced semen analysis is an excellent screening test to evaluate couples considering IUI<sup>2</sup>.

The success rate appeared is higher in the young female age group, short duration of infertility, secondary infertility, unexplained infertility, a higher number of motile sperm inseminated and dual insemination in a cycle<sup>3</sup>.

Advanced female age, poor postwash sperm motility, and a history of corrective pelvic surgery are significant risk factors for poor IUI success rates. Poor postwash sperm motility in combination with either of these other two risk factors resulted in no successful pregnancies<sup>4</sup>.

We opted for the method of IUI for all our female patients, by stimulating ovulation at the time of planned ovulation, with application of medications that enable us to program the time of ovulation, but always with the prior preparation of seeds, in order to achieve maximum of husband fertile potential.

Gynecologists practitioners agree that the efficiency of insemination is not large and it is in great inconsistent with the above mentioned theoretical considerations. For an explanation of the unexpected inefficiency of insemination probably are responsible mechanisms, which have not yet been sufficiently clear to us and the fact that insemination is

not a simple "collision" of egg cell and spermatozoid or mechanical penetration of spermatozoid into egg cell. Fructification is much more than that and represents a kind of cascade reaction between spermatozoid and the accompanying complex of egg cell and egg cells themselves. The essence of this process is series of receptive reactions of spermatozoa and pelucid zones (shell egg cell), as well as spermatozoid and egg cells, which are likely very compromised in patients who enter into the category of "suitable" for insemination, and these are usually patients with oligospermia, hypo sperm and astenosperm. Simply said, before the fertilization, spermatozoa must "present" to zone pelucidi and egg cell, or by their receptors "to unlock" the zone pelucidi and egg cell. To make matters more complicated, after penetrating the egg cell, sperm goes further "tests" which are again based on the interaction of complementary molecules. Any error or lack some of these phases, makes insemination unsuccessful. This could be an explanation for the discrepancy between the large medical logic and low efficiency of insemination.

Cytotec (Misoprostol) applied in the last fornix of vagina after insemination can improve aspirational movements of uterus and blood supply of endometrium, which is in base a function of prostaglandins in the sperm<sup>12</sup>.

IUI implies entering a specially prepared partner's sperm in the uterus, where a fundamental prerequisite for insemination represents passable fallopian tubes. The most common indication for insemination is reduced fertilizing man's power, small or weaker sperm mobility, unfavorable quality of cervical mucus or the presence of anti-spermatozoid antibodies, as well as unknown causes of infertility. It can be carried out in natural or stimulated cycle. With the monitoring cycle: Ultrasonic folliculometre, quality assessment (receptivity) of endometrium, (eg, 3D Angio / Doppler ultrasound examination) the level of estrogen and LH timing, the successfulness of this method is 7-20% (according to different authors)<sup>5</sup>.

IUI can be accompanied with some complications, which according to intensity and severity can be from mild to the very serious. Less severe complications include pain (contraction of the uterus), nausea, vomiting and fever. More serious complications include endometritis, adnex, tub ovarian abscess, parametritis and peritonitis. In a separate group of complications are allergic complications and even anaphylactic shock. Serious complications of insemination are extremely rare phenomenon. All complications are more frequent and more intense if the IUI has been done by

“untreated” sperm. The frequency and intensity of complications were significantly lower if insemination is performed by “treated” sperm.

We believe that our results, in the cases of the implementation of intrauterine insemination as one of the method of assisted reproduction, are satisfactorily and consistent with published results in the reference literature.

According to the results, we think that intrauterine insemination, as cheap and minimally invasive method, should be always carried out when certain conditions acquired, as one of the steps, in order to overcome the problems of primary or secondary sterility.

### CONCLUSION

IUI is usually the first step in treating couples with unexplained infertility.

Controlled ovarian stimulation, with intrauterine insemination, has proved successfully in the treatment of marital infertility, especially in cases of ovulation disorders, disorders of cervical factors, disorders of man`s sperm gram , mild forms of endometriosis and infertility of unknown causes.

IUI is a cheap and minimally invasive method compared to other methods of assisted reproduction. Numerous reports indicate that the pregnancy rate is much higher if IUI is combined with controlled ovarian stimulation. The IUI procedure is simple and may be performed even if the woman is not receiving medication to improve her egg production. Many physicians will encourage women to take medications to stimulate the ovaries in order to increase egg production and, hopefully, the chance of achieving pregnancy.

Although our work shows a small sample, we think that our results are in accordance with the reference and published in the literature, and that can be used successfully in evaluation of success of this assisted reproduction method ,in the treatment of marital infertility.

The success rate of IUI is 10% - 12% per cycle. It is recommended that 3 - 6 cycles of treatment are attempted before considering other options. Overall IUI pregnancy rates have increased from 5.8% per cycle in 1991 to 13.4%

per cycle in 1996, during which time the average age of patients undergoing IUI has increased from 36.1 ( $\pm 0.2$ ) to 39.2 ( $\pm 0.1$ ) years<sup>8</sup>.

Careful patient selection criteria coupled with successful ovarian stimulation is the model for IUI success<sup>9</sup>.

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