Fertility, Gynecology and Andrology
Volume 3 · Issue 1 · e136798

OPEN PEER REVIEW

The Effect of Probiotic Supplementation in Intrauterine Sperm Insemination Pregnancy Rate

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SUBMITTED	REVISED	ACCEPTED	DOI
10 Apr 2023	7 May 2023	9 May 2023	10.5812/fga-136798

About this report

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1 Original submission

1 comment · 18 Apr 2023

Associate Editor

MAJOR REVISION 18 Apr 2023

Dear Authors,
Please find attached the file containing the comments of the associate editor and the reviewers. Please answer the comments point by point and make the necessary changes.

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Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Greetings to the respected reviewers,

Thank you for your valuable comments.

The corrections you requested have been made.

Is the aim to examine the success of IUI or the pregnancy outcomes? Please clarify, because the abstract states pregnancy [outcome.

The effect of probiotic supplementation in intrauterine sperm insemination pregnancy rate

Describe the method completely: did you have two arms? What did you give to each of them? What were your outcomes?

In the intervention group, two weeks before IUI, Lactovage suppository was prescribed once per night, while in the control group, no extra interventions were done. All the patients underwent IUI in the same way. The primary outcomes of the .study were biochemical and clinical pregnancy rates

Because it was not significant, this sentence is not correct.

Conclusion: While the pregnancy rate in women with probiotic therapy was higher, it was not significant. Future randomized studies are needed to definitively examine probiotic therapy and establish its benefit in women candidates for IUI.

You submitted the article to a gynecology journal; there is no need to define IUI.

Removed.

What do you mean? The sentence is not understandable.

The reproductive tract microbiome of the male or female can impact fertility .functions such as implantation, and establishment of pregnancy (4, 5)

Are you sure?

The therapeutic potential of probiotic therapy remains an exciting opportunity in .IUI in improving vaginal microbiome and pregnancy outcomes

How did you prove this?

bacterial vaginitis (related symptoms or signs in the woman's complaint or physical examination)

The causes of infertility should be stated. The reason the patient was a candidate for IUI should be explained.

candidates for IUI (women with cervical or tubal abnormality, lack of ovulation, ,unknown or mixed infertility causes)

The randomization and allocation method should be explained further.

The eligible participants were allocated to the study groups (intervention or control) using the random allocation rule. First, 97 letters A and 97 letters B are written on special papers that are not marked inside. Then all of them are placed in a bag and for each patient, after obtaining informed consent, a paper is removed randomly and without replacement, and based on the letter written on it, the .desired intervention is performed for the patient

Which company is it from? The contents and dose of the drug.

Lactovage suppository capsule (Zisttakhmir pharmaceutical company, Iran) which include 10^9 CFU Lactobacillus rhamnosus and inulin was prescribed once per night ,(totally 14 capsules)

Why was a placebo not used?

There was no drug structurally similar to Lactovage, and producing a placebo would have increased the costs of the project.

What information did you collect? Explain the questionnaire.

Participants were asked to fill out a questionnaire about their demographic and obstetrics history, and their hormonal profile, including follicle stimulating hormone (FSH), luteinizing hormone (LH), thyroid stimulating hormone (TSH), and prolactin was investigated from the medical records.

How was the sample size calculated?

The sample size was calculated by considering the confidence limits of 95% and the error coefficient of 0.5%. Based on the sample size formula, 194 people (97 .women in each group) were selected

Be sure to explain that you monitored the patients for possible complications.

.Furthermore, the patient's monitoring was done for any possible complications

The reference for this definition should be cited.

Biochemical pregnancy was defined as a positive β-hCG blood test after the second week of IUI. Clinical pregnancy was defined as pregnancy sac observation .after the sixth week of IUI (13)

All abbreviations below the table should be explained, and all units should be stated.

Variable	Lactovag	Control	P-value
Marriage duration (yrs.)	6.4±4.09	6.31±3.1	0.867
Primary infertility (yrs.)	3.36±2.41	3.81±2.20	0.179
Women´s age (yrs.)	30.36±4.72	30.66±4.49	0.625
Women´s partner age (yrs.)	34.78±4.51	34.99±4.34	0.746
BMI (kg/m^2)	25.83±3.6	25.93±2.71	0.83
TSH (mIU/L)	2.63±1.46	2.7±1.62	0.738
FSH (mIU/mL)	5.96±2.48	6.09±2.37	0.707

PRL (ng/mL)	108.84±18.20	97.26±14.41	0.618

BMI: body mass index, TSH: thyroid-stimulating hormone, FSH: follicle-stimulating hormone, LH: luteinizing hormone, PRL: prolactin.

Is it possible to perform further analysis, for example regression or ....

Table 2 was added.

The reference should be cited.

Removed.

Please compare the results of every article that is cited with the results of your own work as well.

The results of this study showed that the biochemical and clinical pregnancy rate was higher in the women with Lactovage therapy, although this increase was not significant.

In line with our study, Moreno et al. (14) study demonstrated that the existence of an endometrial microbiota pathological modification which is considered a non-Lactobacillus-dominated microbiota is associated with poor reproductive outcomes including decreases in implantation, and clinical pregnancy. Furthermore, the ongoing pregnancy, and live birth rates were lower in those women while these rates were not evaluated in our study.

Although recent evidence indicated that the loss of lactobacilli dominance causes to infertility, preterm birth, maternal infections, and higher risk of sexually transmitted diseases (15-17), it seems using probiotic supplements can restore the vagina microbiota.

In this regard, a review study by Dai Z et al. (18) in 2015 in China showed that the use of probiotics and intestinal bacteria by affecting the metabolism of amino acids improves sexual performance, health, and fertility in both couples.

On the other hand, van Ostrom et al. (19) study showed that the prevalence of BV was higher in infertile women with tubal infertility causes, and probiotic therapy in addition to BV elimination, can improve their fertility outcomes (20). In our study, the tubal infertility causes were so rare, might result in no significant findings.

Old articles should be replaced; preferably, most articles should be from 2018 onward.

1. Alqawasmeh O, Fok E, Yim H, Li T, Chung J, Chan D. The microbiome and male infertility: looking into the past to move forward. Human Fertility. 2023 Apr 5:1-3.

4. Feng T, Liu Y. Microorganisms in the reproductive system and probiotic's regulatory effects on reproductive health. Computational and Structural Biotechnology Journal. 2022 Mar 30.

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6. Kavousi M, Ghaebi NK, Najafi MN, Mokaberinejad R, Feyzabadi Z, Salari R. The effect of a natural vaginal product based on honey on the success of intrauterine insemination (IUI) in infertility treatment. Avicenna journal of phytomedicine. 2019 Jul;9(4):310.

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9. Younge, N.; McCann, J.R.; Ballard, J.; Plunkett, C.; Akhtar, S.; Araújo-Pérez, F.; Murtha, A.; Brandon, D.; Seed, P.C. Fetal exposure to the maternal microbiota in humans and mice. JCI Insight 2019, 4, e127806.

2 Revision 1

0 comments

No public comments in this round.