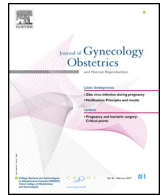




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Review

Immobilization versus immediate mobilization after intrauterine insemination: A systematic review and meta-analysis

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ABSTRACT

Introduction. – The objective of this systematic review and meta-analysis was to investigate a possible association between immobilization and pregnancy rate in patients undergoing intrauterine insemination.

Material and methods. – To ensure the quality of the methodology, the PRISMA criteria were met at all stages of the development of this meta-analysis. We searched the Cochrane Library, EMBASE, PubMed MEDLINE, ScienceDirect and reference lists of eligible studies from inception to March 2017, without any restriction. We also interviewed the ClinicalTrials.gov database for unpublished articles. Finally, we sought potentially eligible studies in meeting abstracts. Two reviewers independently extracted study characteristics and outcome data. Estimates were pooled using random effects models and sensitivity analyses. We selected studies that compared bed rest to immediate mobilization after intrauterine insemination. The primary outcome was the ongoing pregnancy rate per couple.

Results. – Of 176 identified abstracts, four primary studies, all of them randomized controlled trials, met the inclusion criteria, including 1361 couples. The overall relative risk of ongoing pregnancy rate in bed rest versus immediate mobilization was 1.67 95% CI [0.86; 3.22]. The overall relative risk of the live birth rate was 1.11 95% CI [0.56; 2.20].

Conclusion. – This systematic review and meta-analysis was not able to demonstrate that bed rest after intrauterine insemination effectively increases in pregnancy rate. For everyday practice, no specific strategy, bed rest or immediate mobilization, can be recommended at this time.

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Introduction

Background

Intrauterine insemination, a frequently used assisted reproductive technology [1], shortens the route traveled by sperm by short-circuiting the cervical canal. Prepared so as to maximize the number of mobile spermatozoa, the sperm is directly inseminated in the uterine cavity to facilitate the encounter with the oocyte [2]. This is followed by immediate mobilization or a period of bed rest in the supine position, depending on the medical team [3–6]. There is no consensus regarding the length of this bed rest, but conventionally it is 10 to 20 minutes [3–6].

In natural conception, the sperm is subject to physical stress during ejaculation and female genital tract contractions, which produces oxidative damage [7]. Only one hundred sperm reach the fallopian tube [2]. In intrauterine insemination, the sperm is prepared before insemination and is washed from the particles of seminal fluid, mimicking what happens when the sperm passes through the female genital tract in natural conception [8]. More than one million prepared spermatozoa at least must be inseminated in the uterine cavity in according to increase the pregnancy rate [8].

Studies evaluating sperm transport through the female genital tract show that sperm reaches the fallopian tube about 2 to 10 minutes after ejaculation [9–12]. These data suggest that sperm migration at the fertilization site is independent of position. Until now, studies have yielded conflicting results and the question of the association between immobilization after intrauterine insemination and pregnancy rate has remained unresolved: an

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association between immobilization and pregnancy rate has been found in some [3–5] but not all [6] studies.

Objective

In view of the current controversy, we used a systematic review and meta-analysis of the literature to investigate a possible association between immobilization and pregnancy rate in patients undergoing intrauterine insemination.

Materials and methods

To ensure the quality of the methodology of this work, the PRISMA guidelines [13] were followed at all stages of design, implementation, and reporting (Table A).

Search methods for the identification of studies

We systematically searched PubMed (with and without keywords Medical Subject Headings MeSH), EMBASE, ScienceDirect, and the Cochrane Library from inception to April 1st, 2017. The search was initially done without restriction with regard to language, study design, or publication date. We also interviewed the ClinicalTrials.gov database for unpublished articles. We finally sought potentially eligible studies in the abstracts of meetings of the European Society of Human Reproduction and Embryology (ESHRE) and the American Society for Reproductive Medicine (ASRM). Consequently, the searches covered the vast majority of relevant journals and congresses. Search terms included: “intrauterine insemination, IUI, bed rest, immobilization, supine position, immediate mobilization, immediate ambulation, pregnancy rate”.

Eligibility criteria

Selection criteria were determined before data collection. We selected studies that met our inclusion criteria: randomized controlled trials, case-control or cohort studies published in English that compare bed rest with immediate mobilization after intrauterine insemination, with a view to improving the pregnancy rate. We searched electronic databases (PubMed, EMBASE, ScienceDirect, and the Cochrane Library) and meeting abstracts (ESHRE, ASRM). Reviews, editorials, letters, case reports, and substudies of eligible studies were not selected.

The primary outcome was the ongoing pregnancy rate per couple, defined as a viable intrauterine pregnancy, determined by a fetal heart beat on transvaginal ultrasound at 12 weeks of gestation [4]. The secondary outcome was the live birth rate.

Study selection and data extraction

Two independent reviewers (D.C., R.C.) screened all titles and abstracts and obtained full-text reports for those considered potentially eligible. Only randomized controlled trials were included. We found no case-control or cohort study in the literature. Each trial was ranked based on methodological rigor and potential introduction of bias. Data were independently extracted by two investigators (D.C., R.C.) and were analyzed for originally reported characteristics, randomization method, and calculation of statistical power. The results of both reviewers were compared.

Statistical analysis

We used random effects models, according to the method of DerSimonian and Laird [14]. Relative risk (RR) was more than 1 for

a favorable effect on pregnancy rate of bed rest after intrauterine insemination. Heterogeneity was measured by the I² statistical test [15]. Measures of association (RR) were performed with the use of Review Manager software (RevMan) [computer program]. Version 5.3. Copenhagen: the Nordic Cochrane Centre, the Cochrane Collaboration, 2014 was used for statistical analysis.

Results

Literature flow chart

Our literature search identified 176 potentially eligible articles, in PubMed MEDLINE ($n = 6$), EMBASE ($n = 153$), the Cochrane Library ($n = 8$), ScienceDirect ($n = 25$), and conference abstracts ($n = 1$) from 1993 to July 5, 2016. Finally, 4 studies were included in the quantitative analysis (Fig. 1). Two studies were found in PubMed [3,4], one study was found in ScienceDirect [5], and one study was found in an abstract from the ESHRE 2016 Annual Meeting [6].

Study characteristics

The 4 studies were published between 2000 and 2016 (Table 1) and were all designed as a random control trial ($n = 4$) [3–6]. The time of bed rest after intrauterine insemination varied from 10 to 20 minutes. The immobilization group and immediate mobilization group were comparable in all studies. The ongoing pregnancy rate was calculated in each study. The inclusion criteria were comparable in the different studies. Intrauterine inseminations were performed after a spontaneous cycle or stimulated cycle with clomiphene citrate, or recombinant or urinary follicle stimulating hormone. Follicular growth was monitored by transvaginal ultrasound alone or transvaginal ultrasound associated with blood sampling. Ovulation was triggered by HCG in each study and women were inseminated between 36 and 40 hours later with prepared sperm. The sample sizes of the four selected studies varied from 95 to 479 couples, for a total of 1361 couples.

Visual examination of the funnel plot (Fig. 2) revealed mild asymmetry, with more positive small studies published than negative studies, which is a typical publication bias. The quality was good, as all studies included were randomized controlled trials (Table 2). The only bias found was the blinding of both patients and physicians.

Effect of intervention

Ongoing pregnancy rate

The RR of the ongoing pregnancy rate was 2.91 95% CI [1.05; 8.04] in Saleh et al., 1.53 95% CI [1.05; 2.24] in Custers et al., and 3.50 95% CI [1.46; 8.39] in Orief et al., and was statistically significantly in favor of bed rest. However, Van Rijswijk et al. report an RR of 0.80 95% CI [0.63; 1.02] in favor of immediate mobilization, though statistical significance was not reached. The overall RR of ongoing pregnancy rate in bed rest versus immediate immobilization was 1.67 95% CI [0.86; 3.22] (Fig. 3).

Live birth rate

The live birth rate in the bed rest group was calculated in two studies [4,6]: it increased significantly in the first study [4] but decreased in the second [6]. The overall RR of the live birth rate was 1.11 95% CI [0.56; 2.20] (Fig. 4).

Discussion

Main findings

This meta-analysis demonstrated no statistically significant association between bed rest and ongoing pregnancy rate. Until

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