Review of: "Comparative Study between Using Only Vaginal Misoprostol and Using Vaginal Misoprostol and Estradiol Cream for Induction of Labour: Randomized controlled trial"

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Potential competing interests: The author(s) declared that no potential competing interests exist.

The study proposed by Mortada et al. is a randomized clinical trial. The objetive of the study is to verify if labor induction with misoprostol+estradiol is superior to misoprostol alone. The end point is not properly defined and the authors are fully aware of all the requirements from the CONSORT guideline.

The study is underpowered and there are many confounding factors that were not considered. Althought their efforts were worthy to be praised, it falls short to provide high quality evidence.

Next, I provide an explanation why their work should be rejected.

Clinical Trial REgistration and data sharing: High quality RCTs need to be registered, for example ClinicalTrial.gov, before initiating the trial.

Data should be share ina public repository, as GitHub or Harvard Dataverse.

Neither of these were observed.

The CONSORT guidelines is marginaly used by the authors.

Introduction

The rationale for the study is not provided. The article from Dasgupta et al (Reference 6) was cited and no explanation was given why this trial should be repeated.

Material and Methods

The authors should use subheadings

Trial design

Is this a superior, non-inferiority or equivalence trial? Please clarify.

Changes to the trial design

Were changed made in the trial, compared to original design? Please clarify.

I believe it will be hard to show, since the trial registration was not provided.

Participants

The inclsion criteria are provided, but not in details.

> *Eligible patients (according to our inclusion criteria which were female patients with gestational age from 36 - 41 weeks, with singleton living fetus < 4 k.gs with cephalic presentation, had no labor pain, or liquor abnormalities with Bishop score < 5), were randomly allocated to one of two treatment arms in a single-blind manner by the computer-generated system.*

How gestational age was confirmed? Induction of labor with 36 weeks is not adequate, unless there are medical indications. Please provide explanation.

How the fetal weight was defined?

Please correct liquor to amniotic fluid (AF).

The term abnormal AF is vague. The presence of thick meconium is an abnormality that cannot be seen in clised cervix.

Bishop score is a common score for unfavourable cervix. However, cervix dilatation is another problem. You may have a 4 cm dilated cervix, and a closed cervix, and both can be Bishop <5.

Exclusion criteria should be expanded. Please prvide more information about

> *abnormal umbilical artery Doppler indices or non-stress test,*

Study settings

Please, provide the day when it started and ended. Where is Ain Shams University Maternity Hospital? In which country?

> *April 2021 to October 2021 at Ain Shams University Maternity Hospital*

Interventions

It is not clear how the cream was applied with the misoprostol. All patients had an especular exam?

Did the cream was weighted, using a digital scale ?

Figure 1 does not provide information about the digital scale.

Outcomes

If the inclusion criteria is open for criticism, the outcome is vague too. If the authors want to use just the BISHOP score or the 6 cm dilatation of the cervix?

Who timed the period of the study from start until the outcome?

Who examined the patient's cervix to determine if they reached the outcome? It is mentioned

> *Neither women nor the staff was known whether the woman under observation was assigned to only misoprostol or misoprostol with estradiol group.*

Please clarify, since misoprostol was added every 4 hours.

Changes to outcomes

Any changes to trial outcomes after the trial commenced, with reasons

Sample size

I redid the sample size calculatin and the resutls were different. For a superior clinical trial, using a SD of 3.76, sample size would be 40 in each group; however, the higher SD should be applied (5.27); the sample size should be 79 in each arm.

However, the authors do not provi de SD of their results, which makes the sample size calculation impossible.

Randomization sequence generation

It was not informed. This is a crucial topic.

Randomization type

It was not informed. This is a crucial topic. Was it made in blocks of 4? 1:1 ratio?

Randomization allocation concealment mechanism

It was not informed. This is a crucial topic.

Randomization implementation

It was not informed. This is a crucial topic.

Blinding

Although the authors wrote

> *The repeated doses, evaluation and labor were done by the supervisors and expert staff. Neither women nor the staff was known whether the woman under observation was assigned to only misoprostol or misoprostol with estradiol group.*

It is not clear who check the outcome.

Similarity of interventions

If relevant, description of the similarity of interventions. E.g., a water based gel was added to the misoprostol alone group.

RESULTS

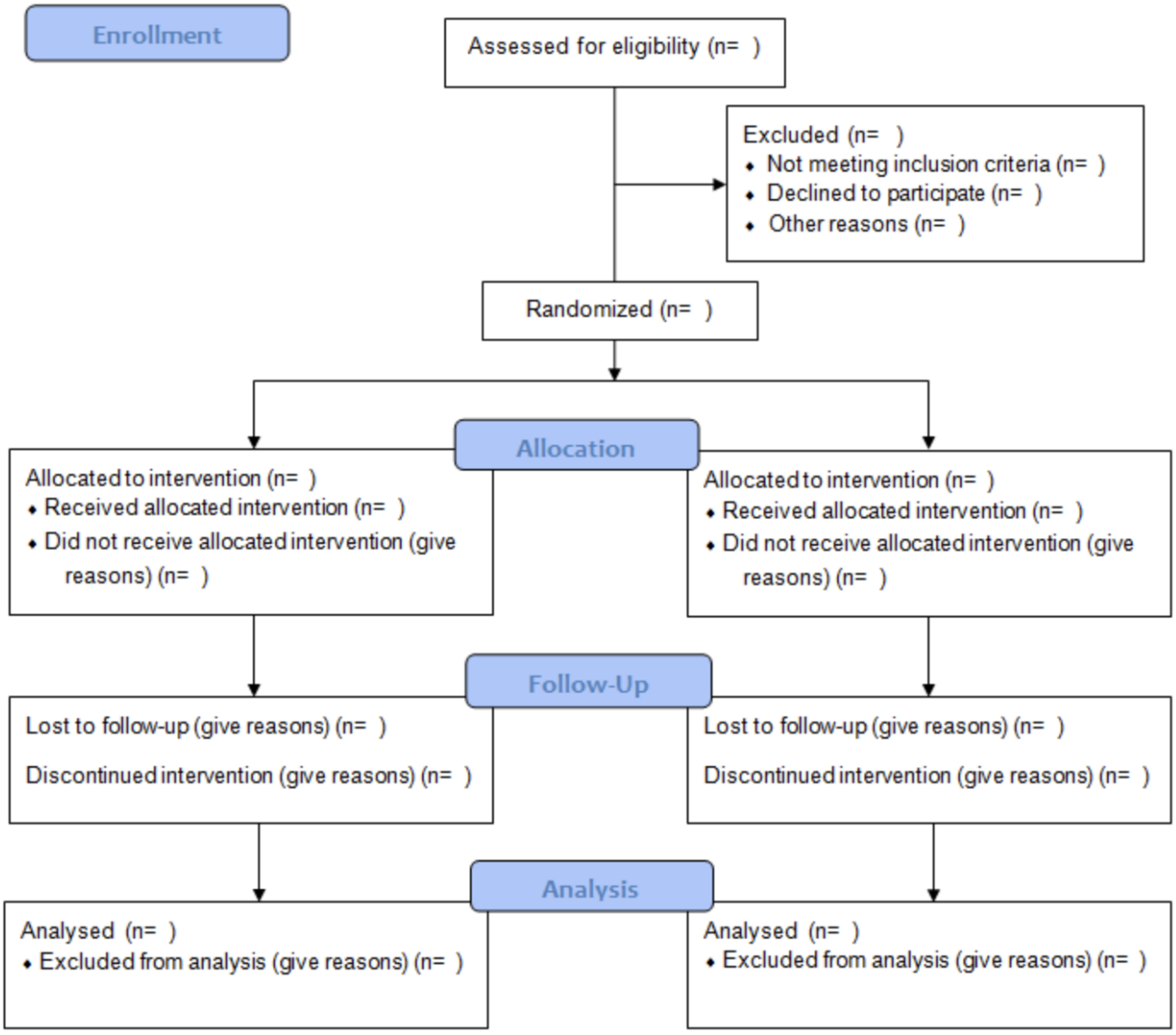
After reading the results, it is clear that other factors were included without further explanation;

> *Among 32 patients in the active phase in the misoprostol group, there were 22 patients (68.8%) received oxytocin with a median time of 5.0 (4.0 - 6.0) hours while Among 38 patients in the active phase in the estradiol group, there were 25 patients (65.8%) received oxytocin with a median time of (5.0 (4.1 - 6.8).*

What were the indications for the use of oxytocin? to perform the rupture of membrane?

There are many data that were interesting, but not necessary linked to the study and it brings doubt about the study. Let's considere a case where the patient started with misoprostl, BISHOP 0, after 4 hours the fetus developed a non reassuring condition and an urgent C-section was done. How this outcome was considered?

Figure 1 is not properly used. Please provide accordingly



Why the authors do not provide mean and SD of their outcome.

Discussion

I suggest the authors understand how to write a discussion section.

Describe the main findings according to the objective. compare their results to the literature. Give explanations for

similarities and differences

Give limitations

Give positive aspects

New opportunities for research from this study.