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# Effect Of Altering Vaginal Ph On Induction Of Labour In Full-Term Pregnancies Using Misoprostol

Obstetrics & Gynecology

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**ABSTRACT**

**Background:** Labor induction is commonly used in United States as obstetrical technique. Absence of favorable cervix leads to decrease in success of vaginal birth.

**Aim of the work:** Increase the success rate of the labor induction process using misoprostol through changing vaginal pH and studying the effects.

**Patients and methods:** This randomized controlled trial was performed at the Department of Obstetrics and Gynecology (Said Galal Hospital – Faculty of Medicine, Alazhar University). The trial enrolled 180 healthy pregnant women who attended for pregnancy termination. All of the participants signed their informed consent to take part in the trial. Women were divided amongst 3 groups as follows, (using vaginal douche pumps): Group A: took a vaginal douche of 100 ml normal saline solution (NaCl 0.9%). Group B: Took a vaginal douche of 100ml sodium bicarbonate 5% solution. Group C: took a vaginal douche of 100ml acetic acid 5% solution.

**Results:** On induction with Misoprostol, douching the vagina with acid had the best results, with Group C taking the shortest time (20.46 hours) to reach active stage of labour, followed by Group A (21.45 hours), and finally Group B. (22.59 hours). With a P-value of 0.013, the difference between the groups was statistically significant.

**Conclusion:** Washing the vagina with an acidic solution appears to enhance Misoprostol's effect in inducing labour in full-term pregnancies, as evidenced by the minimal mean time to obtain active labour stage.

**Keywords:** *Misoprostol; induction of labour; full-term pregnancies; vaginal pH.*

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## INTRODUCTION

Misoprostol originally marketed as a treatment for peptic ulcers, then it has been used to augment the effectiveness of abortion and labor induction. Although the US Food and Drug Administration does not approve the use of misoprostol for this use officially, pregnancy was removed from the label as an absolute contraindication [1] Furthermore, its relatively low cost, widespread availability and lack of need for refrigeration render it a valuable tool in common obstetric practice [2].

Although initially known as oral tablets, this drug is also commonly used as a vaginal suppositories. Before taking these tablets, they should be thoroughly humidified. And according to the pharmacokinetics of the drug, it should liquefy better in an acidic medium [3].

There are studies discussing the efficacy of misoprostol in different pH media in 1st [4] & mid-trimesteric abortions [5,6]. Despite this, there is limited research on its effect in labor induction [1].

The goal of our research was to see how changing vaginal pH affected misoprostol-induced labour in full-term pregnancies.

## PATIENTS AND METHODS

This randomized controlled trial was carried out at Al-Azhar University's Faculty of Medicine's Said Galal University Hospital..

Between January 2021 and July 2021, 180 healthy term pregnant women who were scheduled for pregnancy termination were enrolled in the study. All of the participants signed their informed consent to take part in the study.

As three distinct procedures were matched, a constant variable was examined. According to Ramsey et al. [1]; he conducted similar research on the required time from the start of the induction process until the active stage of labour in two groups and discovered that the mean time for the first group was 16.3 hours and the mean time for the second group was 17.1 hours, with a standard deviation of 1.4. The total sample size was 180 people, divided into three groups of 60 people, with a power index of 80% and a type 1 error rate of 5%.

Patients included in the study had cephalic singleton pregnancies with gestational age 40-41 weeks, and was primigravidas and second gravidas, fetal weight less than 4kgs, lack of spontaneous uterine contractions, a Bishop score less than 4, reassuring non-stress test, vaginal pH [7] and with sufficient pelvic outlet.

We had excluded the following, non singleton pregnancy, previous CS, ROM or Polyhydramnios, fetal weight more than 4kgs , vaginal pH more than 4.9, prostaglandins hypersensitivity, cases who failed induction for any other cause other than unsuccessful ripening, for e.g. fetal suffering or arrest of progress due to malposition, history dependent cause (cardiac disease, neurological disease, congenital anomalies,etc ) and contracted pelvis.

After achieving inclusion and exclusion criteria, we divided patients into 3 groups: Group A: the acid group, Group B : the alkaline group, and Group C: the normal saline group. Randomization was done using a closed-envelope system and a computer-generated model. After the woman was registered, the ward nurse opened the envelope.

Initial Modified Bishop score was evaluated for all women after registeration in their corresponding sets and the data noted. Non-stress test was performed for all participants if reassuring go to the following test, if not reassuring we exclude this patient.

Patients took their initial 100ml vaginal wash according to their corresponding sets using a douche pump.Normal saline solution (0.9 % ) was previously available in 500ml bottles.Acetic acid was utilised at a concentration of 100% before being diluted to a concentration of 5%. This was done by using a pipette to take 5ml of the solution and combining it with 95ml distilled water in a bottle measuring beaker to make 100ml of acetic acid 5% for vaginal douching. Sodium bicarbonate salt was used to make a 5 % $NaHCO_3$ solution.

They were subsequently given 25 micrograms of Misoprostol E1 (Vagiprost® Adwia Pharmaceuticals, Egypt) every six hours with a 24-hour restriction (total of 4 conceivable doses). Before each dose, 100ml of the relevant solution was washed once more.

Modified Bishop score and the cervical length had been recurring at 4- hourly breaks, till the active stage. The Modified Bishop involves the same principle but has replaced the assessment of effacement with reassessing the cervical length using TVS.

| Points | 0 | 1 | 2 | 3 |
|---|---|---|---|---|
| Cervical Length via TVS (cm) | >4 | 2-4 | 1-2 | <1 |

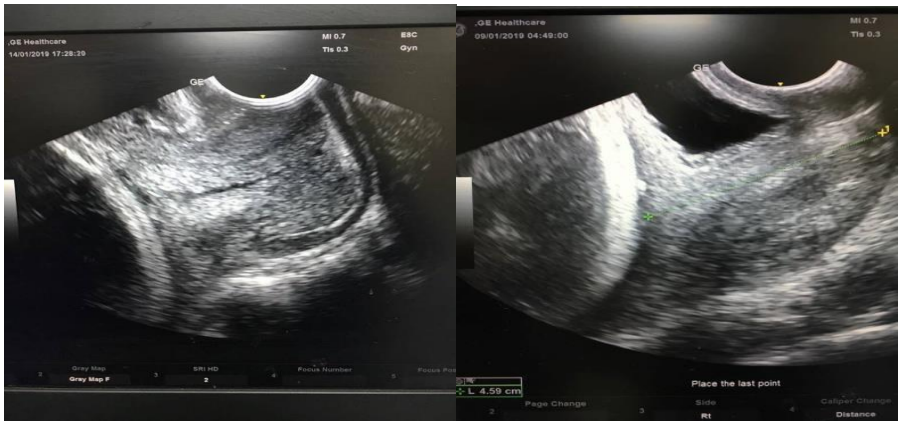


**Fig. 1:** Cervical length seen being measured by TVS.

When active stage of labor was reached, considering Modified Bishop score as less as 6, patients took an identical oxytocin augmentation protocol when needed. If after 24 hours active stage was not reached, the induction process was discontinued, and the on-call consultant was informed to decide on the appropriate treatment regimen.

| Bishop 1 (4hrs after start of induction) | Bishop 2 (8hrs after start of induction) | Bishop 3 (12hrs after start of induction) | Bishop 4 (16hrs after start of induction) | Bishop 5 (20hrs after start of induction) | Bishop 6 (24hrs after start of induction) |
|---|---|---|---|---|---|
| | | | | | |

**Table 1:** Serial Modified Bishop Scoring:

| Cervical Length 1 (mm) (4hrs from the beginning of induction) | Cervical Length 2 (mm) (8 from the beginning of induction) | Cervical Length 3 (mm) (12hrs from the beginning of Induction ) | Cervical Length 4 (mm) (16hrs from the beginning of induction) | Cervical Length 5 (mm) (20hrs from the beginning of induction) | Cervical Length 6 (mm) (24hrs from the beginning of induction) |
|---|---|---|---|---|---|

**Table 2:** Serial cervical length measurement:

**Statistical Methods:**
The statistical package (SPSS) was used for data entry and encryption. It was designed to analyze the relative frequencies and mean deviation of various quantitative and qualitative variables. And to compare groups ANOVA (analysis of variance) method was used. Although Chi square test was done to compare categorical data.

## RESULTS

During the time between January 2021 and July 2021 at the Obstetrics and Gynecology Department, Said Galal hospital, Faculty of medicine Al-Azhar University, we recruited 180 healthy term pregnant women in our study and split them into 3 groups; Group A: was commenced on normal saline (NaCl 0.9%), Group B: was commenced on alkaline solution (sodium bicarbonate 5%) and Group C: was commenced on acidic solution (acetic acid 5%). The following clarifies the spreading of their demographic data.
**Maternal age**: all recruited women of the 3 groups are of the same age group with mean (21.09) for group A, (21.8) for group B and (22.31) for group C

**Gestational age:** according to inclusion criteria, the study is conducted to full-term pregnancies 40 weeks and 41 weeks only so the mean ranges of gestational age of the three groups are so close.

**Estimated fetal weight:** all recruited participants had average range of fetal birth weight. Mean EFW for group A is (3.385), for group B is (3.260) and for group C (3.242).

**Parity:** across different groups primigravidas represented a minimum of 60% of participants in each individual arm of the study (Group C to be precise), whilst second gravidas only represented 11% of participants in Group B. This tells us that the majority of postterm pregnancies are more likely to occur with primigravidas, rather than multiparous patients.

| | | Solution | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | Group A (n=60) | | Group B (n=60) | | Group C (n=60) | | P value |
| | | Mean | SD | Mean | SD | Mean | SD | |
| Age (years) | | 21.09 | 2.40 | 22.31 | 3.50 | 21.80 | 3.48 | 0.095 |
| Gestational Age (weeks) | | 40.61 | 0.49 | 40.78 | 0.42 | 40.69 | 0.47 | 0.109 |
| EFW (kilograms) | | 3.385 | 0.277 | 3.260 | 0.245 | 3.242 | 0.276 | 0.082 |
| Parity | PG | 49 (81.6%)) | | 53 (88.3%) | | 36 (60%) | | ----- |
| | P1 | 11 (18.4%) | | 7 (11.7%) | | 24 (40%) | | |

**Table (3)**: Patient Characteristics across the study.

| | Solution | | | | | | |
|---|---|---|---|---|---|---|---|
| | Group A | | Group B | | Group C | | P value |
| | Mean | SD | Mean | SD | Mean | SD | |
| 1st Bishop score (at 4 hours) | 3.38 | 0.81 | 3.09 | 0.85 | 3.75 | 1.28 | 0.001 |
| 2nd Bishop score (at 8 hours) | 4.09 | 1.23 | 3.50 | 0.99 | 4.70 | 1.51 | < 0.001 |
| 3rd Bishop score (at 12 hours) | 4.97 | 1.69 | 4.19 | 1.18 | 5.50 | 1.72 | < 0.001 |
| 4th Bishop score (at 16 hours) | 5.66 | 1.93 | 5.14 | 1.70 | 6.35 | 1.87 | 0.002 |
| 5th Bishop score (at 20 hours) | 6.12 | 2.24 | 5.58 | 2.11 | 6.79 | 2.00 | 0.035 |
| 6th Bishop score (at 24 hours) | 4.00 | 0.86 | 3.90 | 0.76 | 4.33 | 0.65 | 0.267 |

**Table (4)**: Serial Modified Bishop Scores assessment in the 3 solution groups.
Moreover, there was no significant statistical difference (P-value 0.267) between the mean readings at the 6th measurement for failed induction participants, meaning that they all had similar Bishop Scores after 24 hours, regardless of the type of solution used in induction of labor.
**Serial cervical length measurements:** As already seen with the Bishop scores, the measurements at the 1st cervical length are already statistically significant in favour of Group C and are consistent in that regard throughout all readings.
From the 1st to 5th cervical length, the length of the cervix is shown to decrease steadily, indicating an improvement in cervical effacement as it is incorporated into the lower uterine segment.
The only exception to this is the 6th cervical length, for reasons previously mentioned with the Bishop Scores. However, in this case, the cervical lengths for Group C participants are significantly shorter than the other two groups (P-value 0.002). Despite this, all measurements taken at this stage are for those who failed the induction attempt.

| | Solution | | | | | | |
|---|---|---|---|---|---|---|---|
| | Group A | | Group B | | Group C | | P value |
| | Mean | SD | Mean | SD | Mean | SD | |
| 1st Cervical length (in mm, taken at 4 hours) | 34.80 | 3.75 | 36.94 | 3.58 | 36.77 | 6.64 | 0.023 |
| 2nd Cervical length (in mm, taken at 8 hours) | 32.38 | 4.37 | 35.13 | 3.81 | 32.67 | 6.94 | 0.005 |
| 3rd Cervical length (in mm, taken at 12 hours) | 29.52 | 5.62 | 32.70 | 4.42 | 29.05 | 6.86 | 0.001 |
| 4th Cervical length (in mm, taken at 16 hours) | 27.00 | 6.58 | 29.87 | 6.34 | 26.37 | 6.54 | 0.008 |
| 5th Cervical length (in mm, taken at 18 hours) | 25.95 | 7.86 | 28.58 | 7.13 | 24.47 | 6.58 | 0.028 |
| 6th Cervical length (in mm, taken at 24 hours) | 33.40 | 3.59 | 34.33 | 2.76 | 30.08 | 4.17 | 0.002 |

**Table (5)**: Serial cervical length measurements in the 3 groups.

This Figure shows the serial cervical lengths portrayed in the form of a line chart. It is evident that in all cases the cervical length decreases, but with Group C, the gradient of the slope is steepest. This tells us that the rate of decrease in cervical length (cervical effacement) is also greatest in Group C.

| | Solution | | | | | | |
|---|---|---|---|---|---|---|---|
| | Group A | | Group B | | Group C | | P value |
| | Mean | SD | Mean | SD | Mean | SD | |
| **Time to active stage (hours)** | 21.45 | 3.00 | 22.59 | 2.58 | 20.46 | 3.77 | 0.013 |

**Table 6**: Mean time till reaching active stage of labor.

The above helps illustrate the data related to our initial result. Group C needed the minimal time till active stage of labor was reached.

| | Solution | | | | | | |
|---|---|---|---|---|---|---|---|
| | Group A | | Group B | | Group C | | P value |
| | Mean | SD | Mean | SD | Mean | SD | |
| **Total time to delivery (hours)** | 26.30 | 3.31 | 26.78 | 3.50 | 26.50 | 3.26 | **0.716** |

**Table 7**: Total time taken to delivery.

**Results of the induction trials:** Group C shows the hightest success rate (80%) as 48 of 60 participants proceeded to labor, while only 12 cases who failed induction and required C.S

| | Solution | | |
|---|---|---|---|
| Participants who | Group A (n=60) | Group B (n=60) | Group C (n=60) |
| Proceed to labor (rate) | 40 (66.6%) | 30 (50%) | 48 (80%) |
| Failed induction (rate) | 20 (33.3%) | 30 (50%) | 12 (20%) |

**Table 8:** Results of the induction trials

## DISCUSSION

Firstly, no statistical significance was seen throughout our data's demographic range. The P-value for comparing the mean age of the three groups is 0.095, whereas the P-value for comparing the mean gestational age is 0.109. Finally, With a P-value of 0.013, the variance between the groups was statistically significant.

Acid solution has had a visible impact on shortening time till reaching active stage of labor in our participants. The acid group took the minimal time (20.46 hours), then saline group (21.45 hours) and finally the alkaline group (22.59 hours) to attain active stage of labor. The variance between the 3 groups was statistically significant and promotes our study with a P- value of 0.013.

Karim and coworkers [3], studied the effect of antacid intake with oral Misoprostol administration and found that when misoprostol was administered with an antacid, there was no significant change in the rate of absorption, but the bioavailability was reduced by about 16%. Now although our study involves a different route of administration of the drug, they both support similar outcomes.

Participants in our study who recieved normal saline solution instead of alkaline solution during induction got to the active stage of labour faster (mean of 21.45 hours) than those who received alkaline solution (mean of 22.59 hours), confirming our findings.

Behrooz and coworkers [5] conducted a trial using many of the same variables as Karim et al., with the exception of the acetic acid concentration, which they utilised at a 3 percent concentration. Group A took shorter time to cause abortion than group B (12.68 hours vs 23.98 hours, P 0.001).

Finally, our study's main focus was on induction patients who delivered vaginally. Those who delivered by Caesarean section for any reason other than failed ripening, (for e.g. fetal distress) were excluded from our study.

## CONCLUSION

Misoprostol's effect on induction of labour in full-term pregnancies is supported by the fact that it takes the least amount of time to reach the active stage of labor in acidic media.

This information can be used to improve the induction process and reduce the number of Cesarean sections around the world, particularly in Egypt, where Cesarean section rates have been reported to have reached an all-time high of 63 percent, according to some recent research.

Testing could involve different forms of weak acid, other than acetic acid, such as citric (C6H8O7) or formic (CH2O2) acid and we could alter the preparations used to allow different concentrations to be tested.

Finally, we also recommend measuring the vaginal pH before each wash, instead of only with the initial douching. This will help assess whether the vaginal pH was maintained at the desired level or not after each wash and if we would possibly need to increase the frequency of douching.

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