Original Article

Effect of Progesterone Therapy versus Diet Modification on Constipation during Pregnancy

Mohamed M. Farghali[1,2], Ibrahim A. Abdelazim[1,3], Ahmed M. Awadalla[1], Amr A. Aziz Khalifa[1], Yasser Elshehawy[1], A. E. Omu[4], Assem A. M. Elbiaa[1,2]

[1]Department of Obstetrics and Gynecology, Ain Shams University, Cairo, Egypt, [2]Department of Obstetrics and Gynecology, Sabah Maternity Hospital, [3]Department of Obstetrics and Gynecology, Ahmadi Hospital, Kuwait Oil Company, Ahmadi, [4]Department of Obstetrics and Gynecology, Faculty of medicine, Kuwait University, Kuwait

ABSTRACT

Background: Pregnant women may experience constipation for the first time or their existing constipation symptoms increase in severity during pregnancy. **Aim:** To compare the effect of progesterone versus diet modification in the treatment of constipation during pregnancy. **Subjects and Methods:** Women aged ≥18 years with functional constipation according to the Rome III criteria from obstetrics outpatients' clinic and midwife practices included in this study. Participants divided into two groups; control group managed with diet modifications and study group pregnant women with threatened miscarriage and advised to take vaginal progesterone ≥1 week. Participants completed a nonvalidated questionnaire created by the authors during the whole week before intake of progesterone or diet modifications and after treatment phase. Independent Student's t-test and Chi-square (χ^2) test were used for statistical analysis to compare between two studied groups. Primary outcome measures; change in defecation frequency. **Results:** Sensation of anorectal obstruction and sensation of incomplete evacuation were significantly less in Group B (progesterone therapy) compared to Group A (diet modification) (54% [154/281] and 62.98% [177/281] vs. 89.76% [614/684] and 91.08% [623/684], respectively) ($P = 0.04$ and 0.03, respectively). Straining during defecation and manual maneuvers to facilitate evacuation were significantly less in Group B compared to Group A (63.7% [179/281] and 19.9% [56/281] vs. 94.59% [647/684] and 86.54% [592/684], respectively) ($P < 0.01$ and 0.02, respectively). Episodes of abdominal pain and presence of reflux episodes were also significantly less in Group B compared to Group A (18.5% [52/281] and 17.43% [49/281] vs. 84.11% [589/684] and 75% [513/684], respectively) ($P = 0.01$ and 0.03, respectively). **Conclusions:** Estrogen, rather than progesterone, may be a detrimental factor of constipation during pregnancy via decreased bowel movement. Progesterone therapy seems to be effective in the treatment of functional constipation during pregnancy. A randomized placebo controlled trial is required to confirm the data of this study.

KEY WORDS: Constipation, diet modification, pregnancy, progesterone

INTRODUCTION

Constipation is a very common clinical problem.[1] Pregnant women may experience constipation for the first time or their existing constipation symptoms increase in severity during pregnancy.[2]

The reported prevalence of constipation in pregnant women varies between 11% and 38% and occurs mostly during the third trimester, although symptoms can also be present from 12 weeks' gestation.[3] Constipation due to infrequent bowel movements or difficult passage of stools is a common cause of painful defecation and fecal impaction.[4]

Address for correspondence
Prof. Ibrahim A. Abdelazim,
Department of Obstetrics and Gynecology, Ain Shams University, Cairo, Egyptand Ahmadi Hospital, Kuwait Oil Company, Ahmadi, Kuwait.
E-mail: dr.ibrahimanwar@gmail.com

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Constipation usually manifested by straining during defecation, lumpy or hard stools, sensation of incomplete evacuation or anorectal obstruction, manual maneuvers to facilitate defecation, and/or less than three defecations per week.[5]

The pathophysiology underlying functional constipation is undoubtedly, multifactorial, and not well understood. Progressively, rising progesterone and estrogen levels have suggested as the cause of constipation during pregnancy.[6]

Besides discomfort of constipation symptoms, straining during defecating can damage the pudendal nerve and impair the supportive function of the pelvic floor musculature.[7] Furthermore, disturbed defecation can result in the development of uterovaginal prolapse.[8]

Therefore, it is important to recognize the symptoms of constipation and treat these complaints in early pregnancy. In clinical practice, laxatives and fiber are frequently used. Nowadays, there are few effective interventions published preventing or treating constipation during pregnancy.[9] There is weak evidence that increased fiber intake treating or improves constipation during pregnancy.[9] Vazquez conducted a systematic review and found that stimulant laxatives may be more effective than bulk laxatives in improving constipation in pregnancy, although adverse effects, such as abdominal pain and diarrhea, could limit their use.[10]

In addition, Vazquez found that dietary fiber may improve constipation in pregnant women compared with placebo and it is not clear whether increasing fluid intake improves constipation in pregnancy or not.[10]

Although progesterone has been the hormonal explication for many gastrointestinal symptoms that occur in pregnancy, including constipation, a recent study suggested the possibility that estrogen rather than progesterone may be responsible for the delay in gastric emptying and constipation in pregnancy.[11]

Oh *et al.* showed that administration of estrogen-induced constipation via a decrease in a bowel movement in mice but progesterone did not.[11] Oh *et al.* conclusion does not show agreement with the reports suggesting that progesterone is an important risk factor for constipation in women.[11-15]

This study designed to compare the effect of progesterone versus diet modification in the treatment of constipation during pregnancy.

SUBJECTS AND METHODS

A total of 965 pregnant women with chronic constipation finally analyzed in this study after informed consent and approval of the Local Institute Ethical Committee of Maternity Hospital, Sabah area, Kuwait, from April 2012 to March 2015 [Figure 1].

Pregnant women <24 weeks with threatened miscarriage and functional constipation according to the Rome III criteria (lasting for at least 2 weeks with symptom onset during pregnancy) included in the study group. The presence of singleton pregnancy, with positive fetal heart activity, gestational age <24 weeks by date, and confirmed by ultrasound.

Functional constipation diagnosed if there was at least ≥2 of Rome III criteria; (1) straining during defecations, lumpy or hard stools in defecations, sensation of incomplete evacuation or anorectal obstruction/blockage, manual maneuvers to facilitate defecation for at least 25% of defecations, fewer than three defecations per week. (2) Loose stools are rarely present without the use of laxatives or (3) insufficient criteria for irritable bowel syndrome.

Women with endocrine disorders (hypothyroidism), Hirschsprung's disease, spinal anomalies, anorectal pathology, inflammatory bowel disease, previous gastrointestinal surgery excluded from this study. In addition, women with pregnancy-induced hypertension, gestational diabetes mellitus, antepartum hemorrhage or placenta previa, women allergic to progesterone preparations, women on progesterone therapy for 2 weeks before inclusion in this study, multiple gestation, uterine anomalies or fetal anomalies or absence of fetal cardiac activity also excluded from this study.

All participants completed a nonvalidated questionnaire created by the authors about their defecation frequency, sensation of incomplete evacuation, sensation of anorectal obstruction, straining during defecation, manual maneuvers to facilitate defecation during the whole week before intake of progesterone, or diet modifications. In addition, gastrointestinal symptoms such as abdominal pain, reflux episodes, and diarrhea evaluated.

Furthermore, a general medical history and the use of medication recorded. Information and education about functional constipation given to studied women. Before the start of the progesterone treatment, all subjects received rectal tap water enema once daily for 3 days to achieve rectal disimpaction and to create a homogeneous study group. No limitation on the use of tap water enema by our Institutional Review Board.[16]

Participants divided into two groups; control group (684 women), managed with diet modifications as treatment for their constipation by dietitian and study group (281 women) who developed threatened miscarriage and advised to take 400 mg progesterone vaginally (Cyclogest, Actavis, United Kingdom) daily for ≥1 week each until their bleeding stopped [Figure 1].

Diet modification includes increased fiber intake in the form of vegetables (carrots, romaine lettuce, broccoli, beetroot, and cucumbers) and fruits (apples, peaches, and melons). Unpolished rice contains water-soluble fibers; psyllium husk is a natural product that contains several types of fiber. Plenty of water throughout the day and glass of prune juice every morning will prevent constipation.[10]

During the treatment phase, the pregnant women filled daily diary containing similar questions as the questionnaire used at baseline evaluation. Data from the defecation diary summarized into weekly outcomes to be able to compare parameters of the study in the studied groups regarding its frequency and its difference from baseline.

Medications adverse effects and compliance evaluated at baseline and at 2, 4, and 6 weeks after starting progesterone therapy or diet modifications.

Primary outcome measures; change in defecation frequency. Secondary outcome measures; sensation of incomplete evacuation, sensation of anorectal obstruction, straining during defecation, manual maneuvers to facilitate defecation, abdominal pain, reflux episodes, medications adverse effects, and compliance.

Sample size and statistical analysis

Using G*Power software version 3.17 (Heinrich Heine Universität; Düsseldorf; Germany) for sample size calculation, setting the α-error probability at 0.05, power (1-β error probability) at 0.95%, and effective sample size (w) at 0.3. The effective size (w) was calculated as follows: $w = \sqrt{\chi^2 / N}$, where χ^2 is the Chi-square test and N is the total sample size. A number of participants' ≥220 needed to produce a statistically acceptable figure. Collected data were statistically analyzed using Statistical Package for Social Sciences; computer software version 18 (Chicago, IL, USA). Mean and standard deviation (SD) were used to represent numerical variables, while number and percentage were used to represent categorical variables. Independent Student's t-test used for numeric parametric variables, and χ^2 test used for categorical variables analysis. $P < 0.05$ was considered statistically significant.

RESULTS

There was no significant difference between two studied groups regarding; mean age, parity, weight, body mass index, and gestational age at inclusion in this study [Table 1].

There was no significant difference between two studied groups regarding, number of women with ≥3 defecations/weeks and frequency of defecation each week [Table 2].

Table 1: Demographic data of the two studied groups

Variables	Group A diet modification (n=684)	Group B progesterone therapy (n=281)	P
Age (years)	30.7 (5.3)	32.2 (4.2)	0*
Parity	3 (1.4)	4 (2.1)	1.0*
Weight (kg)	89.6 (7.2)	94.1 (6.7)	0.08*
BMI (kg/m²)	30.4 (4.3)	32.1 (5.3)	0.9*
Gestational age at inclusion (weeks)	13.1 (1.03)	14.24 (0.54)	0*

*Nonsignificant difference. Data presented as mean (SD). Statistical analysis done using Student's t-test. BMI=Body mass index, SD=Standard deviation
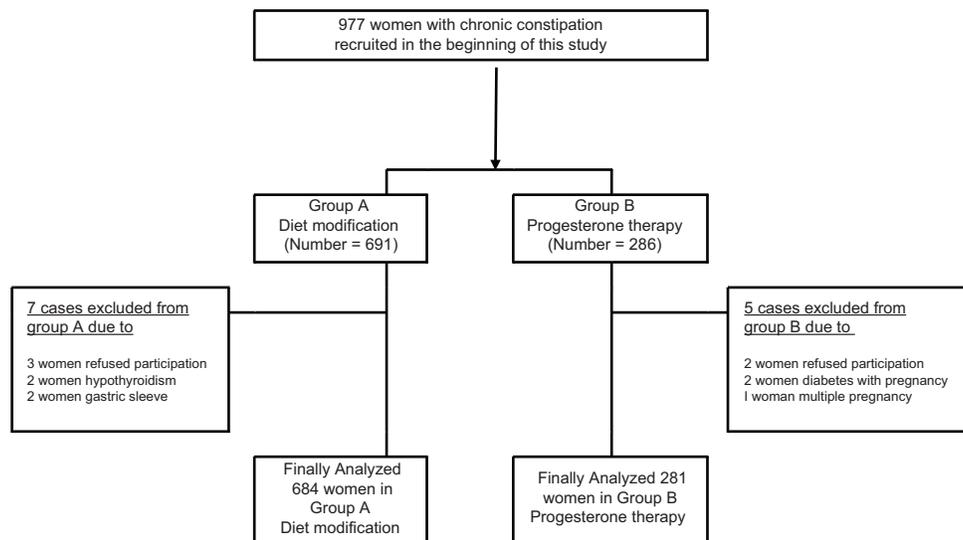

Figure 1: The study course, excluded cases and reasons for exclusion

977 women with chronic constipation recruited in the beginning of this study

Group A Diet modification (Number = 691)

Group B Progesterone therapy (Number = 286)

7 cases excluded from group A due to

3 women refused participation
2 women hypothyroidism
2 women gastric sleeve

5 cases excluded from group B due to

2 women refused participation
2 women diabetes with pregnancy
1 woman multiple pregnancy

Finally Analyzed 684 women in Group A Diet modification

Finally Analyzed 281 women in Group B Progesterone therapy

Table 2: Treatment outcome of the two studied groups			
Variables	Group A diet modification (n=684) (%)	Group B progesterone therapy (n=281) (%)	P, significance
Defecation frequency/week	3.1 (0.8)	6.7 (3.2)	1*
Defecation frequency ≥3 week	152 (22.2)	143 (50.88)	0*
Sensation of anorectal obstruction	614 (89.76)	154 (54)	0.04**
Sensation of incomplete evacuation	623 (91.08)	177 (62.98)	0.03**
Straining during defecation	647 (94.59)	179 (63.7)	<0.01**
Manual maneuvers to facilitate defecation	592 (86.54)	56 (19.9)	0.02**
Episodes of abdominal pain	589 (84.11)	52 (18.5)	0.01**
Presence of reflux episodes	513 (75)	49 (17.43)	0.03**

**Significant difference, *Nonsignificant difference. When data presented as mean (SD), statistical analysis done using Student's t-test, When data presented as number and percentage, statistical analysis done using Chi-square test. SD=Standard deviation

Sensation of anorectal obstruction and sensation of incomplete evacuation were significantly less in Group B (progesterone therapy) compared to Group A (diet modification) (54% [154/281] and 62.98% [177/281] vs. 89.76% [614/684] and 91.08% [623/684], respectively) ($P = 0.04$ and 0.03, respectively).

Straining during defecation and manual maneuvers to facilitate evacuation were significantly less in Group B compared to Group A (63.7% [179/281] and 19.9% [56/281] vs. 94.59% [647/684] and 86.54% [592/684], respectively) ($P < 0.01$ and 0.02, respectively).

Episodes of abdominal pain and the presence of reflux episodes were also significantly less in Group B compared to Group A (18.5% [52/281] and 17.43% [49/281] vs. 84.11% [589/684] and 75% [513/684], respectively) ($P = 0.01$ and 0.03, respectively) [Table 2].

Two women used rescue medication (Bisacodyl/Dulcolax®); one patient used Bisacodyl once in week 1, five times in week 2, and daily in week 3 and 4. The second woman used Bisacodyl only once in week 4. No side effects reported with any medications used during this study. The compliance with progesterone therapy and diet modification was 100%.

DISCUSSION

Females often affected by constipation than males, especially during pregnancy. Although progesterone has been the hormonal explication for many gastrointestinal symptoms that occur in pregnancy, including constipation, a recent study suggested the possibility that estrogen rather than progesterone may be responsible for the delay in gastric emptying and constipation in pregnancy.[11]

Hence, this study designed to compare the effect of progesterone versus diet modification in the treatment of constipation during pregnancy.

There is limited evidence that dietary fiber and fluid intake improve constipation in pregnant women.

However, because of health benefits, increase fluid intake recommended as one of the first measures to relieve constipation. Painful perineum after episiotomy and prolonged recumbency after cesarean deliveries can aggravate constipation.[6,17]

In clinical practice, laxatives and fiber are frequently used in the treatment of constipation during pregnancy. Laxatives such as lactulose (synthetic nondigestible sugar Duphlac®, Abbott Maidenhead, UK) and Bisacodyl (Dulcolax/Durolax®, Boehringer Ingelheim Limited, Bracknell, Berkshire, RG12 8YS, UK) have proven to be safe for mother and fetus.[18]

Unfortunately, their side effects, such as abdominal pain and diarrhea, limit their use.[10] Polyethylene glycol 3350 (PEG, GlycoLax/MiraLax®, Kremers Urban Pharmaceuticals, New Jersey, USA), based laxatives technically meet the ideal criteria for constipation treatment; however, present data are insufficient to exclude any adverse effects on the fetus.[19]

To the best of our knowledge, this is the first study investigating the use of progesterone in constipated pregnant women. Based on the results of this study, progesterone could be of additional value in the prevention and treatment of constipation in pregnant women. An increase in defecation frequency observed during this study in progesterone group, but this increase was insignificant. Furthermore, sensation of anorectal obstruction, sensation of incomplete evacuation, straining during defecation manual maneuvers to facilitate evacuation, episodes of abdominal pain, and presence of reflux episodes were significantly less in Group B (progesterone therapy) compared to Group A (diet modification).

Many studies suggested that the findings in men, nonpregnant women, elderly, and children are not applicable to constipated pregnant women, because of differences in pathophysiology and hormone levels during pregnancy mainly progesterone.[20,21]

The association of female sex steroid hormones and constipation are still not clear. Oh *et al*. showed that

administration of estrogen-induced constipation via a decrease in bowel movement in both male and female mice but progesterone did not.[11] This result suggests that estrogen rather than progesterone may be a detrimental factor of constipation; however, this conclusion does not show agreement with some reports suggesting that progesterone is an important risk factor for constipation in women, and this hypothesis was supported by results indicating that females had greater frequency of constipation during pregnancy.[12-15]

A recent study suggested the possibility that estrogen rather than progesterone may be responsible for the delay in gastric emptying and increase in colonic transit time observed in pregnancy.[11]

Parenteral administration of estradiol, the predominant estrogen during reproductive years to rats resulted in inhibited gastric emptying.[22,23]

On the other hand, female rats treated with progesterone did not show a decrease in colon myoelectric signal.[24]

CONCLUSIONS

Estrogen rather than progesterone may be a detrimental factor of constipation via decreased bowel movement. Progesterone therapy seems to be effective in the treatment of functional constipation during pregnancy. A randomized placebo controlled trial is required to confirm data of this study.

The strength of this study is coming from being the first study investigating the use of progesterone in constipated pregnant women. In this study, due to the presence of a control group, the placebo effect of progesterone excluded and because of the controlled design, there is detailed information available on the natural course of constipation during pregnancy.

A limitation of this study is the nonvalidated questionnaire used at baseline, which could have caused recall bias resulting in possible underreporting of defecation frequency per week and other defecation-related parameters before the study.

Conflicts of interest
There are no conflicts of interest.

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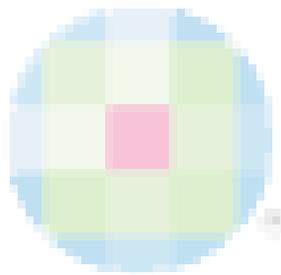
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