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Decreased plasma motilin concentrations in pregnancy

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Abstract

Plasma motilin concentrations were measured in 37 women during the second and third trimester of pregnancy and one week after delivery. The mean plasma motilin concentrations, both fasting and after a glucose load and a mixed meal, were significantly ($p < 0.001$) reduced during pregnancy, returning to the normal range one week post partum. Pregnancy appears to have a profound inhibitory effect on plasma motilin, and this may in part be responsible for the gastrointestinal hypomotility associated with pregnancy.

Introduction

There has been considerable interest recently in the effect of pregnancy on gastrointestinal motility.¹⁻³ Clinical observations such as heartburn, constipation, and gall bladder stasis have been variably attributed to the muscle-relaxing effects of progesterone and the physical impediment of the uterus. Progesterone reduces lower oesophageal sphincter pressure and gastrointestinal motility and also delays gall bladder emptying.⁴⁻⁶ It is still not certain, however, whether these effects are direct or mediated via the action of a gastrointestinal hormone.

Motilin is a hormonal peptide⁷ that has gastrointestinal smooth-muscle stimulating effects. Its target organs include the lower oesophageal sphincter,⁸ the stomach,⁹⁻¹⁰ small¹¹⁻¹² and large intestine,¹³ and the gall bladder.¹⁴⁻¹⁵ We investigated the possibility that motilin secretion is altered in pregnancy.

Subjects and methods

Three groups of patients were recruited before 16 weeks' gestation to study the effect of maternal adiposity on glucose tolerance during pregnancy.¹⁶ A total of 37 subjects were studied, nine whose weight was less than 80% of their ideal body weight, 10 whose weight was between 90 and 110% of their ideal body weight, and 18 with a weight greater than 120% of ideal body weight. These women were studied at 16 and 36 weeks of pregnancy and one week post partum. After an overnight fast the subjects were given a conventional three-hour 50-g oral glucose tolerance test and half-hourly blood samples were taken via an indwelling intravenous cannula. After this the subjects were given a mixed meal of about 2.09 MJ (500 calories), containing 40% fat, 40% carbohydrate, and 20% protein, and further half-hourly blood samples were taken over a period of three hours. The blood samples were centrifuged immediately and the plasma stored at -20°C .

Details of the plasma motilin radioimmunoassay used have been published.⁷⁻⁹ The antibody used (M1) does not crossreact with any of the known gut hormones, and appears to be N-terminal specific. This assay can detect changes in plasma motilin of 3 pmol/l with 95% confidence. To avoid interassay variation, all the samples in the present study were estimated in one assay (intra-assay variation was 5%). The mean fasting motilin concentration ($\pm$ SEM) observed in normal non-pregnant subjects in this laboratory is 48 ± 6 pmol/l.⁷

The research protocol was approved by the ethics committee of St Mary's Hospital and informed consent was obtained from each subject before the study.

The mean and standard error of the mean (mean $\pm$ SEM) have been used throughout. The Wilcoxon signed rank test was used to test for differences in the motilin concentrations at 16 and 36 weeks of pregnancy and post partum. The mean of the values obtained 30 minutes before and immediately before the glucose load have been taken as the mean fasting value. The mean of the values 150 and 180 minutes after the glucose load have been taken as the "basal" value before the meal.

Results

There was no difference in the plasma motilin concentrations in the groups studied and no correlation between body weight and motilin concentrations; the data from the three groups have therefore been pooled.

The figure shows the results obtained. The mean fasting plasma motilin concentration at 16 weeks of pregnancy was 23 ± 2.8 pmol/l (median 20, range 5-91 pmol/l). This was not significantly different from the concentration at 36 weeks of pregnancy (21 ± 2.5 pmol/l, median 17, range 4-58 pmol/l). The concentration one week after

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delivery (57 ± 4.9 pmol/l, median 51, range 18-134 pmol/l) was, however, significantly higher than that observed during pregnancy in the same subjects ($p < 0.001$) and was in the normal range for non-pregnant women.

Plasma motilin concentrations (pmol/l) (mean $\pm$ SEM) in 37 women at 16 weeks of pregnancy (solid dots), 36 weeks of pregnancy (open circles), and one week post partum (squares). The 50 g glucose load was given at 0 minutes and the meal at 180 minutes.

Plasma motilin concentrations fell after the glucose load. The mean value 150 minutes after glucose was 17 ± 2.2 pmol/l at 16 weeks of pregnancy and 16 ± 2.0 pmol/l at 36 weeks; both these values were significantly below that observed one week post partum (38 ± 3.9 pmol/l; $p < 0.001$).

Plasma motilin concentrations rose after ingestion of the mixed meal. The postprandial plasma motilin rise 30 minutes after ingestion of the meal was 10.3 ± 1.3 pmol/l at 16 weeks and this was lower than that at 36 weeks (15.6 ± 1.9 pmol/l; $p < 0.01$). These rises were both smaller than that observed one week post partum (23.0 ± 3.1 pmol/l; $p < 0.001$).

Discussion

Motilin is a gastrointestinal hormone that has recently been isolated and is thought to be one of the factors controlling gastrointestinal motility.⁷ Intravenous infusions of this hormone adjusted to produce a rise in plasma motilin concentrations which lie within the physiological range have been shown to greatly accelerate gastric emptying,⁹⁻¹⁷ to stimulate the lower oesophageal sphincter,⁸ and to reduce intestinal transit time.¹⁸ Other actions of motilin include stimulation of the electrical and mechanical activities of the small bowel¹¹⁻¹² and colon¹³ and emptying of the gall bladder.¹⁴⁻¹⁵

The mean basal motilin concentration observed a week after delivery in the women studied was similar to that reported by the authors in non-pregnant controls⁷ but there was a significant suppression of basal values during early and late pregnancy. The decline in plasma motilin concentrations observed after the oral glucose load and the increase after the mixed meal, which is thought to be due to fat,¹⁹ are in keeping with previous findings in non-pregnant subjects,¹⁹ but the magnitude of the changes observed during pregnancy was less than those previously reported.

It is generally held that pregnancy is associated with some degree of gastric atony and bowel hypomotility.¹⁻³ Although the exact cause of this is unknown, recent evidence suggests that progesterone and other steroid hormones may be responsible.¹⁻³⁻⁵⁻²⁰ Progesterone exposure is associated with a reduction

of lower oesophageal sphincter pressure⁴⁻⁶ and a delay in gastrointestinal transit time²⁰ and gall bladder emptying³⁻¹⁷ during the luteal phase of the menstrual cycle. The evidence accumulated thus far does not, however, exclude the possibility that progesterone may cause stimulation of an inhibitory gastrointestinal hormone or the inhibition of a stimulatory hormone. The results presented here are consistent with the latter hypothesis as they show significant suppression of both basal plasma motilin concentrations and those observed after a meal during pregnancy. It is thus possible that low motilin concentrations may contribute towards the gastrointestinal hypomotility of pregnancy.

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ONE HUNDRED YEARS AGO Sir Garnet Wolseley is said to have ordered that the troops under his command should be allowed daily a triple ration of tea; and it is stated that the extra issue of tea is very acceptable to the men. A second ration of coffee is also ordered daily for every man. No more tinned meats have been sent to the seat of war, but 300 tons of other provisions have been despatched to Ismailia by the steamship *Adowa*. These include, as an exceptional article for hospital uses, a quantity of preserved tongues. The medical department has also transmitted to the hospitals a number of dry cold air refrigerators. (*British Medical Journal*, 1882.)