

THE DISAPPEARANCE OF SLEEP – RELATED CHANGES OF SERUM PROLACTIN IN PREGNANT WOMEN

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SUMMARY

Serum prolactin (hPRL) levels in non-pregnant, pregnant and postpartum women during sleep were investigated. The study showed that in non-pregnant women, there is an immediate shift of hPRL release with reversal of sleeping period. Thus, the nocturnal surge for prolactin is sleep-related. In pregnant women, however, while there is an increase in hPRL level during pregnancy, the nocturnal rise of this hormone is not detected and this is observed as early as the first trimester of pregnancy.

INTRODUCTION

It has been previously shown that the highest level of prolactin in normal healthy non-pregnant women during a 24-hour period is at 0200 hours.¹ This is in agreement with the works of Nokin *et al*,² Sassin *et al*,³ and Robyn *et al*,⁴ who found that the hPRL levels are highest during sleep. Sassin *et al*,⁵ have further shown that the nocturnal rise of prolactin is dependent on sleep. In pregnant

women, however, the nocturnal surge of hPRL level during the last month of their pregnancies is not detected.^{2,6} Four days after delivery, the hPRL surge reappears.⁴

The aim of the present investigation is to demonstrate the disappearance of the nocturnal surge of prolactin release in pregnant women.

MATERIALS AND METHODS

Non-pregnant women

Seventeen normal healthy, non-pregnant women (18 to 23 years of age) took part in the study. Of these, ten were factory workers, five were clerical workers and the other two were students.

These subjects were divided into two groups. Group A consisted of 12 subjects who performed normal daily activities. The subjects slept between 2200 and 0600 hours. Blood samples of 2 ml were taken at 1400 hr (awake) and 0200 hr (sleep). The five subjects in group B slept during the day from 1000 to 1800 hours. Blood samples were taken at 1400 hr (sleep) and 0200 hr (awake). Samples were taken during this single reversal of diurnal activity and therefore the subjects had no time to adjust to the change. This was with the intention that any immediate changes in prolactin level would reflect sudden change in the sleeping habit.

Pregnant and postpartum women

Ten subjects (21 to 30 years of age) participated in the study. Of these, two subjects were in their first trimester of pregnancy, three in the second, four were in the third trimester and one subject on the day 7 postpartum period. Additional information on the subjects were taken, i.e. parity and gravida and their last normal menstrual

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period. Blood samples were taken from each subject at eight-hourly intervals during a 24-hour period: at 1800, 0200 and 1000 hours. All volunteers refrained from sexual intercourse during the period of investigation. In the postpartum women, blood samples were taken at least three hours before breastfeeding. This was to ensure that hPRL levels measured were not influenced by preceding suckling stimulus.

Assay procedure and statistical analysis

Radioimmunoassay for prolactin has been described previously.⁷ The significance of the difference between means was assessed by t-test.

RESULTS

Non-pregnant women

The results are summarised in Figure 1. Group A subjects (those who slept at night and awoke during the day) showed an increase in prolactin concentration at 0200 hr of between 31.5 and 154.0

ng/ml (82.3 ± 8.7 ng/ml) compared to that at 1400 hr, 9.0 to 101.5 ng/ml (29.2 ± 7.2 ng/ml). This represents an approximate four-fold elevation of prolactin during sleep at night ($P < 0.01$). For subjects of Group B (those who slept during the day and awoke at night), hPRL level at 0200 hr was between 5.5 and 39.8 ng/ml (27.2 ± 6.2 ng/ml), whereas at 1400 hr it was between 17.5 and 180.0 ng/ml (64.4 ± 29.3 ng/ml) i.e. a three-fold increase of hPRL during day-sleep. The difference between the mean was, however, not significant.

Pregnant and Postpartum women

The results are summarised in Figure 2. The findings showed that the 0200 hr hPRL peaks were absent in all trimesters. The disappearance of the 0200 hr surge was observed as early as the first trimester of pregnancy and the value (36.0 ± 5.0 ng/ml) was not significantly different from those at

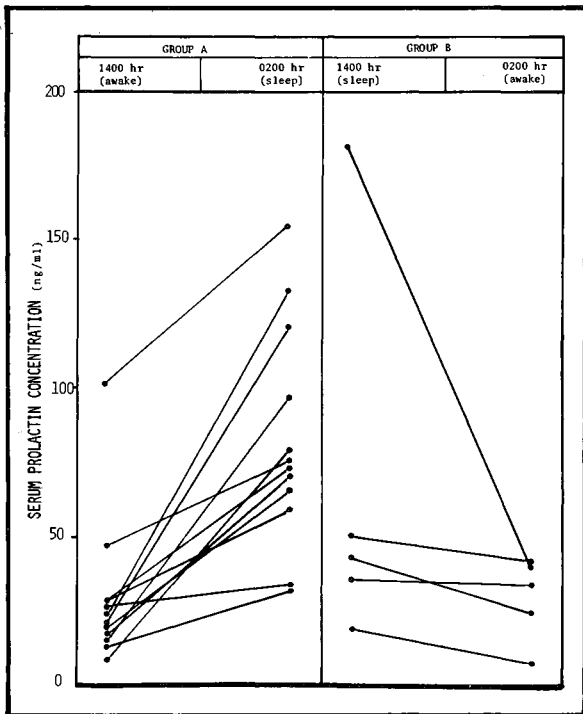


Fig. 1 Sleep-related change of serum prolactin concentrations in two groups of non-pregnant women. Blood samples of group A (slept at night and awoke during the day) were taken at 1400 hr (awake) and 0200 hr (sleep), and for group B (slept during the day and awoke at night) also at 1400 hr (sleep) and 0200 hr (awake).

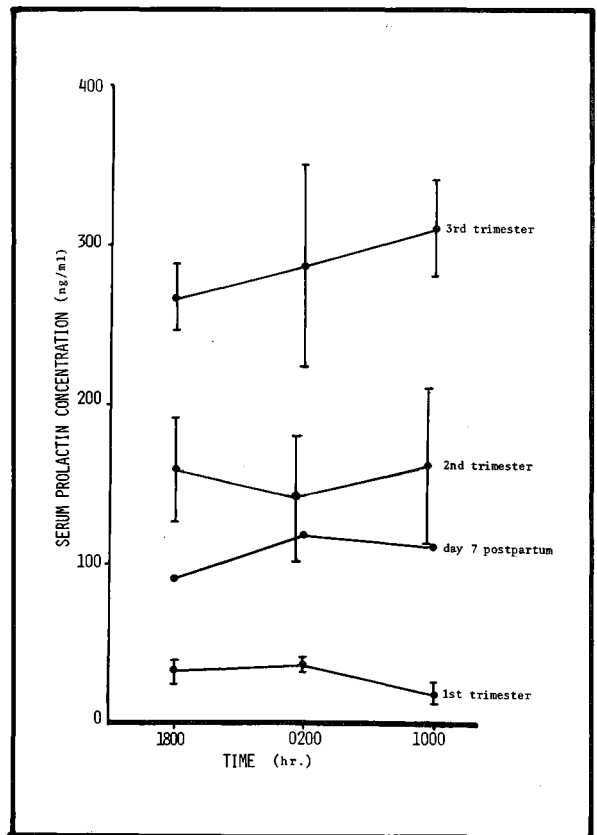


Fig. 2 Mean serum prolactin concentrations in pregnant and day 7 postpartum women during a 24-hour period. Blood samples were taken at 1800, 0200 and 1000 hours. Vertical bars denote standard error of the mean.

1800 hr (33.8 ± 8.8 ng/ml) and 1000 hours (16.4 ± 7.1 ng/ml).

In the second trimester, there was an overall increase in hPRL concentration, and the difference in values between the sampling intervals was not significant (158.7 ± 33.8 , 141.0 ± 38.9 and 162.3 ± 49.5 ng/ml at 1800, 0200 and 1000 hr, respectively).

Prolactin concentration had further increased during the third trimester, and again there was no indication of a peak at 0200 hr (286.2 ± 63.2 ng/ml) when compared with those at 1800 hr (267.0 ± 21.5 ng/ml) and 1000 hours (309.5 ± 30.4 ng/ml).

In the study of a day 7 postpartum subject, the nocturnal rise of hPRL concentration was still absent (90.0, 117.0 and 110.0 ng/ml at 1800, 0200 and 1000 hr, respectively).

DISCUSSION

In this study polygraphic monitoring to identify precisely the sleep onset, waking and specific sleep stages was not carried out. However, the subjects confirmed that they were in deep sleep when awakened at the 0200 and 1400 hr blood sampling times. It should be noted that since the subjects were apprehensive of being cannulated to enable blood to be taken during sleep, the 0200 hr and 1400 hr blood samplings were performed immediately after they were awakened. However, it has been shown that the half life of prolactin is approximately 15 minutes.⁸ Thus, it is unlikely that the prolactin values decline to basal levels within such short time.

The results of the present study have shown that there is an immediate shift of hPRL release with reversal of sleeping period. This suggests that the nocturnal surge for this hormone is sleep-related. This study, therefore, supports the finding of Sassin *et al*,⁵ who showed that hPRL release shifted completely with the shift of sleep onset.

There was an overall increase in hPRL concentrations during pregnancy, and this is in agreement with our previous work.⁷ In the present study, the nocturnal rise of hPRL in pregnant women is not detected. Thus, the absence of night-rise in hPRL in pregnant women is presumably associated with the pregnancy itself. Nokin *et al*,² and Pujol-Amat *et al*,⁶ have also demonstrated a similar disappearance of hPRL peaks in three

women investigated during the last month of their pregnancies. Thus, the present studies, as an extension of work by the aforementioned investigators^{2,6} have also shown that the disappearance of nocturnal surge of hPRL level is observed even during the first trimester of pregnancy. It is unlikely that the nocturnal peak of prolactin is submerged by the higher prevailing levels since, even in the first trimester, when circulating concentrations were only about two times that in non-pregnant women, there is no significant rise.

The present study has also shown that at day 7 postpartum period the nocturnal surge of hPRL is still absent. Although it is impossible to draw a strong conclusion on a basis of a single subject, it seems to suggest that the disappearance of hPRL nocturnal surge is maintained for sometime after delivery, but exactly how long awaits further investigation. Robyn *et al*,⁴ however, showed that four days after delivery the variations in prolactin concentrations during a 24-hour period reappeared. The cause of the discrepancy between the present finding and theirs is unknown. However, Canales *et al*,⁹ showed that it is only at the third week postpartum that administration of oestradiol caused an increase in prolactin. A long term and intensive study involving collection of blood samples up to a several weeks postpartum could possibly clarify the controversy. It is to be noted that there are scant reports in the literature of such studies in view of inherent difficulties in obtaining volunteers. Thus, the underlying causes of nocturnal surge in non-pregnant women and the disappearance of this surge in pregnant women are yet to be investigated.

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