# POSSIBLE LUTEOTROPHIC EFFECT OF PROLACTIN AS EVIDENCED BY OCCURRENCE OF PREGNANCY FOLLOWING ADMINISTRATION OF DA-ANTAGONIST IN A CASE WITH VERY LOW PRL—LEVEL

by

B. N. Chakravarty
N. Gupta
Sudarshan Ghosh Dastidar
and
Sidhartha Chattopadhyay

## SUMMARY

**A case of very low PRL level in which pregnancy was achieved following use of DA-antagonistic in luteal phase is reported.**

*Introduction*

Since the isolation and characterisation of prolactin as a distinct pituitary hormone, being predominently under tonic inhibitory control (known as PIF- DOPAMIN), a large number of evidence has accumulated to suggest that pathological hyperprolactaenaemia is associated with anovulation and amenorrhoea with or without galactorrhoea. When prolactin level is lowered the normal cyclical gonadal activity is restored. (Thorner *et al*, 1976; Tyson *et al*, 1977). Thus the bulk of the work is directed towards the adverse effects of abnormal elevation of prolactin. But little is known about its possible biological (specially luteotrophic) activity in physiological level.

Though prolactin is known to be luteotrophic in sheep and other rodents (Jaffe *et al*, 1973), no such report is available to support similar phenomenon in human. In present clinical practice, apart from diurnal variation, the significance of lower limit of prolactin has not yet been clearly established. The above considerations interested us to investigate whether or not a very low prolactin level could interfere with maintenance of normal corpus luteum activity. In our infertility clinic, women with persistent low prolactin level (less than 5 ng/ml), attempt is being made to achieve modest elevation of prolactin in the luteal phase and following such tentative attempt pregnancy has been achieved in 1 case which is being repored here.

*From: Deptt. of Obstetrics and Gynaecology, N.R.S. Medical College, Calcutta.*
*Accepted for publication on* 5-10-83.

## CASE HISTORY

Mrs. K. aged 28, married for 8 years attended our clinic on 17-4-82 with history of primary infertility. She had regular menstrual cycles and no significant abnormality could be elicited in the history, apart from infertility. The report of husband's semen analysis (2-12-80), hysterosalpingogram (23-12-80), premenstrual endometrial biopsy (19-3-81), and post coital test

(23-5-81) were available at the time of first visit and these reports were quite compatible with fertility potential of the couple.

Laparoscopy was performed on 19-7-82 and the findings were: uterus normal in size, mobile; both tubes were healthy and freely mobile. Pouch of Douglas was clear. Chromotubation demonstrated free spill of dye from both tubes. There was no evidence of endometriotic spot anywhere in the pelvis.

Basal body temperature was discordant initially but subsequently the record showed low monophasic pattern. Hence probable cause of infertility in this case was presumed to be due to endocrine dysfunction leading to either ovulatory defect or inadequacy.

Different ovulation inducing drugs were administered in phases based on regular monitoring of BBT records, cervical mucus and periodic estimation of related reproductive hormones (RIA).

Primary induction of ovulation was planned with clomiphene citrate and HCG. This planning was based on clinical parameters of BBT records and cervical mucus.

She received clomiphene citrate (Tab. Fertyl, Arex-50 mgm twice daily) from day 3 to day 7 and low dose oestrogen (Tab. Lynoral .01 mgm —Organon) 1 tab. a day from day 5 to day 11. On the 12th and 13th day cervical os and cervical mucus were examined (Cervical scoring based on Serono chart) but satisfactory response could not be achieved.

The dose of clomiphene was increased to 150 mgm per day in the next two cycles and inspite of this increased dose, the peripheral biologic effect of positive ovulation could not be detected in the cervical mucus and in the basal body temperature chart. Hence HCG could not be administered in any one of these cycles. This regime of induction continued from August 1982 to October 1982. As ovulation could not be induced with clomiphene and HCG, plasma FSH, LH, TSH and prolactin were estimated.

The reports of analysis of hormones in different periods of menstrual cycle are shown below:

18-10-82 FSH (8th day of menstrual cycle) —4 mIU (Normal 5-20 mIU/ml).

18-10-82 TSH (Random)—2.0 mIU/ml (Normal less than 4 mIU/ml).

22-10-82 LH (12th day of menstrual cycle) —5.5 mIU/ml (Normal 5-30 mIU/ml).

31-10-82 PRL (21st day of menstrual cycle)—4 ng/ml (normal less than 25 ng/ml).

Based on the reports of radioimmunoassay and having failed to induce with clomiphene, gonadotrophins were next used for induction of ovulation.

In the first cycle, HMG (Pergonal-Serono) 1 amp each day was administered on 3rd, 5th, 7th and 9th post-menstrual day. HCG could not be subsequently added because cervical mucus did not become thin or reasonably stretchable indicating persistence of follicular inadequacy.

The dose of HMG was doubled in the next month—the days of administration was extended upto 11th day of this cycle. The cervical score was positive on the 16th day when HCG (Profasi-serono) 10,000 I.U. was injected. The BBT showed distinct biphasic pattern but suggested delayed ovulation and a short luteal phase. Plasma progesterone level was not estimated but inadequacy of luteal phase was suspected based on basal body temperature records.

As pregnancy could not be achieved despite ovulation, PRL was again estimated in the next cycle following similar schedule of induction. Level of PRL was 3 ng/ml 5 days following the 'thermal' shift (ovulation). Next cycle, in addition to HMG and HCG she received chlorpromaine 12.5 mgm (2 tabs. a day) for 7 consecutive days from the day following the ovulation (as speculated by BBT and cervical mucus study). Repeat PRL estimation on the 23rd day of the same cycle revealed value of 15 ng/ml.

She missed her period in the same cycle and BBT showed sustained elevated temperature. As she developed symptoms and signs of early pregnancy urine was tested for HCG (Gravindex test). This was positive on the 5th day following her last menstrual period. The pregnancy so far is continuing uneventfully.

## *Discussion*

As discussed earlier, the role of basal level of PRL in female reproductive endocrine function calls for further research. The classical experiment by McNatty *et al* (1974) clearly demonstrates that granulosa cells could synthesize steroids in *in vitro* culture at a maximal rate when PRL level was optimum. They postulated that 'normal' PRL level is essential for adequate steroidogenesis by

corpus luteum. Robyn *et al* (1973) showed that if PRL level in luteal phase of a large number of patients were aggrevated and compared to their values of follicular phase there does seem to be an increase of PRL level in luteal phase. It has been claimed that in hypophysectomized patients pregnancy can be induced and carried in absence of PRL by administration of pure FSH/LH. However, in view of the very recent observation that PRL is also synthesised in the 'desidual cells' (Rosenberg *et al*, 1980), the above claims should be further reviewed. It is highly interesting and indicative that decidual cells which are mainly developed to sustain pregnancy are a potential source of PRL. This locally produced PRL could in fact might be playing hitherto unknown role in maintainance of corpus luteum. Schultz *et al* (1978) have shown a significant decrease in luteal phase progesterone secretion in normo-prolactaenimic regularly cycling women treated with bromocryptine. This observation also supports our speculation. Furthermore, it is known that the PRL is one of the factors responsible for potentiating the effect of ACTH on androgen production (Vermulan *et al*, 1977) from zona reticularis. Thus a moderate increase of PRL level in luteal phase might also exert its luteotrophic effect mediated via an optimum androgen level (DHEA-S) which is reported to have mild luteotrophic effect (Chakravarty and Mukherjee, 1977).

In the case reported here, low PRL was hypothetically thought to be a factor causing inadequate luteal phase. As it is known that DA-antagonists (Phenothiazines) can elevate PRL level in a short time, chlorpromazine was administered. Subsequently PRL estimation showed elevation (15 mg/ml) and pregnancy followed.

*References*


1. Chakravarty, B. N., Mukherjee, S.: J. Obstet. Gynaec. India. 27: 3, 383, 1977.
2. Jaffe, R. B., Yuen, B., Keye, W. R. (Jr.) and Midgley, A. R. (Jr.): Am. J. Obstet. Gynec. 117, 1973.
3. McNatty, K. P., Sawers, R. S. and McNeilly, A. S.: Nature, 250: 653, 1974.
4. Robyn, C., Delboye, P., Nokin, J., Vekemans, M., Perez Lopez, F. P. and L'Hermite, M.: International Symposium on human prolactin. pp. 98-119. 2nd Pasteels, Edited by S. L. and Robyn C. Excerpta Medics, Amsterdam, 1973.
5. Rosenberg, S. M., Maslar, I. A., Riddick, D. H.: Am. J. Obstet. Gynec. 138, 681, 1980.
6. Schultz, K. D., Geiger, W., Del Pozo, E. and Kunzig, H. J.: Am. J. Obstet. Gynec. 132: 561, 1978.
7. Thorner, M. O., Besser, G. M., Jones, A., Dacie, J. and Jone, A. E.: Brit. Med. J. 4: 694, 1976.
8. Tyson, J. E., Andersson, J., Huth, J., Smith, B. and Zakur, A.: Obstet. Gynec. 46: 1, 1977.
9. Vermulan, A., Sui, E. and Rubens, R.: J. Clin. Endocr. Metab. 44: 1222, 1977.