LH PULSE FREQUENCY IN RELATION TO POSITIVE OESTROGEN-GONADOTROPHIN FEEDBACK IN AMENORRHOEA

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SUMMARY

The relationship between the pattern of pulsatile LH release and the response to oestrogen provocation was studied in twenty amenorrhoic or oligomenorrhoic subjects. In twelve subjects with positive oestrogen-gonadotrophin feedback a definite pulsatile pattern of LH release was demonstrated with a pulse frequency of 60-80 min and an increase from nadir to peak ranging between 30 and 58%. The mean basal LH concentration was significantly higher in this group (P<0.001).

Of eight subjects who had absence of positive feedback, five showed infrequent pulses, 1-2 during the four-hour period. These were of low amplitude and with a percentage increase of 45-70% at nadir to peak. The remaining three did not have a pulsatile pattern of LH release.

Positive feedback, as demonstrated by an oestrogen provocation test was thus found only in patients having 3 or more LH pulses in the 4 h study period; an LH pulse frequency similar to that in the early follicular phase in regularly menstruating women.

Function of the hypothalamic-pituitary-ovidian axis in patients with menstrual disturbance can now be assessed at various levels. Current tests include no, only those of pituitary function alone, but also of oestrogen-gonadotrophin feedback and 24 h study of hormone release pattern. With the use of releasing pulsatile LH/H for induction of ovulation, it becomes pertinent to examine the release point of gonadotrophin secretion in a practical manner prior to commencement of treatment, and to relate these patterns to other modes of gonadotrophin release to categorize suitable dose regimens.

The pulsatile pattern of luteinizing hormone (LH) release has been shown in both humans and laboratory animals (Dierschke et al., 1970; Gay et al., 1970; Katongole et al., 1971; Yen et al., 1972).


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In addition to changes throughout the menstrual cycle, diurnal variation of LH pulsatile release has been demonstrated (Yen et al., 1972; Strickler et al., 1977). Difficulties of assessment of LH pulsatility may be resolved by more frequent sampling (Filiporti et al., 1982), however the significance of the various pulsatile patterns observed in gynaecological patients and the relationships between them and the results of other dynamic endocrine function tests are at present unclear.

We report here the relationship between the pattern of LH pulsatility as assessed by samples collected at 10 min intervals for a 4 h morning period and the existence of positive oestrogen-gonadotrophin feedback in amenorrheic and oligomenorrhoeic women. The presence or absence of this control mechanism was assessed by an established oestrogen provocation test (Shaw et al., 1975; Glass et al., 1975).

PATIENTS, MATERIALS AND METHODS

Twenty subjects (aged 21–31 years) presenting with secondary amenorrhea or oligomenorrhoea at a gynaecological endocrine and infertility clinic were selected for study. Subjects were regarded as being amenorrheic or oligomenorrhoeic if menses had not occurred in the previous 12 or 6 months respectively. All gave informed consent. Thyroid function tests, estimations of pre-treatment plasma concentrations of LH, FSH, prolactin, oestradiol-17β, progesterone, testosterone and x-ray of the pituitary fossa were performed on all subjects.

A 4 h morning LH pulsatility study was undertaken as detailed below. This was followed by a standard combined LHRH/TRH pituitary function test comprising the administration of LHRH (100 µg) and TRH (200 µg) (Relefact LHRH/TRH, Hoechst) intravenously, blood samples being collected at -15, 0, 30, 60 and 90 min following administration. Thereafter 1 mg oestradiol benzoate was given intramuscularly and further samples for LH and FSH were collected at 24, 48, 56 and 72 h. Positive oestrogen-gonadotrophin feedback was said to be present if, after oestrogen administration, plasma LH concentration rose by 10 IU/l or the FSH concentration by 3 IU/l above the mean baseline values. Intact negative feedback, which was present in all 20 patients was defined as a fall in LH and/or FSH concentration following oestrogen administration.

LH Pulsatility study

The subjects were admitted to hospital at 0000 h. A 21 gauge butterfly needle was inserted into an antecubital vein and fixed by strapping and a 3-way stopcock was secured firmly to the end. A 20 ml syringe was filled with normal saline containing heparin in a concentration of 10 IU/ml and attached to one end of the 3-way stopcock and blood samples were collected from the other.

10 ml of blood was withdrawn initially (0 min sample) and thereafter 2.5 ml were taken every 10 min for a period of 4 h. Subjects were usually lying flat, reading or listening to the radio; they were allowed to move around but not to sleep. Blood was centrifuged and plasma collected and stored at -20°C until assayed. All samples from each subject were analysed in the same assay batch. All the samples were analysed for FSH and LH; oestradiol-17β and progesterone were measured in the 0 min sample only.

FSH and LH were measured by double antibody radioimmunoassay using a polyethylene glycol assisted precipitation. LH concentrations were expressed in IU/l in
Результаты

Использование данной методики позволило выявить ряд положительных тенденций в области улучшения качества образовательного процесса. Учитывая, что в ходе реализации проекта были внесены значительные корректировки в программу обучения, можно констатировать, что выбранный подход дал положительные результаты. Изменения, внесенные в учебный план, позволили более эффективно организовать работу с учащимися, обеспечивая их полноценное развитие. В целом, результаты показывают, что предложенные методы и подходы являются перспективными для дальнейшей работы в рамках реализации данного проекта.
DISCUSSION

As mentioned earlier, the results from the two methods were consistent in showing no difference in the group of interest. However, the experimental data has been found to be more consistent with the predicted results. The null hypothesis was rejected at a level of 0.05.

The next step in the analysis is to examine the interaction between the two factors, which in this case is the type of treatment and the dose level. The interaction is significant at a level of 0.01, indicating that the effect of treatment depends on the dose level.

Finally, we would like to mention that the results of this study can be used to refine the treatment protocols for future studies.
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