Reversible inhibition of central precocious puberty with a long acting GnRH analogue

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Summary

A 7 year old girl with precocious puberty was treated with buserelin, a long acting analogue of gonadotrophin releasing hormone. Spontaneous and stimulated gonadotrophin secretion became prepubertal but returned to pubertal values when buserelin was withdrawn, suggesting that normal sexual maturation should follow cessation of treatment.

Buserelin (6-D-Ser-(TBU)-GnRH-(1–9) ethylamide) returns pubertal gonadotrophin responses to intravenous gonadotrophin releasing hormone to prepubertal concentrations in children with precocious puberty.1 One reservation about this treatment, however, has been whether normal sexual maturation will follow its cessation. We report a child in whom pubertal gonadotrophin secretion returned after drug withdrawal.

Patient and methods

A girl aged 7-8 years presented in April 1983 with precocious puberty (Tanner stage P2B4). Ultrasound examination of the abdomen and computed tomography of brain were normal.

Gonadotrophin secretion was assessed during sleep and after intravenous gonadotrophin releasing hormone stimulation. Blood was withdrawn continuously by a Cormed SL-65 continuous blood withdrawal pump throughout the first few hours of sleep monitored by electroencephalogram. Specimens were divided into aliquots collected over 15 minute periods. The following morning an intravenous gonadotrophin releasing hormone test was performed. Serum gonadotrophin concentrations were measured by radioimmunoassay.

Buserelin (400 µg) was administered three times daily by nasal insufflation. Gonadotrophin secretion was assessed three months later. Treatment was stopped after nine months and testing was repeated after a further three weeks.

Results

The biochemical results are shown in the Figure. Pubertal gonadotrophin responses to intravenous gonadotrophin releasing hormone were abolished by buserelin and returned when the drug was withdrawn. During treatment, pulsatile gonadotrophin secretion was diminished. Withdrawal of buserelin was followed by pulsatile secretion of luteinising hormone and, to a lesser extent, follicle stimulating hormone. During and after treatment, basal gonadotrophin concentrations were raised compared with the values beforehand. The lower limits of detection of the gonadotrophin assays were 0-6 IU/l for follicle stimulating hormone and 2-0 IU/l for luteinising hormone. Interbatch coefficients of variance for follicle stimulating hormone were 10-8% at 3-8 IU/l and 3-2% at 10-2 IU/l and for luteinising hormone were 11-3% at 2-9 IU/l and 5-1% at 9-9 IU/l. Serum oestradiol concentrations were 150, 29 and 69 pmol/l before, during, and after treatment respectively. During nine months' treatment there was no clinical progression of puberty.

References


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Before treatment

Buserelin

After treatment

Comitè and co-workers showed the return of pulsatile gonadotrophin secretion after withdrawal of a different gonadotrophin releasing hormone analogue after eight weeks' treatment. They later described clinical and biochemical progression of puberty after completion of 18 months of treatment.

The final proof of reversibility will be when patients are seen to progress normally through puberty and become fertile. Our evidence suggests, however, that the effects of buserelin are reversible.

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References


Discussion

The continuous administration of gonadotrophin releasing hormone to Rhesus monkeys inhibits gonadotrophin secretion. This observation led to the development of long acting analogues that diminish gonadotrophin secretion in man. The mechanism of action of these analogues is uncertain but may be due to ‘down regulation’ whereby sustained exposure of the gonadotroph to high concentrations of gonadotrophin releasing hormone results in diminished responsiveness. While it is likely that this is reversible, there is as yet little evidence that this is the case.

Like others we have found that buserelin inhibits the gonadotrophin responses to intravenous releasing hormone and reduces pulsatile gonadotrophin secretion during sleep. We have now shown that stopping treatment after nine months was followed by the return of pubertal responses to intravenous gonadotrophin releasing hormone and pulsatile gonadotrophin secretion during sleep. Basal gonadotrophin concentrations, however, remained raised, suggesting a sustained effect of the drug.

Figure Gonadotrophin responses to sleep and intravenous gonadotrophin releasing hormone (GnRH) before, during, and after buserelin treatment.

Sleep level 1-4 by depth of line. (W = wake), open columns = luteinising hormone (LH), black columns = follicle stimulating hormone (FSH), open circles = LH, closed circles = FSH.

Figure 873

Buserelin

Figure

PSW is supported by the Cancer and Leukaemia in Childhood Trust.
Favourite words

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SUMMARY A prospective survey of language used by children aged between 2 and 16 years for 'taboo subjects' was carried out on a paediatric surgical ward and in the outpatients clinic. The children were interviewed in the presence of their parent(s). A remarkable diversity of words and phrases was noted. Language was affected by the age and sex of the patient. This survey is of interest to all clinicians who need to communicate with children.

It has been emphasised frequently that good clinical practice depends on adequate history taking: this requires effective communication between doctor and patient and both parties have to understand and be understood. On paediatric surgical wards information about genitalia and 'taboo functions' must be gathered from child and parent. It may take several attempts and a variety of phrases to achieve this with children. As this problem has received so little attention in medical reports, we carried out a survey to define the vocabulary of the taboo words used by children.

Patients and methods

The study took place in the children's ward and the outpatient department at Southampton General Hospital. One hundred children and their parent(s) were studied by questionnaire which was filled in by the investigators. Details of the child's age and sex were noted. The children were asked to give their favourite word for the following anatomical parts: penis, vagina, anus, and testicles and the following physiological functions: defecation, anal flatulence, micturition, and vomiting.

Table 1 Favourite words for anatomical parts

<table>
<thead>
<tr>
<th>Part</th>
<th>Word (s)</th>
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<tbody>
<tr>
<td>Penis</td>
<td>Willy (36); don't know (20); penis (14); winkle (4); widgie (4); dinkle (3); others—willy warbler, twinkle, ding-a-ling, my body, diggle, big worm, prick, tail, wotsit, privates, winkle, dilly dat, peanut, little man, hosepipe, nudder, dick, tinkle, bum.</td>
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<tr>
<td>Vagina</td>
<td>Don't know (61); fanny (14); vagina (6); others—pinkie, willy, tweet, fluffy bit, tumnny, foo foo, no willy, luly, front bottom, special tummy, crumpet, tappenny, ninny, foo, chuckarella, can't, wee wee, twinkle, private.</td>
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<tr>
<td>Anus</td>
<td>But (46); bottom (29); don't know (21); arse (3); backsides (1).</td>
</tr>
<tr>
<td>Testicles</td>
<td>Don't know (76); balls (10); testicles (10); others—goolies, privates, nuts, rugby balls.</td>
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