described for agenesis of the corpus callosum as seen
on ventriculography\(^1\) and CT scanning\(^2\) can be seen
in the present case on ultrasound scanning, with the
exception of dilatation of the 3rd ventricle and its
interposition between the lateral ventricles. This was
not found on the CT scans of the present case either.
The degree of dilatation and interposition of the 3rd
ventricle is said to be variable\(^3\) and absence of this
finding may mean that the agenesis is incomplete.\(^4\)

Although rare, agenesis of the corpus callosum
should be easily recognisable on neonatal ultrasound
head scanning.

I thank Dr E M O'Neill, for permission to report
this case and Dr I Holland, General Infirmary,
Leeds, for the CT scans.

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Correspondence to Dr F Sheehy Skeffington, H F Hawley
Perinatal Research Fellow, c/o Ward 10, Barnsley District
General Hospital, Gawber Road, Barnsley S75 2EP,
Yorkshire.

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Controlled trial of imipramine in diurnal enuresis

ROY MEADOW AND IAN BERG

Department of Paediatrics and Child Health, St James's University Hospital, Leeds

SUMMARY Twenty-seven children with diurnal
enuresis were studied in a double-blind randomised
controlled trial of imipramine. Outcome was not
related to such features as age, gender, maximum
functional bladder capacity, or evidence of psychi-
atric disturbance. Although the condition in several
children improved, no evidence emerged to suggest
that imipramine was superior to placebo in the
treatment of the condition.

Day wetting is a troublesome problem which not
uncommonly affects children of school age, especially
those who wet the bed. The characteristic features of
this diurnal form of enuresis have been described
elsewhere.\(^1\)\(^2\) Unfortunately, no effective method of
treating wetting, which occurs during the day when
the child is up and about, has so far been found.\(^3\)

Imipramine is a drug which relieves bed wetting, at
least temporarily.\(^4\)

It was therefore decided to carry out a trial of
imipramine in persistent day wetters to see if diurnal
enuresis could be lessened.

PROCEDURE

Children treated at the paediatric outpatient depart-
ment of a large undergraduate teaching hospital
were studied. In each instance a history was taken, a
physical examination was carried out, and a mid-
stream specimen of urine was examined. No other
special investigations were done routinely. However,
since the presence of a urinary tract infection is
considered to justify radiological investigation, over
half the children had an intravenous urogram and a
voiding cystourethrogram. Any urine infection was
eradiated before the child was included in the study.
During the trial, the urine was checked regularly and
kept free from infection. Any child over age 5 years
whose daytime wetting was a substantial problem
was taken into the trial until it comprised 27 children.
Although several also had some bed wetting the
main cause of parental concern was the day wetting.

All the mothers completed an Eysenck personality
inventory for themselves, and a Rutter A Question-
naire concerned with their children's behaviour.
Each was asked to give permission so that the child's
school could be visited and the form teacher could
complete a Rutter B Questionnaire and a Conners
Teachers Questionnaire.

At the first visit to the outpatient department
initial clinical assessment included estimation of the
maximum functional bladder capacity. Each mother
was given a chart to record wetting events during the
next 4 weeks before any treatment was started.

On the second visit, it was decided whether the
child's wetting was sufficiently troublesome to
warrant drug treatment. If so, allocation to the
imipramine or the placebo group was made by
opening the next in a series of envelopes containing randomly distributed assignments. Tofranil syrup (25 mg) was given every morning for 4 weeks and 50 mg for the next 4 weeks to those on the drug. The dosage of the placebo syrup was correspondingly doubled. The maximum functional bladder capacity was measured after 4 weeks on the smaller dose and after 4 weeks on the larger dose. There was a follow-up visit after 6 months. Charting of daytime wetting was continued throughout. Two ratings were made. Firstly, the number of completely dry days in a 4-week period—the 'dryness' score—out of a possible maximum of 28. Secondly, an estimate of the severity of wetting, none (0); 'slight' (1) dampening of the pants, insufficient to penetrate outer clothing; 'moderate' (2) sodden pants, with wet patch on outer clothing; 'severe' (3) puddles on seat or floor. A 'wetness' score, out of a possible maximum of 84 over 4 weeks was the sum of the daily scores.

Results

There were 9 boys and 18 girls in the trial. The average age was 8 years (SD ± 2). Clinical assessments were completed in 26 and school forms were completed in 23.

Less wetting occurred during the trial period than before, but no significant differences (P > 0.05) emerged using analysis of variance when the drug (n = 14) and placebo (n = 13) groups were compared, looking at wetness and dryness scores before treatment, on the smaller dose, on the larger dose, and on the follow-up (Table).

The drug and placebo groups did not differ significantly on the Rutter A Scale, the Conners Teachers Questionnaire, or on the Eysenck personality inventory. The placebo group had significantly high T (11.5 versus 5.0) and A (3.6 versus 0.4) scores on the Rutter B Questionnaire (P < 0.05).

Analyses of covariance were carried out using wetness and dryness scores as dependent variables. Differences in values on the smaller compared with the larger doses and those before starting treatment were looked at, taking into consideration age, gender, Rutter A T score, Rutter B P score, and the mother's Eysenck personality inventory N score.

There were no significant differences between drug and placebo groups.

Maximum functional bladder capacities were small (mean 174 ml) in the sample but did not differ between the drug and placebo groups, before starting treatment, or between the smaller and the larger dose. There was no significant change in maximum functional bladder capacity with treatment (P > 0.05).

A comparison between day wetting children (n = 23) and the same number of controls from their class at school showed no significant differences in age (mean 8.3 years in each group) or gender (8 boys and 15 girls in each group). Scores on the Rutter B T scale were significantly higher in the day wetting children (mean = 7.6) compared with the controls (mean = 4.1, P < 0.01). All 5 of the Conners Teachers Questionnaire factors showed significantly higher scores in the day wetting children (cases/controls: factor I 6.4/1.0, F = 8.4, P < 0.01, factor II 4.5/1.3, F = 11.3, P < 0.01, factor III 6.3/3.7, F = 4.1, P < 0.01, factor IV 6.0/2.1, F = 9.3, P < 0.01, factor V = 2.6/0.4, F = 9.1, P < 0.01).

Comments

The two groups of children with daytime wetting were typical in terms of age distribution and the predominance of girls. Their fairly small maximum functional bladder capacities and the excess of behavioural problems at home and at school were also characteristic of diurnal enuresis.1 2

In view of the fact that imipramine relieves nocturnal enuresis, while the drug is being taken,4 it is surprising that we did not find it to affect daytime wetting significantly. It could be argued that since the pharmacokinetics of the drug vary considerably with different patients, larger doses might have been more effective for some children. Because cases were randomly assigned to treatment groups it was possible to use analysis of covariance on looking at the results.5 Yet no significant differences appeared when age, gender, and the various measures of psychological disturbance were allowed for.

Six of the children became reliably dry during the treatment trial, and most others had considerably

| Table Average wetness score and average number of dry days, before treatment, on smaller dose (25 mg), on larger dose (50 mg), and on follow-up |
|----------------------------------|----------------------------------|----------------------------------|----------------------------------|----------------------------------|----------------------------------|----------------------------------|----------------------------------|----------------------------------|
| Group                      | Average wetness score in previous 4 weeks | Average number of dry days in previous 4 weeks | Group                      | Average wetness score in previous 4 weeks | Average number of dry days in previous 4 weeks |
|                            | Before treatment | On smaller | On larger | 6 month follow-up | Before treatment | On smaller | On larger | 6 month follow-up |
| Imipramine (n = 14)      | 40 | 28 | 21 | 20 | 4 | 9 | 11 | 10 |
| Placebo (n = 13)         | 36 | 27 | 26 | 30 | 6 | 12 | 15 | 9 |
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less wetness. This overall improvement is presumably explained by placebo effect and spontaneous remission rate. The failure of maximum bladder capacities to show any substantial increase corresponding to this improvement is further evidence of the unsatisfactory nature of this measure.3 6

Our trial suggests that imipramine, which is potentially dangerous because of the risks of accidental or deliberate overdose, should not be used for the treatment of children with diurnal enuresis.

We thank Ciba-Geigy for supporting this trial, and Mrs Wendy Pearson for assistance.

References


Correspondence to Professor S R Meadow, Department of Paediatrics and Child Health, St James’s University Hospital, Clinical Sciences Building, Beckett Street, Leeds LS9 7TF.

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Familial benign copper deficiency

K MÉHES AND EVA PETROVICZ

Department of Paediatrics, County Hospital, Győr, Hungary

SUMMARY Hypocupraemia with normal caeruloplasmin levels was found in a 21-month-old boy admitted to hospital because of repeated seizures and failure to thrive. He had blonde curly hair, spurring of the femora and tibiae, and mild anaemia, but his mental development, electroencephalogram, and structure of the hair on microscopical examination were normal. There was a general improvement in his condition with supplements of oral copper but as soon as these were reduced or stopped hypocupraemia and seizures resumed. Family investigation showed copper deficiency with mild symptoms in the mother and the maternal uncle. The pedigree suggests possible autosomal dominant or X-linked dominant transmission.

Although several conditions leading to sporadic copper deficiency have been described, only two diseases, Wilson’s hepatolenticular degeneration and Menkes’s kinky-hair syndrome, are regarded as inherited abnormalities of copper metabolism.1

We report on what is perhaps a new form of familial hypocupraemia.

Case report

The propositus, birthweight 2.95 kg, had a normal delivery and no perinatal complications. At age 6 months he was admitted to hospital because of a seizure and subsequent hypotonia. On admission there were no abnormal physical, neurological, or biochemical findings except for moderate anaemia. Serum copper level was not determined. As there were no symptoms he was discharged 6 days later.

During the next year, although his psychomotor development was good, weight gain was poor and he had frequent infections.

At age 21 months he was referred to our department because of seizures and hypotonic attacks. On admission his weight was below the 3rd centile, but height and head circumference were between the 10th and 25th centiles. His appearance was characteristic with a broad nasal bridge, Cupid’s bow upper lip, and blonde curly hair (Fig. 1). The skin on his face was moderately seborrhoeic. Muscle tone, mental development, electroencephalogram, and eyes were normal. Radiological skeletal survey showed broadening and spurring of the femora and tibiae. Skeletal age corresponded to the chronological age. On microscopical examination the child’s hair showed normal structure.

Levels of serum glucose, electrolytes, pH, calcium, magnesium, zinc, immunoglobulins, hepatic and renal function tests, urine analysis, blood and urine amino-acid chromatography, glycosaminoglycan excretion were all normal. Stool bacteriology
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R Meadow and I Berg

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