Imipramine was more effective than mianserin for nocturnal enuresis

Smellie JM, McGrigor VS, Meadow SR, Rose SJ, Douglas MF. **Nocturnal enuresis: a placebo controlled trial of two antidepressant drugs.** Arch Dis Child. 1996 Jul;75:62-6.

Objective
To compare mianserin, a quadricyclic antidepressant, with imipramine, a tricyclic antidepressant, and with placebo in children with nocturnal enuresis.

Design
16-week randomised, double-blind, placebo-controlled trial.

Setting
Centres in Southampton, Leeds, and Aberdeen, United Kingdom.

Patients
80 children aged 5 to 13 years (81% boys) who had nocturnal enuresis (bedwetting ≥ 3 nights per week). Exclusion criteria were history of urinary tract infection or structural abnormality, secondary enuresis, moderate or severe learning difficulty, emotional or conduct disorder, anaemia, blood dyscrasia, epilepsy, neurological or endocrine disorders, or drug allergies. Follow-up was 100% for the treatment period and 95% for the withdrawal period.

Intervention
All patients completed a 4-week run-in period and were allocated to a nightly dose of imipramine, 25 mg (n = 25); mianserin, 10 mg (n = 26); or placebo (n = 29) for 8 weeks. Follow-up was continued for a 4-week withdrawal period. Compliance was assessed by pill count.

Main outcome measures
Improvement in dry nights achieved, degree of wetness per week, and consecutive dry nights.

Main results
For dry nights achieved, 72% of patients who received imipramine showed definite improvement (mean increase of ≥ 2 dry nights/wk) compared with 38% of patients who received mianserin and 38% who received placebo (P < 0.001). {This absolute risk improvement (ARI) of 34% means that 3 patients would need to be treated (NNT) with imipramine for 8 weeks (rather than mianserin) for 1 additional patient to show definite improvement in dry nights, 95% CI 2 to 16; the relative risk improvement (RRI) was 87%, CI 12% to 234%.}* Patients who received imipramine had the lowest degree of wetness per week compared with mianserin (P = 0.002) and placebo (P = 0.002). 84% of patients who received imipramine achieved ≥ 7 consecutive dry nights compared with patients who received mianserin (35%) or placebo (24%) ($P \leq 0.001$); {for imipramine compared with mianserin, ARI 49%; NNT 2, CI 1 to 4; RRI 143%, CI 47% to 341%}*. The groups did not differ 1 month after cessation of treatment.

Conclusion
Imipramine was more effective than mianserin for short-term treatment of children with nocturnal enuresis.

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*Numbers calculated from data in article.

Commentary

The study by Smellie and colleagues confirms the current evidence that imipramine, a tricyclic antidepressant, is effective for the short-term treatment of nocturnal enuresis in children. It also provides evidence that mianserin, a quadricyclic antidepressant, is no more effective than placebo for the treatment of nocturnal enuresis.

Nocturnal enuresis occurs in approximately 15% of 5-year-old children and has a spontaneous annual cure rate of approximately 15% (1). If the condition is distressing for the child and family, treatment can be implemented. The treatment of choice remains an alarm system because it offers a permanent cure (2). It requires, however, a motivated child and parents and time for the system to become effective. Medication is most useful in situations where a quickly achieved short-term period of dryness is needed, such as when the child will be sleeping away from home. The relapse rate after discontinuing medication is high. The 2 main choices of medication are desmopressin, an analogue of vasopressin, and tricyclic antidepressants, including imipramine. Desmopressin is preferred to imipramine because it is safer. The side effects of desmopressin are usually mild and include headache, nausea, abdominal and nasal discomfort, epistaxis, and hyponatraemia. To date, long-term, permanent side effects have not been reported. A small but nonetheless important risk exists for sudden death in children who take tricyclic antidepressants (3). Desmopressin is also expensive. Imipramine can serve as an alternative medication to desmopressin for children who cannot take desmopressin because of its cost (£1.00 vs 4 p) or because of its side effects.

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