Open Study of Low-Dose Amitriptyline in the Treatment of Patients with Idiopathic Fecal Incontinence

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INTRODUCTION: Amitriptyline, a tricyclic antidepressant agent with anticholinergic and serotoninergic properties, has been used empirically in the treatment of idiopathic fecal incontinence with good results. METHODS: An open study was conducted to test the response to amitriptyline 20 mg daily for four weeks by 18 patients (2 males) of median age 66 years with idiopathic fecal incontinence. Incontinence scores, number of bowel movements, computerized ambulatory anorectal pressures, and pudendal nerve terminal motor latencies were evaluated before and after four weeks of therapy. Twenty-four control subjects (10 males) of median age 61 years were also assessed.

RESULTS: Amitriptyline improved incontinence scores (median pretreatment score = 16 vs. median posttreatment score = 3; P < 0.001) and reduced the number of bowel movements per day (P < 0.001). Amitriptyline also decreased the frequency (median pretreatment frequency = 4.5 per hour vs. median immediate posttreatment frequency = 1.2 per hour; P < 0.05); control median frequency = 0.3 per hour) and the amplitude of rectal motor complexes (median pretreatment rectal pressure = 94 cm H2O vs. median immediate posttreatment rectal pressure = 58 cm H2O (P < 0.05); control median rectal pressure = 36 cm H2O) and improved anal pressures during these events (P < 0.001). CONCLUSIONS: Amitriptyline improved symptoms in 89 percent of patients with fecal incontinence. The data support that the major change with amitriptyline is a decrease in the amplitude and frequency of rectal motor complexes. The second conclusion is that drug increases colonic transit time and leads to the formation of a firmer stool that is passed less frequently. These in combination may be the source of the improvement in continence. [Key words: Fecal incontinence; Anal sphincter; Anorectal manometry]


T ricyclic antidepressants have been used empirically in the treatment of idiopathic fecal incontinence with satisfactory results. The aim of this study was to test the efficacy of amitriptyline in patients with idiopathic incontinence and to provide a rational basis for further clinical trials. Our primary hypothesis was that amitriptyline, which has serotoninergic, anticholinergic, and antimuscarinic properties, might improve the function of the anal sphincter in patients with incontinence.

P ATIENTS AND METHODS

For a 12-month period from June 1995, consecutive patients with idiopathic fecal incontinence of more than six months' duration were recruited from our Gastrointestinal Unit. Eighteen patients (2 males) of median age 66 (range, 30–81) years were enrolled. Their median duration of symptoms was four years (range, 10 months to 15 years). Twenty-four healthy subjects (10 males) of median age 61 (range, 32–79) years were also assessed.

Study Design

The design of the study was an open trial of low-dose amitriptyline. All incontinent patients received amitriptyline 20 mg daily at bedtime, and each treatment was given for four weeks. Patients were evaluated at the start of the trial and after four weeks of therapy. The controls consisted of volunteers recruited from medical and nursing staff, patients admitted for surgery unrelated to defecatory disorders, and members of the public. The controls did not receive amitriptyline and were evaluated only at the initial clinic visit. The study was approved by the Infirmary Medical Committee, and a consent form was read and signed by all participants.

Clinic Visits

At the initial clinic visit all patients who presented with cardiovascular disease, epilepsy, hyperthyroid-
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ism, impaired liver function, urinary retention, prostatic hypertrophy, psychosis or with a history of traumatic childbirth (episiotomy, forceps delivery, obstetric tears), abuse of alcohol or drugs, prior adverse reaction to amitriptyline, pregnancy or lactation or in therapy with oral contraceptives, antidepressant drugs, antiepileptics (benzodiazepine, barbiturates) drugs and cimetidine were excluded from this study.

Incontinence was scored using a scale of 1 to 18. Continence to flatus, fluid and solid stool was assessed in terms of frequency of incontinent episodes and a score given for each as follows: A) incontinence less frequent than once per month: score for flatus, 1; score for fluid stool, 4; score for solid stool, 7. B) incontinent episodes between once per month and once per week: score for flatus, 2; score for fluid stool, 5; score for solid stool, 8. C) incontinent episodes more than once per week: score for flatus, 3; score for fluid stool, 6; score for solid stool, 9. The magnitude of the score reflects increasing severity of incontinence both in terms of frequency and nature of the incontinent episodes.

Urgency of defecation was defined as an overwhelming desire to defecate that precluded all other activity. Fecal leakage and soiling were defined as incontinence of small amounts of stool without immediate awareness.

All participants underwent thorough physical examination, including perineal and rectal examination and rigid sigmoidoscopy, to exclude local anorectal conditions that could be responsible for fecal incontinence. Assessment included endoanal ultrasonography (EUS), pudendal nerve terminal motor latency (PNTML), and computerized ambulatory anorectal manometry. EUS was performed with a rotating 7-MHz transducer (Brueel-Kjaer type 1840, Naerum, Denmark). Integrity of the internal anal sphincter (IAS), external anal sphincter (EAS), perineal body, and puborectalis muscle were assessed. Patients with disruption of the anal sphincter were excluded.

PNTML was measured by using the St. Mark's pudendal nerve to deliver an electrical stimulus. A Medelec Mystro (Dantec Neuromatic 2000 M, Woking, United Kingdom) provided the stimulus and its oscilloscope measured the latency.

The technique of 24-hour ambulatory manometry has previously been described in detail. In brief, anorectal manometry was performed using the Gaeltec 7-MPR system (Gaeltec, Isle of Skye, United Kingdom). Once the catheter was in position, usually around midday, subjects were allowed to leave the unit, and they returned the next day. All subjects were instructed to complete a diary of events including a desire to open bowels, passage of flatus, defecation, and micturition. Each event was also marked on the recorders memory by pressing an event marker device and noting the time on the recording clock. On completion of the recording, information on the ambulatory recorder was downloaded to a personal computer (Archimedes Taxan 410 personal computer, Acorn, Cambridge, United Kingdom). Transient IAS relaxation was defined as a rise in rectal pressure greater than 5 cm H2O with a fall in anal pressure of 5 cm H2O or more that was associated with desire to pass gas or feces. Rectal motor complexes (RMCs) were defined as episodes of rectal activity neither associated with actual passage of flatus or defecation nor with IAS relaxation.

Patients attended the clinic after a four-week treatment period. Each visit included an interview with reassessment of the incontinence score, a clinical examination, and the ambulatory recordings of anorectal pressures. Details of any adverse effects were documented.

**Statistical Analysis**

All results are expressed as median values. Statistical analysis was performed using the Mann-Whitney U test and the results considered to be significant at the 5 percent level (P < 0.05).

**RESULTS**

Eighteen patients with fecal incontinence fulfilled the entry criteria and were recruited. There were two males, and the age range was 30 to 81 years, with a median of 66 years. All patients completed the trial and were included in the efficacy analysis. Four patients (22 percent) experienced adverse effects (drowsiness or dry mouth) during therapy; however, they were able to tolerate their side effects, and amitriptyline was not discontinued.

**Clinical Data**

Four patients were smokers (median number of cigarettes, 12), and six patients were receiving noncontraindicated medications (beta-blockers, nonsteroidal anti-inflammatory drugs, salbutamol and thyroxine). Twelve patients had an obstetric history with a median of two (range, 1–4) vaginal deliveries. A his-