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Ephedrine hydrochloride: Novel use in the management of resistant non-neurogenic daytime urinary incontinence in children

Neil Featherstone*, Joanna Stanwell, Susan Affleck, Kate Wang, Feilim Murphy, Su-Anna Boddy

Department of Paediatric Surgery & Urology, St George's Hospital, Blackshaw Road, Tooting, London SW17 0QT, UK

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Abstract *Objective:* To determine whether the adrenoceptor agonist, ephedrine hydrochloride, is an effective treatment for resistant non-neurogenic daytime urinary incontinence in children.
Methods: From 2000 to 2010, eighteen children with resistant non-neurogenic daytime urinary incontinence were treated with oral ephedrine hydrochloride at our institution. Sixteen were female and two were male. Median age at treatment was 12 years (range 5—15 years). Two children had spina bifida occulta. There were no other co-morbidities. Multiple anticholinergics were prescribed and dose maximized to support a bladder and bowel training programme, without achieving continence in this resistant group of children. Pre-treatment urodynamics were normal in 10, but revealed an open bladder neck in 8 patients. None showed detrusor over-activity. Oral ephedrine hydrochloride was started at 7.5 mg or 15 mg twice daily and titrated up to a maximum of 30 mg four times daily according to response.
Results: Median follow-up was 7 years (range 6—8 years). Seventeen children (94%) reported improvement in symptoms and six (33%) achieved complete urinary continence. All patients maintained compliant bladders on post-treatment urodynamics. Seven of the 8 previously open bladder necks were closed. No patients reported any significant side effects. Patients with open bladder necks on pre-treatment urodynamics were more likely to show a full response to ephedrine (odds ratio 15; 95% CI 1.2—185.2).
Conclusions: Oral ephedrine hydrochloride is an effective treatment for carefully selected children with resistant non-neurogenic daytime urinary incontinence.

* Corresponding author. Tel.: +44 208 6721255; fax: +44 208 7250711.
E-mail address: neilfeatherstone@doctors.org.uk (N. Featherstone).

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Introduction

In the paediatric population, ephedrine hydrochloride, a potent α and β adrenoceptor agonist, is used by paediatric urologists in children with myelomeningocele and neurogenic bladder, as an adjunct to clean intermittent catheterization and anticholinergic medication, either in oral or intravesical form [1—4].

Ephedrine is thought to act via constriction of the internal urethral sphincter and relaxation of bladder muscle [5]. *In vitro*, ephedrine has been shown to relax strips of urinary bladder muscle via β receptors (reversed by the β-adrenergic receptor blocker timolol) and contract strips of urethral muscle via α receptors (reversed by the selective α-1-adrenergic receptor blocker prazosin) in rabbit tissue [6].

To the best of our knowledge, ephedrine has not been reported as a treatment for resistant non-neurogenic daytime urinary incontinence in children. We aimed to determine if ephedrine hydrochloride was a useful therapeutic agent in this challenging group of children.

Patients and methods

Ethical approval was obtained prospectively from the local ethics committee.

During a ten-year period between 2000 and 2010, eighteen children were treated with oral ephedrine hydrochloride for resistant daytime urinary incontinence at St Georges Hospital, London, UK (approximately 0.5% of the daytime urinary incontinence referrals to the paediatric urology service during this period).

Our standard approach was followed in all cases; this included specialist paediatric urology assessment, careful history, physical examination and selective utilisation of spinal/renal tract imaging. All were enrolled on a clinical nurse specialist led bladder training programme. They were given advice on adequate clear fluid intake, advised to avoid caffeinated/fizzy drinks and encouraged to adopt the correct position on toilet. Stimulant laxatives were administered to treat constipation and antibiotics were prescribed for proven urinary tract infections. Anticholinergics were prescribed, usually in the form of oxybutynin, either three times daily or as the once daily slow release preparation. If oxybutynin was not tolerated, either tolterodine or solifenacin were trialed and dose maximised before children were deemed resistant to standard daytime urinary incontinence treatment.

All patients underwent pre- and post-treatment urodynamic investigations (urodynamic lines were placed via the urethra). Pre-treatment urodynamics were performed after anticholinergic medication had been stopped for at least 3 days. Patients were followed-up at 3 to 6 monthly intervals until adulthood.

Oral ephedrine hydrochloride was started in this resistant group of patients at a dose of 7.5 mg or 15 mg (depending on age and weight) twice daily and increased to a maximum of 30 mg four times daily according to response. Response was assessed using volume-frequency charts and standardised bladder diary. Success was reported using definitions conforming to the International Children's Continence Society (non-response defined as a 0—49% decrease, partial response defined as 50—89% decrease, response defined as 90% or greater decrease and full response defined as 100% decrease or less than 1 symptom occurrence monthly) [7]. Ephedrine was weaned once continence had been achieved. All patients were followed-up on a regular basis (3—6 monthly intervals) in a specialist urinary incontinence clinic.

Results

Eighteen patients were treated with ephedrine hydrochloride between 2000 and 2010. Sixteen were female and two were male. Median age was 12 years (range 5—15 years) at time of treatment. Two had spina bifida occulta. There were no other co-morbidities. Median follow-up was 7 years (range 6—8 years).

None of the 18 children showed evidence of detrusor over-activity. Ten had closed bladder necks and eight had open bladder necks evident on video cystography (Fig. 1).

Seventeen children (94%) reported improvement in symptoms and six (33%) achieved complete urinary continence with ephedrine hydrochloride. Table 1 shows the response for patients with open and closed bladder necks. In 7 of the 8 patients with an open bladder neck on pre-treatment urodynamics, the bladder neck was subsequently not seen to open on post-treatment urodynamics. None of our patients reported any significant side effects, despite one accidental overdose. There were no statistically significant differences in the overall response between children with open or closed bladder necks. However, children with open bladder necks were more likely to show a full response to ephedrine (odds ratio 15; 95% CI 1.2—185.2). Both male patients (one with open bladder neck) showed a full response.

Ephedrine was weaned once continence had been achieved after a median of 1 year of treatment. In two patients, symptoms recurred on an initial attempt at weaning and ephedrine was continued for a further 2 years.

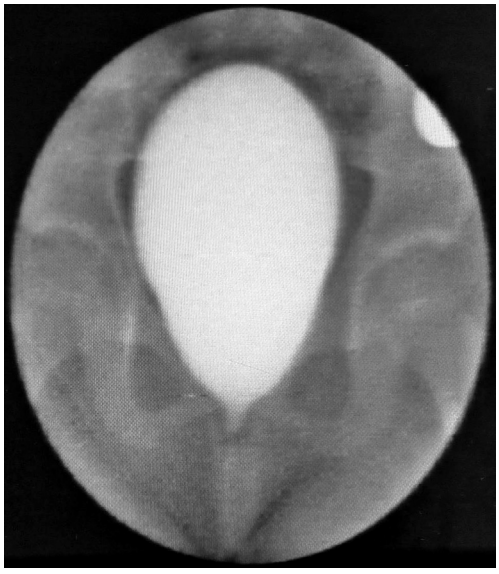

Figure 1 Video cystography demonstrating an open bladder neck during urodynamic investigation.