

ADRENERGIC DRUGS FOR URINARY INCONTINENCE IN ADULTS- EVIDENCE FROM A COCHRANE REVIEW 1

Aims of Study

Urinary incontinence is estimated to affect over 10% of the adult female population. Stress urinary incontinence is conventionally treated with conservative physical therapies and if this is unsuccessful, surgery. However, surgery is not without morbidity. Adrenergic drugs are thought to act by stimulating contraction of the bladder outlet sphincter. Drug treatment of stress urinary incontinence with adrenergic drugs is generally considered to be ineffective or their use severely limited by side effects such as hypertension, pilo-erection and central nervous system stimulation. Despite this pessimism, there is continuing clinical and pharmacological interest in their use, but data from randomised controlled trials are scarce. Adrenergic agonist drugs are rarely used in men, but they could have a place in the management stress urinary incontinence after radical prostatectomy.

Methods

We searched the Cochrane Incontinence Group trials register (January 2002) and the reference lists of relevant articles. Randomised or quasi-randomised controlled trials which include an adrenergic agonist drug in at least one arm for adults with urinary incontinence were selected. Two reviewers independently assessed eligibility, trial quality and extracted data. Data were processed as described in the Cochrane Collaboration Handbook. Data extraction was undertaken independently by two reviewers and cross-checked. Trial data were considered in relation to the eight main hypotheses. Within these categories, sub-categories were used according to the type(s) of drugs being compared. Any difference of opinion related to the data extracted was discussed and resolved with a third person. When appropriate, meta-analysis was undertaken. For categorical outcomes we related the numbers reporting an outcome to the numbers at risk in each group to derive a relative risk. For continuous variables we used means and standard deviations to derive a weighted mean difference. A fixed effects model was used for calculation of summary statistics (pooled estimates) and 95% confidence intervals. Differences between trials were further investigated when significant heterogeneity was found at the 10% level or appeared obvious from visual inspection of the results. For cross-over trials, and trials where continuous data were reported without measures of dispersion (e.g. standard deviations), comparisons were made only on the direction of effect.

Results

Fifteen eligible randomised trials were identified, which included 832 women, of whom 506 received an adrenergic drug (phenylpropanolamine in 11 trials, Midodrine in two and Clenbuterol in another two). Of these, six were crossover trials. No trials included men.

The limited evidence suggested that an adrenergic agonist was better than placebo. For example, higher cure or improvement rates for adrenergics compared to placebo (e.g. for phenylpropanolamine, RR 1.58, 95% CI 0.87 to 2.85; for Midodrine 1.55, 95% CI 1.02 to 2.35; for Clenbuterol 1.96, 95% CI 1.26 to 3.05). However, more adverse events were reported during active treatment, in some cases causing drop out from the trials.

The drugs also appeared to be better than pelvic floor muscle training (PFMT) in two small trials, possibly reflecting relative acceptability of treatment to women (more women cured or improved with drug compared with PFMT RR 1.41, 95% CI 1.09 to 1.81; more women satisfied, RR for satisfaction 2.68, 95% CI 1.33 to 5.40; and higher drop out from PFMT group, 11/75 from drug group vs 28/82 from the PFMT group)

There was not enough evidence to evaluate the use of higher compared to lower doses of adrenergic agonists nor the relative merits of an adrenergic agonist drug compared with oestrogen, whether used alone or in combination.

Conclusions

There is some weak evidence in support of adrenergic agonists as effective treatment for incontinence over placebo treatment. There was not enough evidence to assess their effectiveness in relation to other treatments. They do have minor side effects, but stopping treatment for this reason is uncommon. However, rare but serious side effects such as cardiac arrhythmias and hypertension have been reported. Larger trials would strengthen the evidence base for the use of adrenergic drugs for the treatment of stress urinary incontinence. In particular, their use needs to be evaluated in comparison with other effective treatments such as surgery and pelvic floor muscle retraining, and in combination with these alternatives, both in terms of continence and unwanted effects. A randomised trial in men with post-prostatectomy incontinence should be considered. Trials should use standardised outcomes including both subjective and objective measures of cure and improvement, general health status measures, and quality of life and health economic outcomes.

Reference:

1. Adrenergic drugs for urinary incontinence in adult (Cochrane Review) in The Cochrane Library, Issue 2, 2003. Update Software, Oxford.