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NEW USE FOR AN OLD DRUG: RESULTS OF A DOSE TITRATION STUDY OF INTRA-VESICAL ATROPINE

Aims

Atropine is a potent anti-muscarinic and has been in use for decades. The local use of atropine by intra-vesical installation has been demonstrated to produce a significant increase in cystometric bladder capacity, for patients with spinal injury or MS, with no reported side-effects and no detectable blood levels[1,2]. Used in this way atropine has the potential to suppress detrusor hyperreflexia without systemic side-effects and at low cost. We aimed to examine the dose – response effect of intra-vesical atropine in preparation for a clinical trial comparing it to a conventional oral anticholinergic.

Methods

Eight subjects with a diagnosis of multiple sclerosis, using intermittent catheterisation and oral anticholinergics were recruited to the study. Following a 3-7 day baseline period *without* their usual anticholinergic medication, subjects used increasing doses of intra-vesical atropine over the 12 day intervention phase. Subjects were asked to keep a frequency/volume bladder diary during the study period.

Results

The table below summarises the mean changes (baseline data subtracted from intervention phase data) of the three main outcome measures (i) volumes (both voided and catheterised) (ii) frequency of voiding (iii) frequency of incontinence episodes. Both increased strength and frequency of atropine doses resulted in higher voided volumes, decreased frequency and decreased incontinence episodes. One of the eight subjects did not experience any improvements. All but one subject (who reported dry mouth) experienced no increased side-effects compared to the baseline (no anticholinergic) period. Seven of the eight subjects requested to use intra-vesical atropine after the study.

Dose	2mg				4mg				6mg			
Administration	od	bd	tds	qds	od	bd	tds	qds	od	bd	tds	qds
Day	1	2	3	4	5	6	7	8	9	10	11	12
Mean volumes (ml)	-6	+5	+30	+45	+34	+72	+94	+108	+28	+49	+123	+204
Volumes (SD)	*39*	*58*	*66*	*69*	*80*	*88*	*81*	*132*	*58*	*53*	*115*	*137*
Mean frequency	0	-1	-1	0	-1	-2	-2	-3	-3	-2	-4	-4
Mean incontinence	+2	1	-1	0	0	0	-1	-1	-1	-1	-2	-1

Conclusions: This dose titration study demonstrated a clear dose-response effect, with maximum effect and maximum patient satisfaction at the highest dose (6 mg qds) used. The clinical use of intra-vesical atropine appears promising.

1. Deaney et al. JNNP 1998;65,957-958
2. Enskat et al. Proceedings of ICS(UK) 1999