Systematic review of therapy for neurogenic detrusor overactivity

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Abstract

While many neurologic diseases predispose patients to neurogenic detrusor overactivity (NDO), the only populations that have been systematically studied are adults with multiple sclerosis (MS), adults with spinal cord injury (SCI) and children and young adults with myelodysplasia. First-line pharmacotherapy for NDO is an antimuscarinic drug. However, the evidence base for these agents in this indication is poor. There is some high-quality evidence for the efficacy of detrusor injections of botulinum toxin A in the treatment of NDO, with significant reduction in urgency incontinence episodes, improved urodynamic parameters, and improved quality of life. While few adverse events have been reported with this therapy, there is a need for intermittent self-catheterization in these groups.

Neurogenic detrusor overactivity (NDO) can be seen with various neurological diseases. At present, however, the only such populations that have been systematically studied are adults with multiple sclerosis (MS) and spinal cord injury (SCI) and children and young adults with myelodysplasia. There have yet to be any randomized, controlled studies evaluating therapy for NDO in Parkinson's Disease or dementia. This review will, therefore, focus on the available treatment evidence from the above-mentioned conditions.

Antimuscarinic therapy for neurogenic detrusor overactivity

The first-line, mainstay treatment of NDO is the antimuscarinic drugs. This practice is not, however, based on a great deal of high quality research. Indeed, the body of evidence for their efficacy based on randomized controlled trials (RCTs) is surprisingly poor. In total, there are only five Grade-A studies in adults.[1-5] These studies, which spanned from 1985 to 2007, examined the effect of oral propiverine, oxybutynin, trospium or propantheline or intravesical atropine. The research in MS has also been reviewed in a systematic fashion in a Cochrane review published in 2009.[6] In children with myelodysplasia, there are two RCTs[7,8] and 11 observational studies.[9-19]

Looking at all this evidence, propiverine, trospium, oxybutynin, propantheline and tolterodine have all been shown to produce clinical and some evidence of urodynamic improvement in NDO. Although this evidence is sufficient to conclude that "antimuscarinics are effective in NDO," prescribing more recently introduced antimuscarinics is not evidence-based. Rather, there is an assumption that their demonstrated efficacy in non-neurogenic DO is "carried over" to the NDO group. Indeed, everyday clinical experience does seem to bear that assumption out and even suggests that antimuscarinics may in fact be more efficacious in NDO than in idiopathic DO and that their benefits are longer lasting.

Other oral therapies for neurogenic detrusor overactivity

Desmopressin

The evidence for efficacy of desmopressin in MS for treatment of nocturia and daytime frequency is level 1, based on the results of a meta-analysis published in 2005.[20] However, desmopressin does carry the risk of hyponatremia, particularly in older patients. The recommendation for patients over 65 years of age is to check serum Na levels at baseline and again at 3 days and 7 days after commencing treatment or changing dose.

Cannabinoids

Two studies have looked at the efficacy of cannabinoids on urinary problems in MS and evidence of limited efficacy was found. In one study with orally administered Δ9-tetrahydrocannabinol extract, researchers observed a reduction in incontinence episodes,[21] while in another

study using oral nabiximols (Sativex), there were significant reductions in the number of episodes of nocturia, overall bladder control, number of voids/day and Patient's Global Impression of Change relative to placebo.[22] Notably, in this latter study, the beneficial effects in reducing nocturia was related to severity of baseline episodes (Fig. 1).

Other oral therapies

To date, there are no data available for α-adrenoreceptor antagonists or phosphodiesterase inhibitors, nor the recently introduced ß-adrenoreceptor antagonists in the neurogenic population.

Neurotoxins for neurogenic detrusor overactivity

Intravesical vanniloids

There is some lesser grade evidence for the use of intravesical vanniloids to treat NDO but no such preparations are currently licensed.[23,24]

Botulinum toxin

Despite its relatively recent introduction, there is high-quality evidence for the efficacy of detrusor injections of Botulinum toxin A in the treatment of NDO in MS and SCI in adults and myelodysplasia in children and young people. There are three RCTs in adults which provide evidence for improvement in daily frequency of incontinence episodes and specific quality of life (QoL), and six observational longer-term studies show benefit is sustained. Eleven prospective observational studies in children show comparable efficacy.[25-36]

Moreover, the results of pivotal licensing studies of onabotulinumtoxin A in NDO are currently being presented in abstract form and are showing a significant reduction in urgency incontinence episodes, improved urodynamic parameters, and improved QoL.[37-40] In the registration study presented at the European Association of Urology meeting in March 2011, a total of 154 patients with multiple sclerosis and 121 with spinal cord injury were randomized to receive onabotulinumtoxin A 200 U or 300 U or placebo.[25,26] The researchers showed that both doses of onabotulinumtoxin A were associated with significant improvements vs. placebo in episodes of urgency incontinencemaximum cystometric capacity (MCC), maximum detrusor pressure (MDP), and quality of life.

Few adverse events have been reported, but the need for intermittent self-catheterization (ISC) in these groups of patients is an important consideration. In the registration study described above, 30% of the 200 U group and 42% of the 300 U group required intermittent self-catheterization, compared to 12% of the placebo group.

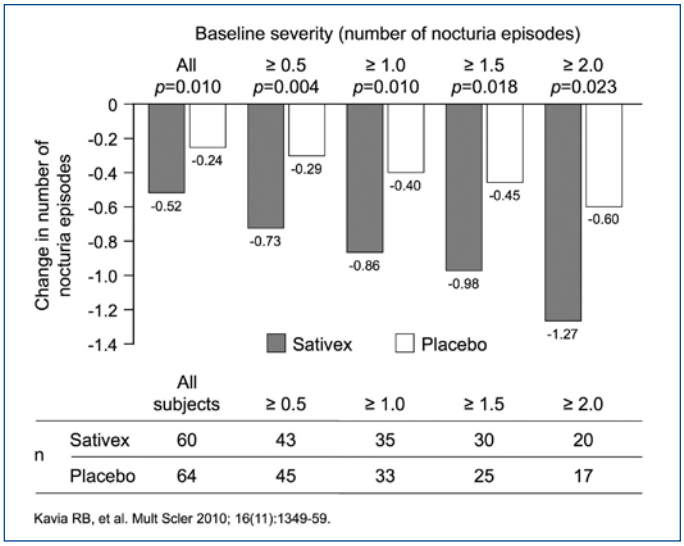

Fig. 1. Treatment of neurogenic detrusor overactivity with cannabinoid therapy: reduction in number of nocturia episodes related to severity of baseline episodes.

Conclusions

The evidence base for antimuscarinics to treat NDO is poor despite these medications being those most commonly used in clinical practice in this group. Few other drugs have had demonstrated efficacy and, with the exception of desmopressin, are rarely prescribed. The evidence for the efficacy of detrusor injections of Botulinum toxin A is already at level 1. Emerging licensing studies make a strong case for this being a highly effective treatment for NDO but with a risk of the need for intermittent self-catheterization.

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This paper has been peer-reviewed.

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