**Peer reviewed**

**Bladder and bowel dysfunction in multiple sclerosis: A review of treatment effectiveness**

**Abstract**

In the present review we located and examined 22 articles reporting trials of treatments for bladder and bowel problems among people diagnosed with multiple sclerosis (MS). Of those studies, 16 included only people with MS. The wide range of measures and methods used precluded any quantitative analysis and hence a narrative review was adopted. There is limited research evidence to guide the treatment of bladder and bowel problems among people with MS. We consider that there is reasonable evidence that oral anticholinergic agents and intranasal desmopressin offer some short-term relief for overactive bladder and nocturia respectively. For those patients with persistent or refractory symptoms there is limited evidence from single trials which suggest that intravesical administration of antimuscarinics or vanilloids, or injection of detrusor muscle with botulinum-A toxin, might be considered. Future research priorities should include: studies that focus on managing bladder and bowel symptoms with samples consisting exclusively of people with MS; research on conservative strategies for the management of bladder symptoms; intervention studies of all types with longer follow-up periods. Finally, there is an urgent need for further research on the management of bowel problems in MS.

**Introduction**

Symptoms of bladder and bowel dysfunction affect the majority of people with multiple sclerosis (MS) at some stage during the course of the disease and feature among the more distressing and disabling symptoms causing severe limitations upon activity levels, social participation and reduced quality of life. The lifetime prevalence of bladder symptoms is around 75%. The prevalence of faecal urgency, with or without incontinence, may be as high as 53%, and the prevalence of constipation up to 73%. In the absence of a cure for MS, alleviating disabling symptoms such as bladder and bowel dysfunction should be an important component of the comprehensive medical management of the disorder.

Typical urinary tract symptoms in MS are those of the overactive bladder (i.e. frequency, nocturia and urgency) with or without urge incontinence), symptoms of poor bladder emptying (e.g. poor stream, feeling of incomplete emptying), or a combination of these. Overactive bladder symptoms are the most common and may be associated with detrusor overactivity. Difficulties with bladder emptying may be related to bladder outlet obstruction or inadequate detrusor activity. Bowel symptoms, especially faecal incontinence, are less likely to be reported than urinary symptoms and have been less frequently studied.

The actual pathophysiology underlying bladder and bowel symptoms in people with MS may be very complicated. Moreover, because of the widespread nature of nervous system lesions in MS, that affect multiple levels of hierarchical control of bladder and bowel function, it is not clear if it is appropriate to extrapolate the findings of treatment studies in other populations, with or without identifiable neurological disease, to the MS population. If there is little evidence specific to the MS population then the temptation or need to generalise probably increases.

A recent comprehensive review of management of neurogenic bladder and bowel dysfunction conducted by Committee 12 (Neurologic Urinary and Faecal Incontinence) from the 3rd International Consultation on Incontinence presented an overview of evidence for neurological disorders as a whole, and separate summaries for particular disorders (e.g. Parkinson's disease, MS). This was a useful approach, enabling some comparison between evidence from wider and more specific populations. There were two other notable features of the report,

---

**E Jean C Hay-Smith**  
Rehabilitation Teaching and Research Unit, University of Otago, Wellington

**Richard J. Siegert**  
Rehabilitation Teaching and Research Unit, University of Otago, Wellington

**Mark Weatherall**  
Rehabilitation Teaching and Research Unit, University of Otago, Wellington  
Member Australian and New Zealand Continence Journal Editorial Committee

**David A. Abernethy**  
Department of Medicine, University of Otago, Wellington, New Zealand

**Corresponding author:**  
E Jean C Hay-Smith  
Rehabilitation Teaching and Research Unit  
Department of Medicine  
University of Otago Wellington  
PO Box 7343, Wellington South, New Zealand  
Email: jean.hay-smith@otago.ac.nz
which are also characteristic of other reviews of treatments for bladder/bowel dysfunction in people with MS that we are aware of; these are the absence of reference to some published trials of conservative management and the lack of discussion about the size of treatment effect.

In this article we review the evidence for the effectiveness of various treatments of bladder and bowel dysfunction in people with MS.

Methods

In August 2005 we searched the following electronic bibliographic databases: Medline, Embase, Cinahl, PsycINFO and the Cochrane Central Register of Controlled Trials. A combination of subject headings and key words were used: multiple sclerosis, incontinence, neurogenic bladder, constipation, urgency, frequency, detrusor, and retention. The condition and symptom specific search was combined with a keyword search for likely reports of randomised trials. Searching was limited to reports of human studies. The reference lists of retrieved articles were searched for reports of possible trials.

Studies were selected if they reported a randomised trial in a study sample wholly or partly comprised of people with a diagnosis of MS, and included participants with one or more of the following symptoms: urinary or faecal incontinence, urinary or faecal urgency, urinary frequency or nocturia, urinary retention, or constipation. The primary inclusion criterion for participants in some studies was detrusor overactivity, which is a urodynamic rather than symptom based diagnosis. However, we assumed patients in these studies had overactive bladder symptoms. All types of intervention were eligible, so long as the treatment was given specifically for bladder or bowel dysfunction. We did not review studies investigating interventions to prevent or treat urinary tract infection. A narrative review is presented since there were few trials and there was little commonality in either the interventions or the outcome measures they reported.

Results

Twenty-four studies were considered for the review. Two trials were not reviewed; one investigated the effect of a drug (terodiline) that was withdrawn from the market because of cardiac side effects, and one trial report was not available in English translation (1). There were nine parallel and 13 crossover designs (2,3). In general, the quality of trial reporting was poor, so it was difficult to appraise the methodological quality of the studies. Two trials were published as abstracts of ongoing studies (4,5), one abstract of a small phase II trial (6), and one was a letter to the editor (7). These three trials gave few details of study methods or data. On the whole, it seemed most studies were at moderate to high risk of bias.

We grouped the 22 included studies according to the predominant symptom or symptom complex, and the type of intervention targeting this symptom and show these in Table 1.

Interventions for Lower Urinary Tract Dysfunction. There were three articles that examined the effectiveness of physical and or behavioural therapies for treatment of lower urinary tract dysfunction. Pelvic floor rehabilitation improved a range of outcome measures at six months in one trial and biofeedback may have improved subjective reports of symptoms in another (8,9,10).

Interventions for Overactive Bladder. Thirteen studies looked at a range of pharmacological interventions for overactive bladder symptoms. Oral anticholinergic agents produced improvements on a range of outcome measures in a number of trials with some evidence from between drug comparisons that oxybutynin may have been better (11,12). Intravesical atropine may improve

<table>
<thead>
<tr>
<th>Predominant symptoms</th>
<th>Interventions</th>
<th>Trials (by first author/year)*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Prostaglandin synthesis inhibitor</td>
<td>Cardozo 1980</td>
</tr>
<tr>
<td></td>
<td>Antidiuretic hormone analogue</td>
<td>Fredrikson 1996*, Hoverd 1998*, Kinn 1990*</td>
</tr>
<tr>
<td></td>
<td>Vanilloids</td>
<td>de Seze 1998, Kim 2003</td>
</tr>
<tr>
<td></td>
<td>Botulinum-A toxin</td>
<td>Schurch 2005</td>
</tr>
<tr>
<td>Nocturia</td>
<td>Antidiuretic hormone analogue</td>
<td>Eckford 1994*, Hilton 1983*, Valiquette 1996*</td>
</tr>
<tr>
<td>Voiding difficulties</td>
<td>Bladder emptying technique</td>
<td>Prasad 2003*</td>
</tr>
<tr>
<td>Constipation</td>
<td>Alpha adrenergic antagonist</td>
<td>O’Riordan 1995*</td>
</tr>
<tr>
<td></td>
<td>5-HT4 agonist</td>
<td>Medaer 1999*</td>
</tr>
</tbody>
</table>

*asterisked trials are those in MS patients only. Non-asterisked trials included non-MS participants.
cystometric bladder capacity. In a small trial of flurbiprofen, which only included three participants with MS, a range of outcome measures were improved compared to placebo but, with more adverse events for flurbiprofen. Three trials examined the usefulness of antidiuretic hormone analogue. Intra-nasal or oral desmopressin have improved voiding frequency and volumes and were preferred by patients in a number of studies although their follow-up times were typically rather short. Single trials of intravesical vanilloid and intramuscular Botulinum-A toxin that included some participants with MS were suggestive of reduced leakage and voids over a relatively short follow-up period.

Interventions for Nocturia. Trials of intra-nasal desmopressin have shown reduced night time voids over a relatively short follow-up period.

Voiding Difficulties. A single trial of abdominal pressure and suprapubic vibration found a small difference in post void residual volumes. A single trial of an alpha-adrenergic antagonist found no difference between the treatment and control groups in urine flow rate, residual volume or on a symptom score for irritative/obstructive symptoms.

Constipation. A single trial of oral prucalopride (5-HT4 agonist) reported in a conference abstract, found that constipation was reduced, although the most common side effect was diarrhoea.

Discussion

In the present review we located and examined 22 articles reporting trials of various treatments for bladder and bowel problems among people with MS. Of these studies included only people with MS. The wide range of measures and methods used precluded any quantitative analysis and hence a narrative review was adopted. While this review identified some clear priorities for research on this topic it was less successful in drawing many firm conclusions concerning the management of such problems with MS patients. Despite the prevalence of MS and the disabling nature of bladder and bowel symptoms, there is only limited evidence from randomised controlled trials, to guide clinicians. The difficulty in going from evidence to practice here, in common with many studies of urinary and bowel problems, stems from the lack of common outcome measures, small numbers of participants in individual trials, and methodological and reporting issues. In addition MS is a disease with highly variable effects on bladder and bowel function and the heterogeneous nature of the pathophysiology of continence problems and symptoms in MS makes conducting trials in this area difficult. Treatments are dependent on not only the diagnosis of MS, but also its exact effect on bladder and bowel function.

We consider that there is reasonable evidence that oral anticholinergic agents and intranasal desmopressin offer some short-term relief for overactive bladder and nocturia respectively. When considered in conjunction with the evidence...
for these interventions with other patient groups experiencing overactive bladder, or nocturnal enuresis, it could be concluded that patients with MS and symptoms of detrusor overactivity or nocturia may benefit. For those patients with persistent or refractory symptoms, there is limited evidence from single trials that suggest that intravesical administration of antimuscarinics or vanilloids, or injection of detrusor muscle with botulinum-A toxin, could be considered.

We found four studies that investigated the use of conservative management strategies such as lifestyle factors, physical and behaviour therapies and other non-surgical/non-pharmacological interventions. Such approaches have been absent from otherwise comprehensive reviews of the treatment of bladder dysfunction in neurological conditions 10. This seems to contrast with our own conversations with colleagues in that they report that advice on lifestyle factors (including fluid intake and diet) toileting habits, the use of absorbent products and collection devices play an important role in their clinical practice. The value of conservative management seems worthy of further research. While it may not be feasible where physical disability is advanced or when there is evidence of cognitive impairment some patients might prefer it to taking medicines and one study found good adherence to pelvic floor muscle training 21.

While the research evidence guiding the management of bladder and bowel symptoms in people with MS is quite limited, the priorities for further research seem fairly clear. There is a need for more studies that focus on managing bladder and bowel symptoms with samples consisting exclusively of people with MS. While there is good evidence from non-neurological samples that some treatment approaches are useful, the physical and cognitive impairments that are common among MS patients, suggest that it would be unwise to generalise from studies with otherwise healthy people to people with MS 15. Unfortunately people with neurogenic conditions are often specifically excluded from studies investigating treatments for bladder and bowel dysfunction, for example the antimuscarinic drug trials. Findings from trials in neurologic and non-neurologic populations may or may not be indicative of response in MS; in the absence of a reasonable body of MS specific evidence it is not clear to what extent, if any, such generalisation is appropriate. In the current situation there is a need for larger trials that are designed with sub-group analysis in mind (e.g. neurologic condition or not, MS or not), and trials that recruit only MS patients.

There is a need for more research on conservative strategies for the management of bladder symptoms in people with MS. The potential for effective treatment with some therapies such as pelvic floor muscle training and bladder training may have been discounted because MS is a disease of the central nervous system, affecting the ability to voluntarily control muscle, or because MS patients may be cognitively impaired and thought unable to cope with self-management strategies. Given that many people with MS experience fatigue and other consequences of the condition Vahtera and colleagues 21 report a reasonably good level of adherence to pelvic floor muscle training. MS patients may value the opportunity to try such interventions, particularly if side effects are unlikely.

There is a need for intervention studies of all types with longer follow-up periods. In some studies treatment periods were short 22, 24, 26, 27, 29, 33, 34, e.g. two weeks, and in most cases outcome was assessed at the end of the treatment period when it is likely the treatment effect would be at its maximum. None of the trials followed participants in the longer term, e.g. a year or longer. The extent to which treatments continue to be effective is likely to be of considerable interest to people with MS, given the progressive and long-term nature of the condition.

There is an urgent need for further research on the management of bowel problems in MS. In common with the epidemiological research treatments for bowel dysfunction have received much less attention than bladder dysfunction. Only one small phase II trial was found 18 and although Medaer and colleagues in that trial on prucalopride stated that constipation was reduced, the most common side effect of treatment with the enterokinetic drug was diarrhoea. It is quite possible that faecal urgency and diarrhoea would be even more bothersome than constipation for MS patients. If diarrhoea is a common side effect of this type of drug, MS patients may prefer other more predictable ways of managing constipation, such as suppositories or micro-enema. No studies addressing the effectiveness of treatments for faecal urgency or incontinence in people with MS were found.

Implications of our review for practical management of bowel and bladder symptoms in MS are:

For bladder symptoms there is a need for careful review of the underlying pathophysiology to guide effective therapy in any individual.

Conservative management strategies, consistent with symptoms and presumed underlying pathophysiology, should be tried. Evidence does not yet conclusively demonstrate effectiveness of these strategies in MS.

Where overactive bladder symptoms are present or detrusor overactivity is demonstrated anti-cholinergic agents may be effective.

Where nocturia is present desmopressin may be effective.

If symptoms of overactive bladder do not respond to conservative measures and relatively simple medication approaches then a better definition of the bladder pathophysiology, for example by performance of urodynamics, may guide therapy. Refractory detrusor overactivity may respond to new therapies such as intra-vesical Botulinum-A toxin. Neither a staged approach to diagnosis and management nor randomised controlled trials of Botulinum toxin have specifically been performed in people with MS.

The approach to bowel problems in MS should, in the absence of evidence, be guided by an evaluation of likely pathophysiology of the bowel symptoms. Thus strategies for constipation should
include conservative measures such as adequate fluid intake and mobility, and where possible an appropriate approach to toileting to take advantage of the gastro-colic reflex. Either dietary interventions or pharmaceutical approaches to increasing the bulk of bowel motions may be appropriate, followed by use of stimulants and/or local rectal preparations. More advanced techniques such as biofeedback may be appropriate but the effectiveness in patients with MS has not been established.

In conclusion future research priorities should include: studies that focus on managing bladder and bowel symptoms with samples consisting exclusively of people with MS and large trials designed with sub-group analysis of neurological patients (specifically MS patients) in mind; research on conservative strategies for the management of bladder symptoms; intervention studies of all types with longer follow-up periods. Finally, there is an urgent need for further research on the management of bowel problems in MS.

References


