Ther Adv Gastroenterol
2014, Vol. 7(6) 232–237
DOI: 10.1177/1756283X14540028

Avoiding analgesic escalation and excessive healthcare utilization in severe irritable bowel syndrome: a role for intramuscular anticholinergics?

James S. Pearson, Christine Pollard and Peter J. Whorwell

Abstract

Objectives: In patients with severe irritable bowel syndrome (IBS), abdominal pain can be the predominant symptom impacting on all aspects of their lives and resulting in excessive healthcare utilization. Furthermore, the use of analgesics can become excessive in this group of patients, sometimes leading to opiate dependency. Typically, the pain is often described as spastic in nature and we have speculated that parenteral anticholinergics might provide effective relief when all other measures have failed. For several years, we have therefore been asking general practitioners to consider teaching such patients to administer intramuscular hyoscine butylbromide for pain episodes and this study is an audit of this approach.

Methods: Patients in whom the use of intramuscular hyoscine butylbromide had been recommended to their general practitioner in the last three years were interviewed over the telephone in order to document the efficacy of this approach as well as any potential disadvantages.

Results: A total of 122 general practitioners were advised to try this approach, with 58 agreeing to teach the technique and prescribe the medication. Of the 58 patients who used the medication, 50 (86%) found it gave them pain relief, which was complete in six (10%), substantial in 36 (62%) and mild in eight (14%), with 15 (26%) decreasing the use of analgesics and 13 (32%) of the 41 taking opiates able to reduce or stop them completely. Side effects were few and largely consisted of those associated with anticholinergics. Only four patients stopped medication because of side effects and no major skin reactions were reported.

Conclusions: The use of intramuscular hyoscine butylbromide shows promise in the management of IBS when severe unmanageable abdominal pain is a major problem. This approach appears to be safe and has the potential to reduce analgesic escalation, opiate dependency and attendances at accident and emergency departments.

Keywords: intramuscular hyoscine butylbromide, irritable bowel syndrome, narcotic bowel syndrome

Correspondence to:
Peter J. Whorwell, MD, PhD
Neurogastroenterology Unit, Wythenshawe Hospital, Manchester M23 9LT, UK
peter.whorwell@uhsm.nhs.uk

James S. Pearson, BSc
Christine Pollard, RGN, MSc
Neurogastroenterology Unit, Centre for Gastrointestinal Sciences, Institute of Inflammation and Repair, University of Manchester, Manchester, UK

Introduction

In many patients with irritable bowel syndrome (IBS) a variety of different symptoms can be ranked as the most intrusive. Such symptoms can include typical features such as abdominal pain, abdominal bloating and bowel dysfunction, but noncolonic complaints such as low backache, constant lethargy, nausea and bladder symptoms may be equally disturbing [Whorwell *et al.* 1986; Maxton *et al.* 1989]. However, as the condition becomes more severe there is a tendency for the bowel dysfunction or pain to become the predominant feature. In the group of patients with pain-predominant IBS antispasmodics often fail to achieve any worthwhile improvement and the next step is to try antidepressants, particularly those of the tricyclic variety [Jackson *et al.* 2000; Ford *et al.* 2009]. In nonresponsive individuals

behavioural treatments are often considered and pain modulators such as pregabalin can be tried [Houghton *et al.* 2007]. During this process of attempting to gain some degree of pain control, analgesics are often introduced with paracetamol, usually being the first choice, although it is seldom effective. Anti-inflammatory medications are also often prescribed, although their use should be discouraged because of their detrimental effect on the gut as well as the fact that they do tend to exacerbate the symptoms of IBS [Agrawal and Whorwell, 2006]. In the absence of any improvement, opiate type medications such as codeine, tramadol, morphine and related medications are, therefore, frequently introduced. Unfortunately, all these latter analgesics are drugs of dependency and there is now emerging evidence that they can actually exacerbate pain and lead to narcotic bowel syndrome [Grunkemeier *et al.* 2007; Choung *et al.* 2009; Agostini *et al.* 2010; Tuteja *et al.* 2010; Drossman *et al.* 2012; Farmer *et al.* 2013; Manickam and Saad, 2013]. Consequently, this process results in physicians being faced with patients taking escalating doses of addictive medications and still failing to gain satisfactory pain control. In addition, such individuals place a major burden on healthcare resources not only in primary care but also in secondary care where they are often submitted to multiple investigations as well as being frequent attendees at accident and emergency departments, sometimes requiring hospital admission [Talley, 1999; Spiegel, 2009].

Intravenous hyoscine butylbromide has been used for decades in radiology and endoscopy departments for the purpose of relieving spasm where it is highly effective and remarkably safe. In addition, it is often administered intramuscularly in accident and emergency departments to patients in whom gastrointestinal spasm is thought to be the cause of abdominal pain. Unfortunately, when administered orally, only 8% of this drug is absorbed and it might be anticipated that it would only be effective in reducing the strength of relatively mild contractions [eMC, 2013]. Therefore, it seems likely that the use of intramuscular hyoscine butylbromide might be a more effective way of delivering this drug, which could be used for the control of severe abdominal pain outside the hospital setting.

Patients with IBS can suffer from a variety of different types of abdominal pain but, in a large proportion, the pain is of a colicky nature, with many women likening it to that of the contractions associated with childbirth [Agrawal and Whorwell, 2006]. This suggests that the pain is caused by gastrointestinal spasm and this is supported by the observation that antispasmodic drugs do seem helpful in a proportion of patients [Ford *et al.* 2008]. It remains a matter for debate as to whether this pain is caused by excessive contractions being felt normally or normal contractions being sensed abnormally but, whatever the mechanism, it seems logical to conclude that reducing the strength of a contraction should reduce pain. We have previously found that in patients with IBS admitted to hospital for the control of their symptoms, the administration of intramuscular hyoscine butylbromide can provide rapid, safe and effective control of their pain. This led us to speculate that the outpatient use of intramuscular hyoscine butylbromide might result in effective pain relief in the more severe cases of IBS and have the potential for preventing the use of addictive analgesics or facilitating their reduction in those individuals already receiving them. Consequently, we have recently been asking general practitioners (GPs) to consider teaching their patients with IBS and refractory, colicky abdominal pain unresponsive to conventional medication self-administration of intramuscular hyoscine butylbromide. This paper reviews our experience to date with this approach, which appears to be safe and effective.

Methods

It was felt that approaching patients attending the outpatient department at the University Hospital of South Manchester could lead to selection bias. Consequently, to avoid this potential problem, outpatient clinic letters for the last 5 years ending 31 May 2013 were searched using the following terms: irritable bowel syndrome, hyoscine butylbromide, injection, intramuscular and i/m. This resulted in the identification of 122 GP letters for which we had recommended a trial of intramuscular hyoscine butylbromide in a patient in whom dietary measures, antispasmodics and antidepressants had failed to have any impact on their pain. In the clinic letters, GPs were asked whether they would be happy to teach patients to administer 20 mg of intramuscular hyoscine butylbromide for the control of episodes of severe abdominal pain. A leaflet was enclosed with the clinic letter explaining the rationale behind the use of parenteral hyoscine butylbromide and advice on how to adopt this approach, as well as information related

to possible side effects and drug interactions (see the appendix). All patients included in the study met the ROME III diagnostic criteria for IBS, exhibiting colicky abdominal pain rather than the continuous, unremitting pain of functional abdominal pain syndrome.

Patients identified in this way, when a GP letter had been sent at least 6 months previously, were sent a letter informing them about the survey and the fact that we would be calling them in order to complete a telephone questionnaire about their experience with the use of intramuscular hyoscine butylbromide. They were also reassured that their participation in the survey was entirely voluntary. The questionnaire aimed to capture the patient experience in a semi-structured way as well as documenting the patient's perception of the GP's attitude to this approach.

Results

A total of 122 patients were identified in whom the use of intramuscular hyoscine butylbromide had been recommended. Of these, 102 were able to be contacted, with the remaining 20 being lost to follow up for a variety of reasons, such as change of address, no longer registered with the GP or a change in name. Of the 102 contactable patients, 58 were injecting hyoscine butylbromide intramuscularly, the mean age was 41 (range 17–64), 50 (86%) were women, 11 (19%) had IBS with constipation (IBS-C), 13 (22%) had IBS with diarrhoea (IBS-D) and the remaining 34 (59%) had an alternating bowel habit (IBS-A). All patients had tried oral hyoscine butylbromide with little or no effect up to a dose of 120 mg daily. A total of 41 (71%) were taking some form of opiate medication. Furthermore, all patients had tried a variety of antispasmodic agents as well as a tricyclic antidepressant or a selective serotonin reuptake inhibitor. There was considerable reluctance among GPs to adopt this form of treatment, with 52 (51%) initially refusing to teach patients how to administer intramuscular hyoscine butylbromide. However, after discussion with our specialist nurse, a further 12 GPs agreed to initiate treatment, leaving 40 GPs (39%) who were still reluctant to proceed. Consequently, 62 patients were prescribed intramuscular hyoscine butylbromide but in two patients, in whom attacks were infrequent, this approach had not yet been tried and a further two patients refused to undertake the survey, leaving 58 eligible patients.

Table 1 summarises the results of the questionnaire, showing that in 86% of patients there was a degree of pain control with an impact on the management of their IBS. The frequency of administration of hyoscine butylbromide varied between once a month and three times daily, with some patients waiting until the pain reached a crescendo while others intervened at an earlier stage in the evolution of their pain. Similarly, the duration of benefit reported was very variable, with a mean of 5 h but a range of half an hour to several weeks. A total of 11 patients reported that they had been able to resume full-time work, and importantly, 15 (26%) had been able to significantly reduce their analgesic use, with six reporting a reduction in opiate consumption and seven (12%) being able to come off opiates completely. A total of 54 (93%) said they would recommend this form of treatment to someone in similar circumstances.

Table 2 summarises the side effects experienced by this group of patients and the majority, such as dry mouth, blurred vision and dizziness, were what might be expected for an anticholinergic medication and no patient discontinued treatment because of these problems. A total of 20 patients (34%) experienced no side effects at all and only 4 patients (7%) discontinued treatment because of side effects.

Another potential problem with intramuscular injections is the possibility of reactions at the injection site and these are listed in Table 3. Thirty eight (66%) of the patients experienced no problems at all and 13 (22%) reported pain at the injection site but this was usually only mild and transitory. Two patients (3%) mentioned lumps at the injection site with the remaining four (7%) reporting a burning sensation while injecting. Only three patients discontinued injections because of injection site problems. There were no reports of inflammation or infection.

Discussion

This study evaluating the use of intramuscular hyoscine butylbromide as a pain control measure in severe refractory IBS shows that when prescribed for use in the community, it can be safe and effective. A total of 72% of patients reported that the injections had a major impact on their pain, with 10% saying that they resulted in almost complete relief of their pain and 62% stating that they had made a significant difference to their

Table 1. Effects of intramuscular hyoscine butylbromide.

Total number of patients receiving hyoscine butylbromide	58	
Number of patients exhibiting some degree of pain control	50	86%
Degree of pain control exhibited		
Complete	6	10%
Substantial	36	62%
Mild	8	14%
No effect	8	14%
Back in work since commencing hyoscine butylbromide	11	19%
Average duration of relief in hours	5	
Cessation of opiates	7	12%
Reduction of analgesics	15	26%
Recommend to someone in a similar situation	54	93%

Table 2. Side effects.

No side effects	20	34%
Dry mouth	26	45%
Blurred vision	18	31%
Dizziness	6	10%
Urinary difficulties	3	5%
Drowsiness	4	7%
Constipated	2	3%
Nausea	2	3%
Tachycardia	1	2%

Table 3. Reactions at the site of injection.

No problems	38	66%
Pain	13	22%
Lumps	2	3%
Burning sensation while injecting	4	7%
Inflammation	3	5%
Infection	0	0%
Patients discontinuing injections due to pain at injection site	3	5%

management. In 14% of patients this approach to pain management made no difference. Unprompted, 45% of patients stated that this method of pain management had 'changed their life'. Other benefits that emerged were improved socialising (35%) and resumption of full-time work (19%). It should be noted that patients with IBS can have other disabling symptoms, such as urgency and faecal incontinence. Consequently, relieving their abdominal pain may not always lead to normal social activities, even though quality of life may have been significantly improved. Patients using intramuscular hyoscine butylbromide reported no hospitalisations or visits to accident and emergency departments since commencing this approach to treatment. However, subjects were not asked to try and recall previous hospitalisations before the initiation of treatment as it was felt such information would be subject to recall bias and, therefore, not particularly reliable. Despite this, 14% of patients did volunteer the fact they had had frequent hospital admissions prior to the commencement of treatment. If this pattern could be reproduced with wider use of this approach, it is likely to have a major impact on reducing the use of healthcare resources by this group of patients. Ideally, a placebo-controlled trial of this approach would be desirable. However, for a condition for which the pain is so severe, it would be difficult to envisage a study design which would receive a favourable ethical decision.

The prevalence of side effects with intramuscular hyoscine butylbromide was low, with only four patients (7%) having to discontinue treatment because of this problem. The most common side effects encountered were blurred vision (31%) and dry mouth (45%), with 26% of patients encountering these two symptoms concomitantly. Five percent of patients reported some difficulty with passing urine but in all of these individuals it was transient and did not require catheterisation. With regard to the injection site, 66% of patients experienced no problems, 22% some transient pain and 3% reported some swelling at the injection site. It is important to warn patients about the possibility of blurred vision as otherwise this symptom can be rather alarming, although sight is not significantly impaired and it is only temporary. The occurrence of this problem can be used to reinforce the efficacy of this approach by informing the patient that if the treatment is relaxing the muscles of the eye, it will also be relaxing the muscles in the gut. We have not encountered any major problems with interactions with any other medications used in IBS. However, we do advise caution in patients taking tricyclic antidepressants and recommend that the first dose should be 10 mg, which can then be increased to 20 mg if no problems arise. The usual precautions taken with any anticholinergic are advised and potential contraindications include myasthenia gravis, paralytic ileus, pyloric stenosis, prostatic symptoms and glaucoma. Caution should be exercised with asthmatics on high doses of beta agonists or anticholinergics.

It is notoriously difficult to get these patients off opiates and therefore it is notable that this approach facilitated the reduction of opioid medications in some patients and in other cases opiates were completely discontinued. This is particularly important as it is well known that opiates can have a detrimental effect on gastrointestinal motility, which can induce symptoms rather similar to IBS. In some patients the prolonged use of opiates can lead to narcotic bowel syndrome and the continued use of the medication can lead to an actual exacerbation of the very pain that is being targeted, although the mechanism underlying this paradoxical effect has yet to be clearly defined [Grunkemeier *et al.* 2007; Choung *et al.* 2009; Agostini *et al.* 2010; Tuteja *et al.* 2010; Drossman *et al.* 2012; Farmer *et al.* 2013; Manickam and Saad, 2013]. Our results suggest that the administration of intramuscular hyoscine butylbromide might help to prevent the escalation of analgesia, leading to narcotic bowel syndrome and may also have utility in weaning patients off these particular medications.

The concept of the self-administration of an intramuscular injection in the community for a 'benign' condition is not necessarily going to be instantly acceptable, particularly to medical practitioners who have not witnessed the decline of a patient with severe IBS into the world of opiate addiction and narcotic bowel syndrome. This problem is highlighted by the fact that 40% of GPs contacted refused to engage with this particular approach. When it is adopted, we always advise that the patient must have taken the drug orally in the past in order to avoid any idiosyncratic reaction to the medication. However, lack of efficacy following oral administration should not be considered a problem because of the drug's particularly poor absorption characteristics. In those general practices agreeing to adopt this approach, the patients were taught the technique by various members of the primary care health team and the process worked well. It is essential that the first dose is administered in the surgery to avoid any unexpected reactions and to familiarise patients with any anticholinergic effects they might experience, especially blurred vision. Once competent, the patients are advised to use the drug when the pain is particularly severe, and consequently, the pattern of use is dependent upon pain frequency. We advise against preventative injections but there is a strong clinical impression that if a patient leaves administration until the pain has reached an absolute crescendo then the drug may not be quite so effective. It is recommended that the dose should not exceed three 20 mg doses in 24 h and in this survey 43% were using the drug daily, 29% more than once a week and 12% less than once a week. With regard to injection sites, 67% used the thigh, 12% the upper arm, 22% the buttock and the remainder used the anterior abdominal wall with some patients alternating between sites.

The administration of intramuscular hyoscine butylbromide appears to provide a safe and effective way of managing this subset of patients in whom abdominal pain is exceptionally severe. It also offers the potential for preventing an escalation of analgesic use and possible dependency.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of interest statement

JSP and CP declare no support from any organisation for the submitted work, no financial relationships with any organisations that might have an interest in the submitted work in the previous 3 years, no other relationships or activities that could appear to have influenced the submitted work. PJW has received research grants or honoraria from Danone, Almirall, Shire, Abbott, Boehringer Ingelheim UK and Norgine that might have an interest in the outcome reported in the submitted work.

References

Agostini, S., Eutamene, H., Cartier, C., Broccardo, M., Improta, G., Houdeau, E. *et al.* (2010) Evidence of central and peripheral sensitization in a rat model of narcotic bowel-like syndrome. *Gastroenterology* 139: 553–563.

Agrawal, A. and Whorwell, P. (2006) Irritable bowel syndrome: diagnosis and management. *BMJ* 332: 280–283.

Choung, R., Locke, G., Zinsmeister, A., Schleck, C. and Talley, N. (2009) Opioid bowel dysfunction and narcotic bowel syndrome: a population-based study. *Am J Gastroenterol* 104: 1199–1204.

Drossman, D., Morris, C., Edwards, H., Wrennall, C., Weinland, S., Aderoju, A. *et al.* (2012) Diagnosis, characterization, and 3-month outcome after detoxification of 39 patients with narcotic bowel syndrome. *Am J Gastroenterol* 107: 1426–1440.

eMC (2013) Buscopan. Electronic Medicines Compendium. http://www.medicines.org.uk/emc/

medicine/282/SPC/Buscopan+Tablets/#PHARMACODYNAMIC_PROPS (accessed 2 June 2014)

Farmer, A., Ferdinand, E. and Aziz, Q. (2013) Opioids and the gastrointestinal tract – a case of narcotic bowel syndrome and literature review. *J Neurogastroenterol Motil* 19: 94–98.

Ford, A., Talley, N., Schoenfeld, P., Quigley, E. and Moayyedi, P. (2009) Efficacy of antidepressants and psychological therapies in irritable bowel syndrome: systematic review and meta-analysis. *Gut* 58: 367–378.

Ford, A., Talley, N., Spiegel, B., Foxx-Orenstein, A., Schiller, L., Quigley, E. *et al.* (2008) Effect of fibre, antispasmodics, and peppermint oil in the treatment of irritable bowel syndrome: systematic review and meta-analysis. *BMJ* 337: a2313.

Grunkemeier, D., Cassara, J., Dalton, C. and Drossman, D. (2007) The narcotic bowel syndrome: clinical features, pathophysiology, and management. *Clin Gastroenterol Hepatol* 5: 1126–1139.

Houghton, L., Fell, C., Whorwell, P., Jones, I., Sudworth, D. and Gale, J. (2007) Effect of a second-generation alpha2delta ligand, pregabalin on visceral sensation in hypersensitive patients with irritable bowel syndrome. *Gut* 56: 1218–1225.

Jackson, J., O'Malley, P., Tomkins, G., Balden, E., Santoro, J. and Kroenke, K. (2000) Treatment of functional gastrointestinal disorders with antidepressant medications: a meta-analysis. *Am J Med* 108: 65–72.

Manickam, P. and Saad, A. (2013) Narcotic bowel syndrome: is it more common than before? *J Neurogastroenterol Motil* 19: 273.

Maxton, D., Morris, J. and Whorwell, P. (1989) Ranking of symptoms by patients with the irritable bowel syndrome. *BMJ* 299: 1138.

Spiegel, B. (2009) The burden of IBS: looking at metrics. *Curr Gastroenterol Rep* 11: 265–269.

Talley, N. (1999) Irritable bowel syndrome: definition, diagnosis and epidemiology. *Baillieres Best Pract Res Clin Gastroenterol* 13: 371–384.

Tuteja, A., Biskupiak, J., Stoddard, G. and Lipman, A. (2010) Opioid-induced bowel disorders and narcotic bowel syndrome in patients with chronic non-cancer pain. *Neurogastroenterol Motil* 22: 424–430.

Whorwell, P., Mccallum, M., Creed, F. and Roberts, C. (1986) Non-colonic features of irritable bowel syndrome. *Gut* 27: 37–40.

Appendix

Hyoscine butylbromide is an antispasmodic which, when taken by mouth, is very poorly absorbed. Consequently in patients with the more severe forms of spastic abdominal pain the drug may not be especially effective, whereas when it is delivered intramuscularly it can often dramatically reduce pain.

We now have quite a large cohort of patients injecting hyoscine butylbromide intramuscularly on an as necessary basis when their pain is especially severe and this strategy has resulted in improved quality of life, as well as a reduction in analgesic consumption, particularly of the opiate variety. We have also noted a reduction in attendances at A&E departments, as the patients feel more in control. We usually recommend a dose of 20 mg and this can be administered up to 3 times a day when the pain is very severe.

Significant side effects are seldom encountered and in particular the injection site does not appear to become inflamed or sore as can happen with drugs such as cyclizine. Blurring of vision can occur and we tell patients this is because the eye has similar muscles in it to the bowel and consequently this particular side effect is unavoidable but it does not mean the eye is being damaged in any way. Some patients do experience palpitations but these seldom cause problems although they are theoretically more likely in those taking tricyclic antidepressants where a starting dose of 10 mg is advisable. Retention of urine is a possibility in older men with prostate problems but we have not seen this so far. We suggest that hyoscine butylbromide is not administered intramuscularly unless it has been taken orally previously, just in case there is an idiosyncratic intolerance to the drug which would obviously become manifest after oral administration.

We would therefore be very grateful if you would consider teaching this patient to administer hyoscine intramuscularly. We recommend that the first dose is administered in the surgery, so that both the medical practitioner and the patient are reassured that no unforeseen adverse events are likely to occur.