Management of Emergency Abdominal Pain

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Emergency abdominal pain: Overview

Abdominal pain is considered the most common complaints of patients admitted to emergency departments amounting to 5-10% of emergency department visits. Acute abdominal pain can represent a spectrum of conditions from benign and self-limited disease to surgical emergencies. Although most abdominal pain is benign, as many as 10% of patients in the emergency department setting and a lesser percentage in the outpatient setting have a severe or life-threatening cause or require surgery. Therefore, a thorough and logical approach to the diagnosis of abdominal pain is necessary.[1,2]

Etiology of abdominal pain

Most abdominal pain arises from an abdominal pathology; while a few causes may be of extra-abdominal origin. Acute abdominal pain may be caused by a variety of factors. The most common cause of abdominal pain which does not require surgery is gastroenteritis. On the other hand, the most common cause of abdominal pain which requires surgery is appendicitis. In older patients (>60 years), the most common cause of acute abdominal pain are biliary disease and intestinal obstruction. In younger patients, however, acute appendicitis is the most common cause of acute abdominal pain accounting for 25% of cases.[3-5]

Evaluation

Evaluating abdominal pain requires an approach that relies on the likelihood of disease, patient history, physical examination, laboratory tests, and imaging studies. When evaluating a patient with acute abdominal pain, the physician should focus on common conditions that cause abdominal pain as well as on more serious conditions. Apart from the age of the patient, it is necessary to understand the time of pain, location and character of pain and pattern of pain radiation. The location of pain should drive the evaluation. Although location of abdominal pain guides the initial evaluation, associated signs and symptoms are predictive of certain causes of abdominal pain. The presence of nausea, vomiting and bowel habits should be considered. The menstrual history of female patients should also be considered.[1,3]

Management of abdominal pain

Management of emergency abdominal pain requires rapid initial evaluation of pain intensity administration, appropriate analgesic agent by the appropriate route based on the clinical scenario, and early implementation of adjuvant measures. It is necessary to assess the intensity of the pain for proper management. The intensity of pain is a subjective perception, which does not correlate with clinical findings, laboratory parameters or diagnostic imaging findings. Antispasmodics are considered important for treatment of mild-to-moderate pain. Antispasmodic agent, such as drotaverine, has suitable relaxing effect on intestinal smooth muscle that aids in relieving pain and is devoid of anticholinergic side-effects. Drotaverine thus renders effective analgesia in colicky pain.[6-9]

Drotaverine: A propitious choice for emergency abdominal pain

Amongst the various antispasmodics available, Drotaverine hydrochloride is a drug of choice in emergency abdominal pain of different etiologies.8 Drotaverine is a selective inhibitor for phosphodiesterase IV (PDE IV), which regulates the contractile activity of smooth muscles; thereby drotaverine controls the contractile activity of abdominal muscles to provide relief in abdominal spasms.[10,11]

Clinical evidence suggests that it is the drug of first choice in spasmodic pain of smooth muscle spasm like biliary colic, renal colic, intestinal colic, etc. Various post-marketing studies have shown that drotaverine is also effective in the treatment of pain associated with gastric and duodenal ulcer, gastritis, enteritis, cholelithiasis, colitis, cardiac and pyloric spasm and irritable bowel disease (IBS). Drotaverine also normalises the dysmotility of GI smooth muscles and displays significant improvement in stool frequency, consistency, urgency and flatulence in IBS. The anti-spasmodic and pain-relieving effect of drotaverine does not mask the symptoms of acute abdomen, and it does not interfere with diagnostic precision while providing optimum pain control; therefore, it can be initiated for management of emergency abdominal pain even before the actual etiological diagnosis is established.[12,13]

Drotaverine does not have morphine-like effect and therefore does not induce addictive potential. The drug also demonstrates its suitability for both oral and parenteral administration with excellent absorption from the small intestine (90%). Parenteral administration of drotaverine ensures rapid and immediate relief from spasmodic pain. Administered through intravenous (IV) route, the action commences in just 2 minutes. The onset of action with the intramuscular (IM) route is 5 minutes. Oral administration of Drotaverine can be continued for further sustaining its effects (Box 1).[8,10,11,13]

Box 1: Advantages of drotaverine

- Site specific - PDE IV inhibitor; acts directly on abdominal smooth muscles
- Wide therapeutic index (well-tolerated in frequent and repetitive dosing)
- Does not induce anticholinergic side effects (constipation, urinary retention, dry mouth and visual disturbances) as seen with other anticholinergic antispasmodics such as dicyclomine or hyoscyamine
- No addictive potential unlike opioids
- Synergistic combination with NSAIDs such as aceclofenac, mefenamic acid and paracetamol
- Limited drug-drug interactions
- Neither masks the symptoms of acute abdomen nor interferes with diagnosis
- Well tolerated by all age groups
- Effectively maintains a state of spasmolysis
- Onset of action with IV administration: 2 minutes
- Onset of action with IM route: 5 minutes

Abbreviations: PDE IV, Phosphodiesterase IV; NSAIDs, Non-steroidal anti-inflammatory drugs.

Adapted from: 1. Golzari SE, Soleimanpour H, Rahmani F, *et al.* Therapeutic Approaches for Renal Colic in the Emergency Department: A Review Article. *Anesth Pain Med.* 2014;4(1):e16222. **2.** Rai RR, Dwivedi M, Kumar N. Efficacy and safety of drotaverine hydrochloride in irritable bowel syndrome: A randomized double-blind placebo-controlled study. *Saudi J Gastroenterol.* 2014;20: 378-82. **3.** Romics I, Molnár DL, Timberg G, *et al.* The effect of drotaverine hydrochloride in acute colicky pain caused by renal and ureteric stones. *BJU Int.* 2003;92(1):92-6. **4.** Gupta K. Emerging role of Drotaverine in emergency medicine: A review. J Am Med Assoc Ind. *Physicians' Update.* 1999;2 (8):57-64.

Drotaverine has also found an important place in emergency medicine. Its versatile pharmacokinetic properties such as rapid absorption, early onset of action, rapid response to IV dosing and wide therapeutic window favorably contribute to its utility in emergency conditions.[8,10,11] Various studies have been conducted highlighting the role of drotaverine in management of different types of spasmodic pain.

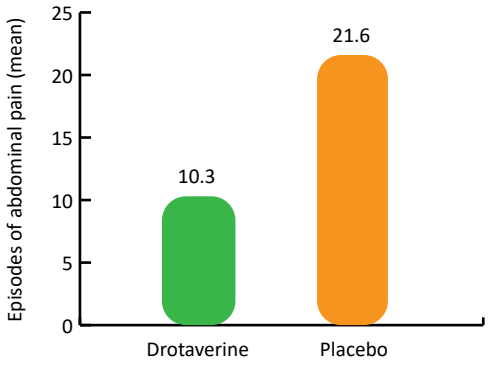
Evidence based efficacy of drotaverine

In the first of its kind pediatric study, Narang et al[14] tried to evaluate efficacy of drotaverine in cases of recurrent abdominal pain. It was observed that the number of episodes of abdominal pain significantly reduced in the drotaverine group in comparison to placebo group [mean (SD) = 10.3 (14) vs. 21.6 (32.4), respectively] (Figure 1). The number of pain-free days were also slightly higher with drotaverine versus placebo [17.4 (8.2) vs 15.6 (8.7), respectively].

Studies have also shown that Drotaverine injection (both IM and IV) relieves pain in patients with clinically proven renal obstruction.[13] Romics et al[11] evaluated the spasmolytic effect of IV Drotaverine hydrochloride in colicky pain caused by renal and ureteric stones in a placebo controlled randomised trial. It was observed that Drotaverine was a more potent medicine in relieving pain with an effectiveness in 79% patients as compared with placebo which was effective in 46% patients ($p<0.001$) (Figure 2).

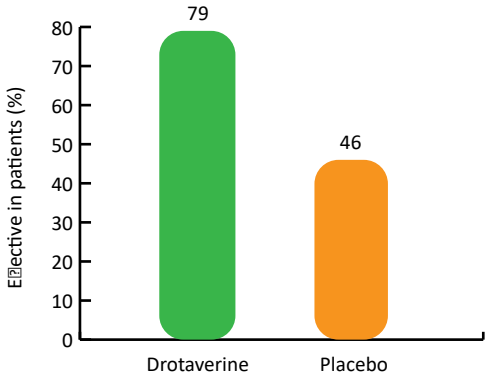
Dash and colleagues[15] conducted a randomized, single-blind study comparing single intramuscular doses of drotaverine

Figure 1: Episodes of abdominal pain in patients receiving drotaverine versus placebo



Adapted from: Narang M, Shah D, Akhtar H. Efficacy and Safety of Drotaverine Hydrochloride in Children with Recurrent Abdominal Pain: A Randomized Placebo Controlled Trial. *Indian Pediatr.* 2015;52(10):847-51.

Figure 2: Effectiveness of intravenous rotaverine versus placebo in patients with colicky pain



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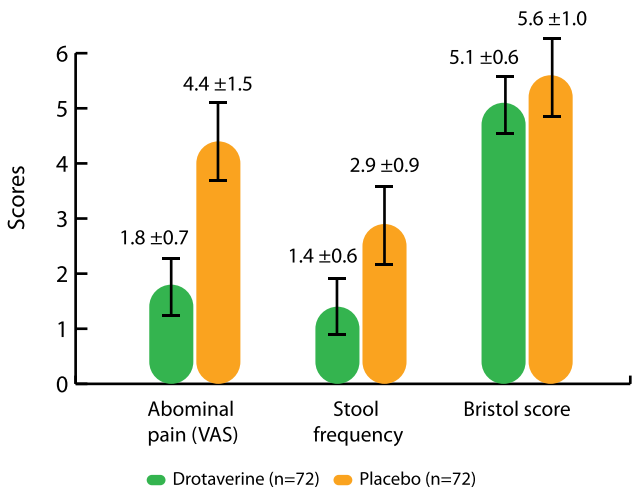
hydrochloride (80 mg) vs diclofenac sodium (75 mg) on 100 patients (n=50 in each group) with renal colic. There was significant decrease in visual analogue scale (VAS) score with both drotaverine (52.4%) and diclofenac (49%) at 30 minutes. Reduction of VAS at 60 minutes was 61.3% with drotaverine versus 60.4% with diclofenac. Treatment was found effective by 45 patients (90%) in the drotaverine group versus 44 (88%) in the diclofenac group. It was concluded that IM drotaverine is an effective and well-tolerated analgesic in renal colic.

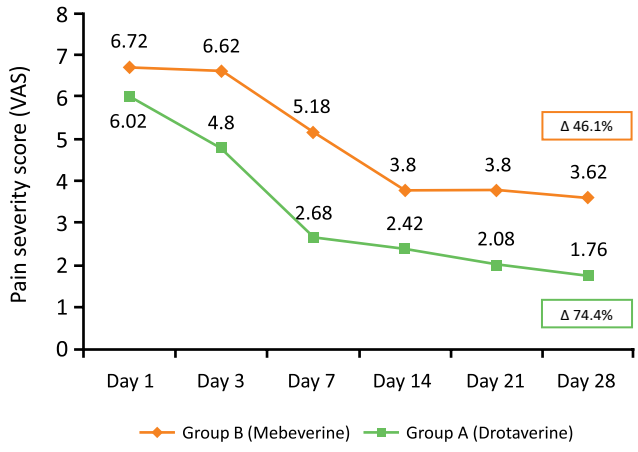
In yet another study, Xue and colleagues[16] aimed to assess the efficacy and safety of drotaverine hydrochloride in alleviating abdominal pain in patients with IBS. It was observed that VAS, stool frequency, and Bristol score were significantly better in

Figure 3: Study outcomes with drotaverine versus placebo in patients with irritable bowel syndrome at the end of 4 weeks treatment



Adapted from: Xue XC, Qi XX, Wan XY. Randomized controlled study of efficacy and safety of drotaverine hydrochloride in patients with irritable bowel syndrome. *Medicine (Baltimore).* 2017;96(51):e9235.

Figure 4: Change in pain severity scores in patients with IBS with drotaverine versus mebeverine therapy



Adapted from: Rai RR, Nijhawan S. Comparative evaluation of efficacy and safety of drotaverine versus mebeverine in irritable bowel syndrome: A randomized doubleblind controlled study. *Saudi J Gastroenterol.* 2021 Feb 24.

the treatment group than those in the placebo group at the end of 4-week treatment (Figure 3). There were no serious and significant differences in adverse events in and between both groups. The findings were suggestive of the promising efficacy of drotaverine in ameliorating symptoms of IBS including abdominal pain.

The efficacy of drotaverine was further substantiated in a randomized control study, wherein Rai and Nijhawan[17] demonstrated that drotaverine was significantly more effective than mebeverine in alleviating pain severity, frequency and stools-related symptoms of IBS. There was a significant reduction in pain severity score from 6.02 at baseline to 1.78 at the end of study (70.4% reduction) in drotaverine group versus 6.72 to 3.62 (46.1% reduction) in mebeverine group (Figure 4). Likewise, patients in drotaverine group demonstrated a significant reduction in pain frequency (from 3 ± 1.0 to 1.1 ± 0.2 versus 3 ± 1.0 to 2 ± 0.1, respectively) and straining (45% versus 15%, respectively) as compared to those in mebeverine group. Thus, it could be substantiated that drotaverine was significantly superior in efficacy as compared to mebeverine in the symptomatic treatment of patients with IBS.

Combination therapy with drotaverine and paracetamol

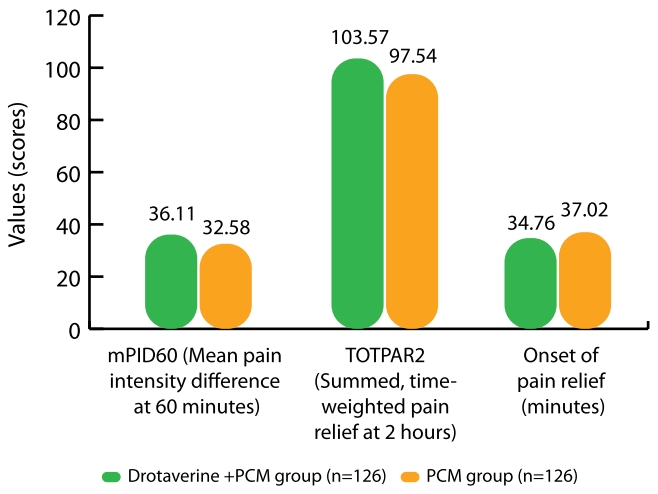
Smooth muscle spasm is often associated with colicky abdominal pain. In such cases, combining a spasmolytic agent with an analgesic may result in prompt and adequate relief, improving both spasm and pain.[14] Paracetamol (PCM) is usually regarded as a safe analgesic/ antipyretic agent, and is believed to be virtually without any gastrointestinal side-effect. While antispasmodics are established in relieving spasmodic pain in gastrointestinal disorders, PCM may have a certain degree of role as it is useful in visceral pain relief.[18,19] By virtue of their different mechanisms of action, the combination of drotaverine and PCM proves to be a potential therapeutic alternative that provides rapid pain relief.[14]

Narang and Koli20 conducted a randomized double-blind controlled trial with an aim to evaluate the efficacy and safety of fixed-dose combination of drotaverine (80 mg) and PCM (500 mg) in amelioration of abdominal pain in acute infectious gastroenteritis. Using VAS, a statistically significant improvement was observed in the mean pain intensity difference at 60 minutes after administration of fixed-dose combination of drotaverine plus PCM. Moreover, a statistically significant improvement was also observed in total pain relief at 2 hours in the fixed-dose combination group. The fixed-dose combination group also demonstrated a significantly better onset of pain relief when using VAS (Figure 5). Thus, findings of this study substantiate that fixed-dose combination of drotaverine plus PCM is an effective and well-tolerated antispasmodic agent in the treatment of abdominal pain associated with acute infectious gastroenteritis.

In another study[21] comparing the effectiveness and safety of drotaverine plus PCM in patients with acute infectious gastroenteritis, it was revealed that pain frequency significantly decreased in 30%, 65% and 90% at 1st, 2nd and 3rd day in patients receiving drotaverine plus PCM (Group A) versus 18%, 45% and 68% in those receiving PCM alone (Group B). Moreover, pain severity was also significantly improved in Group A versus Group B. Global improvement in abdominal pain by patients in Group A was 96% versus 78% in Group B; by clinician it was 99% in Group A versus 85% in Group B. It was concluded that use of fixed-dose combination of drotaverine plus PCM is effective and well-tolerated oral therapy in patients with moderate or severe abdominal pain due to acute infectious gastroenteritis.

Aceclofenac is a novel, long-acting, well-tolerated NSAID with fewer incidences of side effects and established safety

Figure 5: Comparison of pain relief scores and onset of pain relief with paracetamol alone versus in combination with drotaverine



Adapted from: Narang S, Koli J. Efficacy and safety of fixed-dose combination of drotaverine hydrochloride (80 mg) and paracetamol (500 mg) in amelioration of abdominal pain in acute infectious gastroenteritis: A randomized controlled trial. *J Gastroenterol Hepatol.* 2018;33(12):1942-1947.

profile. It provides sustained pain relief by preferentially blocking cyclo-oxygenase II enzyme, which makes it an ideal NSAID for combining with fast acting Drotaverine, for effective pain relief from post-operative procedures. Vinod and Ashish,[22] in a prospective randomized clinical trial involving patients undergoing laparoscopic surgeries, revealed that Drotaverine plus aceclofenac combination brought about statistically significant reduction in VAS pain scores at day 1, 3 and 5, postoperatively. Moreover, the scores for global assessment and general evaluation by clinician were statistically higher in combination group versus aceclofenac only group. The combination group also experienced relatively less adverse events than aceclofenac only group. It could be concluded that Drotaverine plus aceclofenac is more effective than aceclofenac alone for pain relief from postoperative procedures.

Conclusion

Abdominal pain is considered the most common complaints of patients admitted to emergency departments. It is necessary to take a meticulous history and perform a thorough physical examination to ascertain the exact cause. Gastroenteritis represents the most common nonsurgical condition implicated in acute abdominal pain. Pain management merits multifaceted consideration with well-defined role of pharmacologic therapy including antispasmodic agents after accounting for riskbenefit ratio. Antispasmodics are considered important for treatment of mild-to-moderate pain. Drotaverine is a preferred drug in treatment of abdominal pain owing to its characteristic properties. Drotaverine is a highly potent and tolerable spasmolytic agent, suited for oral administration, and capable of relieving or preventing smooth muscle spasms, including those of gastroenterological origin. It is well tolerated and effective even when used in combination with paracetamol or aceclofenac. Combining a spasmolytic agent with an analgesic may result in prompt and adequate relief, improving both spasm and pain.

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