Original Article

DOI: 103126/JNPS.V4113

Efficacy of Hyoscine Butylbromide Versus Drotaverine in Relieving Acute Nonspecific Abdominal Pain in Children- A Non - Randomized Trial

Pradip Kumar Paudel[1], Sudha Basnet[2], Merina Shreshtha[2]

[1]Department of Paediatrics, Province Hospital, Surkhet, Nepal.
[2]Department of Paediatrics, Maharajgunj Medical Campus, Institute of Medicine, TUTH, Maharajgunj, Kathmandu, Nepal

Article History
Received On : Sep 15, 2021
Accepted On : Jun 10, 2022

Funding sources: None

Conflict of interest: None

Keywords: Children, drotaverine, face pain score-revised, hyoscine, nonspecific abdominal pain

Online Access

DOI:https://doi.org/10.3126/jnps.v42i1.39773

***Corresponding Author**

Pradip Kumar Paudel,
Department of Paediatrics,
Province Hospital,
Surkhet, Nepal
Email: drpradippaudel@gmail.com

Abstract

Introduction: Acute abdominal pain is a very common complaint for children presenting to the emergency department (ED). The purpose of this study was to compare efficacy of hyoscine and drotaverine for relieving acute nonspecific abdominal pain in children presenting to ED.

Methods: Total of 52 children aged six years to 16 years were enrolled in a non-randomized trial at Paediatric ED of TUTH from Dec 2017 to June 2018, and randomly allocated to drotaverine or hyoscine groups; 26 in each group. Face pain score-revised tool was used to measure the efficacy of the drug. The primary outcome was to measure the reduction of face pain score (Self-reported) by at least 2 / 10 at 60 minutes after ingestion of study intervention. Other outcomes were requirement of rescue analgesia and adverse effects of drugs.

Results: A total of 20 (77%) in hyoscine and 21 (81%) in drotaverine group responded to oral medication at the end of 60 minutes of oral administration and the difference was not statistically significant (p=0.808). Vomiting was only adverse event present in five (19%) in drotaverine and two (8%) in hyoscine groups, respectively.

Conclusions: In this single center randomized controlled trial, both hyoscine and drotaverine were found to be equally efficacious for relieving acute non-specific abdominal pain in children.

Introduction

Pain abdomen affects children all over the world, involves both gender and all races.[1,2] About 9% of visits to paediatric clinic are for abdominal pain.[3] Frequently, the causes of the abdominal pain are benign medical conditions like gastroenteritis, constipation or acute viral illness and either are self-limiting or improve after treatment.[4-6] Mostly, cause cannot be identified and may be attributed to functional origin.[2,5]

When a child presents with acute abdominal pain, careful history taking and repeated physical examinations are needed to rule out acute conditions where immediate interventions might be required. Analgesics are frequently withheld as analgesia may mask signs of an underlying surgical pathology such as appendicitis.[7] Recent evidence has found that providing analgesia to children does not obscure signs of an acute surgical abdomen.[8] Analgesics not only provide significant pain relief but also permit an adequate abdominal examination as it does not eliminate the tenderness caused by an inflammatory process.[7,8]

Antispasmodics group of drugs like drotaverine and hyoscine are commonly used to relieve gastrointestinal cramps, that are characteristics of visceral pain.[9,10] Other commonly used analgesics in such conditions are NSAIDs like diclofenac, opioids like tramadol, fentanyl, etc. requiring parental route for administration. It was found that hyoscine butylbromide (10 mg) when given orally, found to be beneficial compared to a homeopathic preparation in children, without any serious adverse effects.[8] Hyoscine is available either as tablets or an injectable preparation and therefore not always a good option in children as suspension would be better. Another antispasmodic, drotaverine which was used in children with recurrent abdominal pain, was also reported to reduce episodes of abdominal pain without serious adverse effect.[13] Drotaverine is devoid of anticholinergic side effects as compared to hyoscine butylbromide and also available as suspension formulation thus easier to administer in children. Both the drugs are proven to be effective for treatment of recurrent abdominal pain.[11-13] However, the studies comparing efficacy of both drugs in children with acute nonspecific abdominal pain is lacking. We therefore sought to compare efficacy of the two available oral antispasmodics drotaverine and hyoscine butylbromide in children with acute nonspecific abdominal pain.

Methods

We conducted a non-randomized trial among 52 children of age group six to 16 years with acute nonspecific abdominal pain. We wanted to compare the proportion of children who respond to treatment, defined as reduction of pain intensity by a score of at least 2 / 10 or more using Faces pain scale-revised (FPS-R) tool, at the end of 60 minutes of administration of single oral dose of hyoscine butylbromide or drotaverine at Paediatric ED of TUTH. Sixty minutes was chosen as it reflects the time to peak analgesic action of hyoscine butylbromide[8] and drotaverine (60 – 90 min).[9] We included children with acute abdominal pain of less than seven days' duration presenting to ED without identifiable cause based on history and clinical examination. Pain was assessed immediately before enrollment using FPS-R tool. Children who were unable to swallow pills or communicate verbally, had received analgesics in last six hours, undergone abdominal surgery in last three months, with suspected surgical abdomen, suspected or known previous hypersensitivity reaction to either hyoscine or drotaverine, history and clinical examination suggesting pain abdomen requiring further evaluation to rule out organic etiology, recent abdominal trauma, hemodynamically unstable children, children with history of open angle glaucoma or of myasthenia gravis and who did not give consent were excluded from the study. The mean face pain score at 15 minutes' interval till 60 minute of study between the groups of children that received single oral dose of hyoscine butylbromide or drotaverine and adverse effects within four hours of drug administration were also compared. Rescue analgesia either NSAIDS like ketorolac or opioids like tramadol or fentanyl was given if pain increased.

Single dose of hyoscine butylbromide, 10 mg (Boehringer Ingelheim) or drotaverine 40 mg (Walter Bushnell) was given orally at ED after consent to enroll in the study was obtained. Two tablets of each drug were packaged in opaque and similar looking envelope, one tablet for administration and another one for use in case re-administration required due to vomiting within five minute of first dose. The two groups of children were given butylbromide and drotaverine medicines in non randomized fashion. Participants were non randomly allocated in a 1:1 allocation ratio with block size of 10. The validated FPS-R which was used to assess pain has been shown to have strong positive correlation with the Visual Analogue Scale and the Clinical Analogue Scale[15] and appropriate for use in assessment of the intensity of children's acute pain from age four or five years onwards. This tool consists of drawing of six faces (Scored from 0 - 10) that reflect increasing intensity of pain.[16] The children were asked to point to the face that depicts the level of their pain, with score 0 denoting 'no pain' and score 10 denoting 'very much pain' after well explanation of FPS-R. We used a minimal clinically important difference on the FPS-R of 1 face (score of 2) based on a previous validation study[17] and an adult emergency department study of hyoscine butylbromide and acetaminophen for abdominal pain.[12] With standard deviation (SD) of 1.7, 23 children per group were required to detect difference with 95% CI with 80% power. The sample size was increased to account for dropouts, giving a final sample size of 26 participants per group. Ethical approval was obtained from the Institutional Review Board (IRB) of Institute of Medicine (IOM), Maharajgunj, Kathmandu, Nepal prior to start of the study. All collected data were analyzed by using SPSS software version 20.0 (IBM). Continuous variables were expressed as means ± standard deviation and categorical variables were expressed as percentages. Independent samples t-test was used to compare the mean difference in reduction of face score at each 15-minute interval between the two treatment groups. The P-value was calculated using Fisher Exact test for proportions and a value of < 0.05 was considered significant.

Results

A total of 112 children aged six to 16 years were screened for eligibility over the study period of six months. The male to female ratio was 1:1.3. Of all the screened cases, 60 were excluded and parents of seven children refused to consent. Total 52 children were included, of which 26 children in each drotaverine and hyoscine group were non randomly allocated (Fig. 1). Three cases in each group did not complete one hour of study period due to reported increase in pain score that required rescue intravenous analgesics (Fig.1). Data of all these six cases were included in the analysis based on the prior decision to conduct an intention-to-treat analysis. The last documented pain score before receipt of rescue analgesia was used to denote outcome in these six children. We assumed the pain score to be unchanged if rescue analgesia wasn't used, so we used the same pain score at subsequent recording. The mean age was 11 (± 3.11) and 10.65 (± 3.08) years in drotaverine and hyoscine group, respectively. There were 29 (56%) male children. (Table-1)

Figure 1- Trial Profile

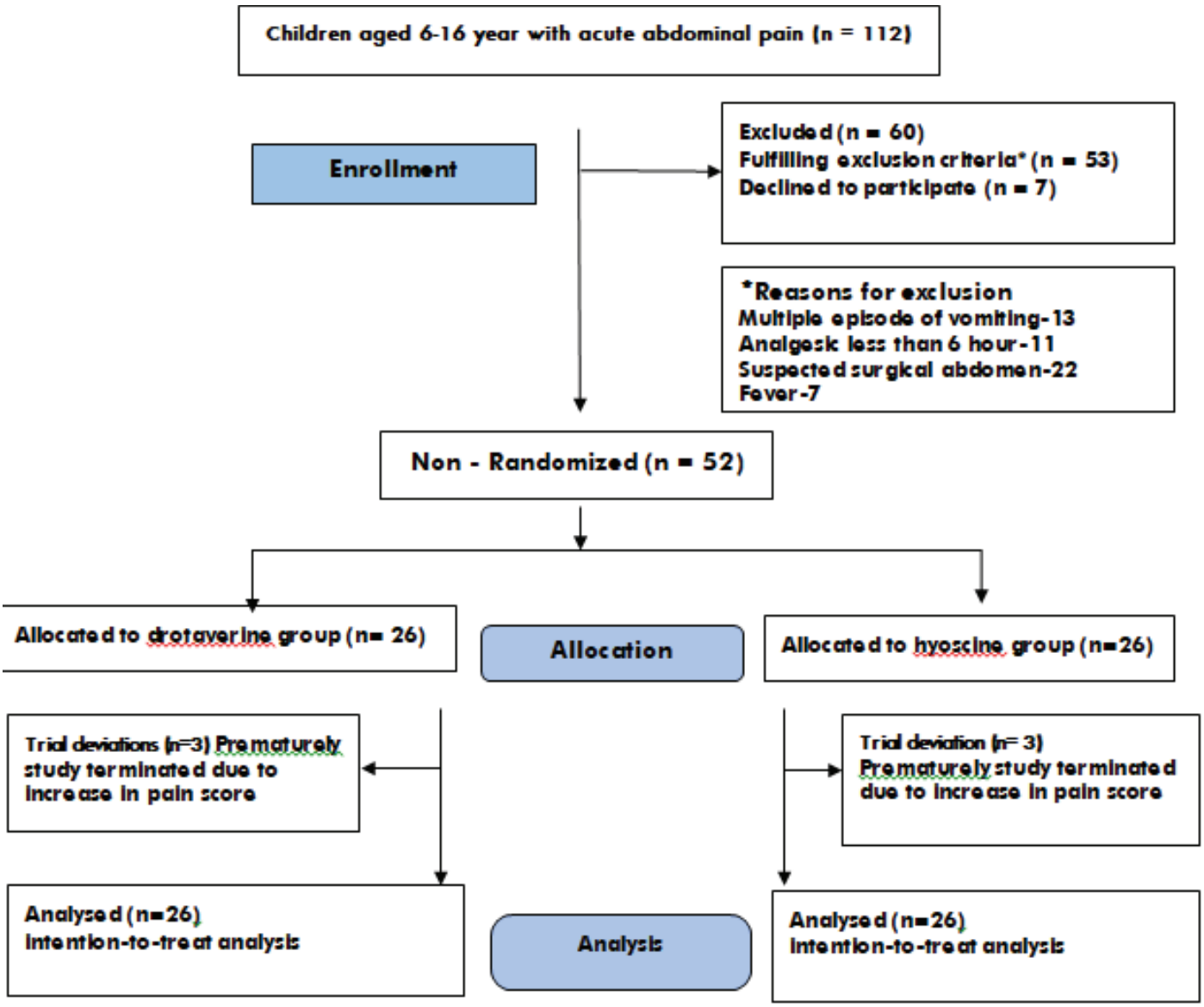


Figure 1. Trial profile of a randomized controlled trial of drotaverine vs hyoscine in acute non-specific pain in children aged 6 to 16 year in Pediatric ER of TUTH, Kathmandu, Nepal.

The mean initial pain score was 6.3 (± 1.6) in drotaverine and 6.7 (± 2.1)in hyoscine group respectively (Table 1). Most of children had duration of abdominal pain of less than 24 hours.

Table 1. Baseline demographic and clinical characteristics of participants

Clinical parameters		Drotaverine groups N = 26 (%)	Hyoscine groups N = 26 (%)
Mean age in years (SD*)		11 (± 3.11)	10.65 (± 3.08)
Female		13 (50)	10 (39.5)
Mean initial pain score (FPS-R) (SD)		6.3 (± 1.6)	6.7 (± 2.1)
Duration of abdominal pain	Less than 24 hours	16 (61.5)	15 (57.7)
	1 to 3 days	8 (30.7)	9 (34.6)
	More than 3 days – 7 days	2 (7.6)	2 (7.6)
Vital signs	Mean Temperature in °F (SD)	98.2 (± 0.37)	98.02 (± 0.63)
	Mean HR per minute (SD)	101 (± 14.45)	96.7 (± 13.7)
	Mean RR per minute (SD)	22 (± 3.3)	21 (± 2.6)
	Mean SBP mmHg (SD)	100.7 (± 12.27)	96.5 (± 7.5)
	Mean DBP mmHg (SD)	67 (± 8.4)	65 (± 7.4)
Character of abdominal pain	Colicky Dull Burning	11 (42.3) 7 (26.9) 4 (15.4)	14 (53.8) 5 (19.2) 4 (15.4)
Associated symptoms	Nausea / Vomiting Loose motion Constipation	9 (34.6) 2 (7.6) 4 (15.3)	6 (23) 1 (3.8) 4 (15.3)

Analyses of efficacy outcomes were based on intention to treat. The proportion of children in drotaverine group i.e, 21 (80.8%) who responded (Reduction of face pain score by at least 2 / 10 or more at the end of 60 minutes of oral drug administration) compared to 20 (76.9%) in hyoscine group which was not statistically significant (p = 0.808) (Table 2).

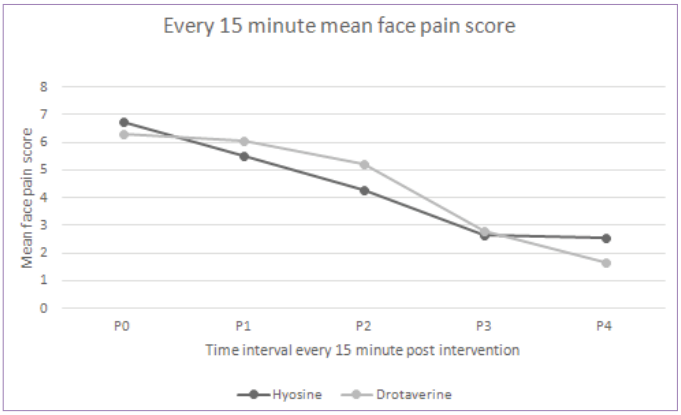
Table 2. Comparison of the proportion of children who respond to treatment at 60 minutes between the two groups

	Hyoscine groups (n = 26)	Drotaverine groups (n = 26)	p-value ***
Response to oral medication (Reduction of face pain score by 2 / 10 or more at 60 minutes)	20 (76.9%)	21 (80.8%)	0.808

***Fisher Exact Test

The independent samples t-test used to compare reduction in face pain score between the two treatment groups post intervention showed no significant difference in mean pain score in both the groups at each 15-minute interval till 60 minutes (Fig. 2).

Figure 2. Line diagram showing change in mean face pain score in the treatment groups over a period of 60 minute.



Rescue analgesia was administered to six participants (23%) in the hyoscine butylbromide and five participants (19.2%) in the drotaverine group (p = 0.2) as they didn't respond to oral therapy. In all cases, either ketorolac or tramadol was administered once decided by treating doctor. Total six cases deviated from trial, equal number in both group, as they didn't complete 60 minute

study duration and received rescue analgesic. Vomiting was the only adverse effect noted in slightly higher proportion (19%) in drotaverine group than hyoscine group (8%) (p - 0.250).

Discussion

The current study compared efficacy of hyoscine and drotaverine in reducing acute non-specific abdominal pain in children aged six to 16 years and found to be equally efficacious. The study found 77% in hyoscine and 81% in drotaverine group had responded to the drug. This difference was not statistically significant (p = 0.808).

Since studies comparing hyoscine with drotaverine in acute abdominal pain in children is lacking, there are studies comparing either hyoscine or drotaverine with placebo in acute undifferentiated abdominal pain. Romic et al compared intravenous drotaverine with placebo in adults with renal colic, and showed significant reduction of pain at 80 minutes in drotaverine arm as compared to placebo.[15] Our study also showed similar reduction of pain severity in children despite the study population in our study being children. In study done by Remington-Hobbs J et al,[16] in adult patient with undifferentiated abdominal pain in ER setting, injectable hyoscine caused clinically significant reduction of abdominal pain in 100% of participants at one hour (-28 mm in VAS). In our study hyoscine was effective in lowering abdominal pain in 77% of the participants only. The reason might be because of different study population and different routes of drug administration.

In a paediatric study that compared hyoscine butyl bromide with Spascupreel, a homeopathic preparation, in children with recurrent gastrointestinal or urethral spasms; had found both agents are equally beneficial, with few adverse effects. Our study also showed both agents to be equally beneficial.[11]

When hyoscine was compared with acetaminophen in children with acute undifferentiated abdominal pain by Poonai N, there was 50% reduction from baseline score at 80 minute in equal proportion of children (55%) in both the groups.[19] Although study setting and participant were similar to our study, marginally higher proportion of children in both group reported reduction of pain score in our study, reason may be explained by larger sample size used in former study.

The conclusions of different studies show that hyoscine or acetaminophen either used oral or intravenous or fixed drug combination has proven efficacious when compared to placebo or either drug.[11,17,19] This study may add Drotaverine to the arsenal of drug available to use in paediatric nonspecific abdominal pain. The suspension formula is expected to be easier to administer in younger children. Among the enrolled children in the present study, around 20% in both groups required rescue analgesics as they did not respond to oral therapy. In a study by Poonai N only 4% required rescue analgesic.[19] The difference could be due to differences in pain perception capacity in children. We could diagnose acute appendicitis in two of these children, despite use of analgesics. Initial examination was not suggestive of surgical abdomen. The repeated examination enabled us to diagnose surgical abdomen despite administration of analgesics. There is ample evidence that providing analgesia to children does not obscure signs of an acute surgical abdomen nor lead to clinically significant differences in negative outcomes.[7] It is justified to give trial of oral antispasmodics for a reasonable period of time provided the child is monitored frequently by performing clinical examination and the finding is reassuring. In our study, in approximately 80% of children with acute nonspecific abdominal pain we could avoid use of intravenous analgesics.

Only few children in the study developed adverse effects like nausea and vomiting in both the groups. We observed each child for four hours after administration of either of the drugs indicating drug may be used safely in children. Since ours is a single centered study with a limited number of patients, generalized of results may not be appropriate. We decided on fixed dose to enable administration of one tablet so that it would be easier for blinding even though drotaverine was available as suspension. The weight-based dosing versus analgesics response could therefore not be assessed. The analgesic efficacy could be studied with the single dose but the adverse effect profile may not be completely studied with a single dosing as adverse effects may appear on cumulative doses.

Conclusions

Hyoscine butylbromide and drotaverine both were found equally efficacious in children with nonspecific abdominal pain. Our results suggest that either hyoscine butylbromide or drotaverine can be considered for children with nonspecific abdominal pain, the latter being more practical as it is available in oral suspension formula. However, more research with larger population in other settings in this area is necessary before making any recommendation.

References

1. Caperell K, Pitetti R, Cross KP. Race and acute abdominal pain in a pediatric emergency department. Pediatrics. 2013;131(6):1098-106. DOI: 10.1542/peds.2012-3672

2. Pant C, Deshpande A, Sferra TJ, Olyaee M. Emergency department visits related to functional abdominal pain in the pediatric age group. J of Investig Med. 2017. Apr;65(4):803-806. DOI: 10.1136/jim-2016-000300

3. Loening-Baucke V, Swidsinski A. Constipation as Cause of Acute Abdominal Pain in Children. J Pediatr. 2007;151(6):666-9.

DOI: 10.1016/j.jpeds.2007.05.006

4. Joshi BG. Etiology of Recurrent Abdominal Pain in Children. J Nepal Paediatr Soc. 2013;33(1):3. DOI: https://doi.org/10.3126/jnps.v33i1.7413

5. Shakya KN, Dangol UMS, Khadka SB. A Study of Abdominal Pain in Children. J Nepal Med Association. 2008;47(197):193-6. PMID: 19079393

6. Sheikh Ali; M, Latif, Tariq. Acute abdominal pain in children; clinical outcome and value of symptoms and sign in diagnosis. Professional Med J. 2015;22(8):1080-6.

7. Green RS, Kabani A, Dostmohamed H, Tenenbein M. Analgesic use in children with acute abdominal pain. Pediatr Emerg Care. 2004;20(11):725-9. DOI: 10.1097/01.pec.0000144913.70500.9e

8. Oguzturk H, Ozgur D, Turtay MG, Kayaalp C, Yilmaz S, Dogan M, et al. Tramadol or paracetamol do not effect the diagnostic accuracy of acute abdominal pain with significant pain relief - a prospective, randomized, placebo controlled double blind study. Eur Rev Pharmacol Sci. 2012;16(14):1983-8. PMID: 23242726

9. Tytgat G. Hyoscine butylbromide: a review of its use in the treatment of abdominal cramping and pain. Drugs. 2007; 67:1343-57. DOI: 10.2165/00003495-200767090-00007

10. Blasko G. Pharmacology, mechanism of action and clinical significance of a convenient antispasmodic agent: drotaverine. J Am Med Assoc India: The Physicians' Update. 1998; 1: 63-69

11. Muller-Krampe B, Oberbaum M, Klein P, Weiser M. Effects of Spascupreel versus hyoscine butylbromide for gastrointestinal cramps in children. Pediatr Int: official journal of the Japan Pediatric Society. 2007;49(3):328-34. DOI: https://doi.org/10.1111/j.1442-200X.2007.02382.x

12. Mueller-Lissner S, Tytgat GN, Paulo LG, Quigley EM, Bubeck J, Peil H, et al. Placebo- and paracetamol-controlled study on the efficacy and tolerability of hyoscine butylbromide in the treatment of patients with recurrent crampy abdominal pain. Aliment Pharmacol Ther. 2006;23(12):1741-8. DOI: 10.1111/j.1365-2036.2006.02818.x

13. 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. DOI: 10.1007/s13312-015-0730-y

14. Von Baeyer CL. Children's self-reports of pain intensity: scale selection, limitations and interpretation. Pain Res & Manag. 2006;11(3):157-62. DOI: 10.1155/2006/197616

15. Simons J, MacDonald LM. Changing practice: implementing validated paediatric pain assessment tools. J Child Health Care. 2006;10(2):160-76. DOI: 10.1177/1367493506062555

16. Romics I, Molnár DL, Timberg G, Mrklic B, Jelakovic B, Köszegi 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. DOI: 10.1046/j.1464-410x.2003.04262.x

17. Remington-Hobbs J, Petts G, Harris T. Emergency department management of undifferentiated abdominal pain with hyoscine butylbromide and paracetamol: a randomised control trial. Emerg Med J. 2012;29(12):989-94. DOI: 10.1136/emermed-2011-200474

18. Bulloch B, Tenenbein M. Assessment of Clinically Significant Changes in Acute Pain in Children. Acad Emerg Med. 2002;9(3):199-202. DOI: 10.1111/j.1553-2712.2002.tb00244.x.

19. Poonai N, Kumar K, Coriolano K, Thompson G, Brahmbhatt S, Dzongowski E, et al. Hyoscine butylbromide versus acetaminophen for nonspecific colicky abdominal pain in children: a randomized controlled trial. Canadian Medical Association Journal. 2020;192(48):E1612-E9. DOI: 10.1503/cmaj.201055