International Journal of Contemporary Pediatrics
Nagendra K et al. Int J Contemp Pediatr. 2022 Aug;9(8):706-712
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291
DOI: https://dx.doi.org/10.18203/2349-3291.ijcp20221821

Original Research Article

A prospective, single-arm, open-label, multicenter study to determine the safety and effectiveness of a fixed-dose combination of camylofin dihydrochloride and paracetamol in Indian children with acute colicky abdominal pain

Nagendra K.[1]*, Sarvanan P.[2], Dinesh Chandra Pandey[3], Minakshi Nalbale Bhosale[4], Kapil Jindal[5], Uttam Hanse[6]

[1]Cheluvamba Hospital, Opposite Mysore Medical College, Mysuru, Karnataka, India
[2]Sapthagiri Clintrac Pvt. Ltd. Sapthagiri Medical Sciences and Research Centre, Bengaluru, Karnataka, India
[3]M. V. Hospital and Research Centre, Lucknow, Uttar Pradesh, India
[4]B. J. Govt. Medical College and Sassoon General Hospital, Pune, Maharashtra, India
[5]Jindal Super Specialty Hospital, Clinical Research Room, Jaipur, Rajasthan, India
[6]GNRC Hospital, Near IIT Sila Grant North, Guwahati, Assam, India

Received: 09 June 2022
Revised: 01 July 2022
Accepted: 02 July 2022

***Correspondence:**
Dr. Nagendra K.,
E-mail: drphoenix777@gmail.com

ABSTRACT

Background: The aim of this prospective, single-arm, open-label, multicenter study was to determine the safety and effectiveness of a fixed dose combination of paracetamol and the antispasmodic camylofin dihydrochloride in Indian children with acute colicky abdominal pain.
Methods: A total of 197 children with acute colicky abdominal pain were enrolled to receive 2 teaspoons (10 mL) of the syrup thrice daily orally for 5 days per local label. Primary objective was to assess safety as incidence of adverse events (AEs) and change in the severity and frequency of AEs from baseline to end of treatment (EOT). Secondary objectives were effectiveness as evaluated by change in mean (standard deviation [SD]) pain intensity (based on the 100-mm visual analog scale [VAS]) and mean change in the frequency of daily pain episodes from baseline to EOT.
Results: In all, 182 (92.4%) patients completed the study. Twenty AEs were reported in 17 patients (8.7%). All AEs were treatment-emergent and of non-serious type. Common AEs included anemia, vomiting, and constipation. At EOT, mean pain intensity significantly ($p<0.0001$) reduced to 3.3 (8.50) with a mean change of -61.5 (19.56) from baseline. Percentage change in mean intensity of pain from baseline to EOT visit was 94.9%. At EOT, the frequency of daily pain intensity significantly ($p<0.0001$) reduced to 1.7 (1.01) with a mean change of -3.5 (2.14) from baseline.
Conclusions: A fixed-dose combination of camylofin dihydrochloride and paracetamol was effective and well tolerated and had a good safety profile in Indian children with acute colicky abdominal pain.

Keywords: Camylofin, Acute colicky pain, Nonsteroidal anti-inflammatory drugs, Spasmolytic

INTRODUCTION

Abdominal pain is a common ailment that requires medical attention.[1] It is an unpleasant, sensory and emotional experience that can profoundly impact the well-being of children.[1-3] Acute spasmodic pain is more common than chronic pain (61% vs 39%) in children[4] and is known to be associated with elevated anxiety, avoidance, somatic symptoms, and increased distress.[5] Acute abdominal pain is observed in self-limiting

conditions such as constipation, gastroenteritis, or viral illness.[6] Abdominal pain exerts a significant burden on the healthcare system[7] and accounts for about 9% of childhood consultations in general practice.[8] Antispasmodics, analgesics, antacids, antidiarrheals, and laxatives are among frequently prescribed medications for the treatment of upper and lower abdominal pain in children.[9] Fixed-dose combination (FDC) drugs have proven advantages like synergistic effects, less risk of drug resistance, good tolerability, complementary mechanism of action, and cost effectiveness. Nevertheless, their safety needs to be established in real world settings.

Antispasmodics are effective in the management of non-specific colicky abdominal pain both in adults and children.[10,11] Camylofin dihydrochloride has been used in clinical practice over the past 50 years.[12] It is a highly effective antispasmodic owing to its direct papaverine like spasmolytic action on smooth muscles and a mild atropine like anticholinergic action.[13] Via its anticholinergic activity, camylofin blocks muscarinic type-3 receptors on smooth muscle cells of the colon and reduces their motility.[14] As its anticholinergic effects are less pronounced, camylofin has a good safety profile with palpitations, dilatation of pupils, and dryness of mouth reported as frequent adverse events (AEs).[12]

Paracetamol (acetaminophen) is among the most commonly prescribed analgesics and antipyretics for management of fever and mild-to-moderate pain in infants, children, and adults.[15] Paracetamol is believed to act on the central nervous system.[16,17] It is an inhibitor of cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2) and suppresses formation of phenoxyl radicals from a tyrosine residue essential for cyclooxygenase activity and prostaglandin synthesis.[18] Though substantial data depicting the efficacy of paracetamol for the treatment of abdominal colicky pain in the pediatrics is not available, several clinical studies have shown the combination of antispasmodic (hyoscine) and paracetamol to be beneficial in abdominal pain.[19,20]

This study was conducted with an aim to garner insights on the use of an FDC of camylofin and paracetamol in children with acute colicky abdominal pain in light of limited clinical evidence pertaining to its safety and effectiveness in pediatric subjects in the Indian setting.

METHODS

Study design

This prospective, single-arm, open-label, multicenter study was conducted between November 2018 and October 2019 across 7 centers in India. The study sites were Cheluvamba hospital, Mysuru, Karnataka; Deep hospital, Ludhiana, Punjab; Sapthagiri Clintrac Pvt. Ltd. Bengaluru, Karnataka; Down Town hospital, Guwahati, Assam; MV hospital and research centre, Lucknow, Uttar Pradesh; B. J. govt. medical college and Sassoon general hospital, Pune, Maharashtra; and GNRC hospital, Guwahati, Assam. The study was conducted in compliance with good clinical practice (GCP) and the applicable Indian regulatory guidelines (Indian council of medical research [ICMR] and Indian GCP guidelines]). The study protocol was reviewed and approved by an independent ethics committee/institutional review board. Well-being of the participating patients was protected consistent with the ethical principles that have their origin in the declaration of Helsinki. Voluntary assent from each patient and written informed consent from parents/guardian/legally acceptable representative (LAR) was obtained prior to performing any study-related procedures.

The study involved a total of 3 site visits; 1 baseline visit on day 1, 1 follow-up visit on day 3 (± 1 day), and 1 follow-up visit on Day 6 (± 1 day) or end of treatment. Patients were administered 2 teaspoons (10 mL) of the FDC, i.e., Anafortan® syrup ([camylofin dihydrochloride 12.5 mg + paracetamol IP 125 mg]/5 mL) thrice daily orally for 5 days as per the local label by a parent, legal guardian, or LAR. Post-therapy follow-up was done for patients with ongoing AEs or serious AEs (SAEs). Follow up was done until AEs were resolved or judged no longer clinically significant, or if a chronic condition, until fully characterized. This follow up was telephonic or by site visit as per investigators' discretion.

Eligibility criteria

Male or female children aged ≥8-12 years, with acute colicky abdominal pain and a history of ≥1 episode of colicky pain reported within 24 hours prior to screening, with no other reported illness, were enrolled. Children who had previously taken the FDC under investigation or any other prescription analgesic, or antispasmodic medication within the previous 1 week before study enrollment were excluded. Children with a history of hypersensitivity/ allergy to study drugs or its constituents, or any other illness or conditions that did not justify their inclusion in the opinion of the investigator or children whose parents, legal guardians, or LARs were unwilling to comply with the study procedures and/or make daily diary entries for their children were also excluded.

Study objectives

The primary outcome safety was assessed by number and percentage of children with AEs including abnormal laboratory (serum chemistry and hematological) parameter levels with severity (as per common terminology criteria for adverse events [CTCAE] criteria) and drug-event relationship at day 3, day 6/end of treatment (EOT); number and percentage of children with change in the severity and frequency of reported AEs from baseline to day 3, day 6 and AE follow up post treatment (as applicable) was presented along with the corresponding 95% CI were assessed.

Tolerability was a secondary outcome and was assessed based on number and percentage of children who discontinued the treatment because of AEs before EOT.

Effectiveness was a secondary outcome and was determined by the change in the mean intensity of pain (based on a 100-mm visual analog scale [VAS] from baseline to EOT (where "meaningful pain relief" is defined as ≥30 mm decrease in pain intensity from baseline); the mean change in the frequency of daily pain episodes from baseline to EOT (as assessed from patient diary); number and percentage of children with ≥30 mm reduction in pain from baseline to EOT (as assessed by VAS); number and percentage of children in each category on a scale ranging from 1 (no change) to 7 (a great deal better) as assessed by physicians' global assessment of pain (based on the effectiveness and tolerability of treatment) at EOT were also assessed.

Number and percentage of children requiring other concomitant analgesics during study period (as assessed by patient diary) and mean change in parent response (based on their perception of child's mood, activity, alertness, oral intake and comfort) rated on a 5-point Likert scale ranging from bad (1) to completely normal (5) from baseline to EOT assessed exploratory outcomes.

Statistical analysis

Because of lack of evidence of safety for camylofin, the sample size was calculated as per available evidence for gastrointestinal-related AE rates associated with paracetamol syrup. It was assumed that camylofin has a similar safety profile. A sample of 197 patients was estimated considering the incidence rate of gastrointestinal-related AEs as 8% with 4% margin at 95% confidence level including 10% drop out rate. All patients receiving at least 1 dose of the FDC constituted the safety population. The study endpoints were analyzed using descriptive statistics. Continuous variables were reported as mean standard deviation (SD), and categorical variables were presented as frequency and number of patients. Statistical tests including paired t test were performed at 5% level of significance. The analysis population for the primary variable was the safety population. In order to assess the treatment effect using different assumptions, the effectiveness variable was also analyzed for the per-protocol (PP) population for sensitivity purpose. The secondary and exploratory variables analyzed for intention-to-treat (ITT) population.

RESULTS

Demographics and baseline characteristics

A total of 197 patients were enrolled in the study. Of these, 182 (92.4%) patients completed the study. Twelve patients withdrew consent, while 3 were lost to follow up. In all, 101 (51.3%) patients were females. The mean (SD) age of study population was 9.5 (1.17) years (Table 1). Of 197 patients, 192 (97.5%) had a history of intermittent colicky pain with a mean of 5.5 (2.55) pain episodes in a day and a mean duration of 13.5 (16.16) minutes. Five (2.5%) patients had history of continuous pain. At the baseline visit, 68 patients (34.5%) had decreased appetite and 62 (31.5%) had nausea associated with abdominal pain.

Safety evaluation

The mean (SD) study drug compliance of overall study patients was 94.3 (9.57%). During the entire study duration, 17 (8.7%) patients reported 20 AEs, all of which were treatment-emergent and of non-serious type (Table 2). Of the 20 AEs, 9 were mild (eosinophilia [2], constipation [2], food poisoning [1], dry mouth [1], nausea [1], crystalluria [1], and hematuria [1]), 10 were moderate (anemia [2], neutrophilia [1], vomiting [2], pyuria [1], increased blood creatinine [1], decreased lymphocyte count [1], increased red blood cell sedimentation rate [1], and crystalluria [1]), and 1 anemia AE was of severe intensity. Of the 20 AEs, 18 AEs were unrelated to study treatment, whereas 1 AE of increased red blood cell sedimentation rate was unlikely and 1 AE of vomiting was probably related to the study treatment. Ten AEs were resolved, whereas the outcomes of remaining 10 AEs were unknown. No adjustment of the study medication was required in response to any of the AEs, and none of AEs led to treatment discontinuation.

Effectiveness evaluation

At EOT, mean pain intensity significantly ($p<0.0001$) reduced to 3.3 (8.50) with mean change of -61.5 (19.56) from baseline. Percent change in mean intensity of pain from baseline to end of treatment visit calculated-94.9%.

Meaningful pain relief was observed in 176 (95.1%, n=185) patients. At EOT, frequency of daily pain episodes significantly ($p<0.0001$) reduced to 1.7 (1.01) with mean change of -3.5 (2.14) from baseline (Table 3). Based upon effectiveness and tolerability of treatment, physicians' global assessment of pain recorded as better and definite improvement in the majority (n=109; 58.9%) of patients, followed by considerable improvement in 54 (29.2%) patients, and moderately better and a slight but noticeable change in 10 (5.4%) patients (Figure 1).

Exploratory evaluation

A total of 8 (4.1%) patients required other concomitant analgesics during the study period, of which 6 (3.1%) patients required drugs for functional gastrointestinal disorders and 2 (1.0%) patients required analgesics.

At visit 3, mean change in parent response recorded for 174 patients and SD of mood, activity, alertness, oral intake and comfort-4.5 (0.84), 4.5 (0.74), 4.5 (0.78), 4.4 (0.85) and 4.6 (0.58), respectively; all parameters showed statistically significant change ($p<0.0001$) from baseline.

Table 1: Demographics and baseline characteristics.

Characteristics	Overall, (n=197) (%)
Age (years), mean (SD)	9.5 (1.17)
Female, n (%)	101 (51.3)
History of colicky abdominal pain, n (%)	
Continuous	5 (2.5)
Intermittent	192 (97.5)
Number of daily pain episodes, mean (SD)	5.5 (2.55)
Location of pain, n (%)	
Right upper quadrant	11 (5.6)
Right lower quadrant	38 (19.3)
Left upper quadrant	11 (5.6)
Left lower quadrant	57 (28.9)
Suprapubic	5 (2.5)
Epigastric	61 (31.0)
Periumbilical	87 (44.2)
Duration of pain episodes (minutes), mean (SD)	13.5 (16.16)
Presence of medical or surgical history, n (%)	118 (60.2)
Blood and lymphatic system disorders	4 (3.4)
Endocrine disorders	1 (0.8)
Gastrointestinal disorders	71 (60.2)
Hepatobiliary disorders	3 (2.5)
Immune system disorders	2 (1.7)
Infections and infestations	33 (28.0)
Investigations	6 (5.1)
Metabolism and nutrition disorders	12 (10.2)
Renal and urinary disorders	6 (5.1)
Respiratory, thoracic and mediastinal disorders	3 (2.5)
Vascular disorders	1 (0.8)

Table 2: Summary of treatment-emergent adverse events by severity and drug-event relationship.

Adverse event	Events, n (%)	Severity	Drug-event relationship	Outcome
Eosinophilia	2 (1.0)	Mild	Unrelated	Unknown
Anemia	3 (1.5)	Moderate (n=2), severe (n=1)	Unrelated	Resolved
Neutrophilia	1 (0.5)	Moderate	Unrelated	Unknown
Constipation	2 (1.0)	Mild	Unrelated	Resolved
Food poisoning	1 (0.5)	Mild	Unrelated	Resolved
Dry mouth	1 (0.5)	Mild	Unrelated	Resolved
Nausea	1 (0.5)	Mild	Unrelated	Resolved
Vomiting	2 (1.0)	Moderate	Probably	Resolved
Crystalluria	2 (1.0)	Mild (n=1), moderate (n=1)	Unrelated	Unknown
Hematuria	1 (0.5)	Mild	Unrelated	Unknown
Pyuria	1 (0.5)	Moderate	Unrelated	Unknown
Blood creatinine increased	1 (0.5)	Moderate	Unrelated	Unknown
Lymphocyte count decreased	1 (0.5)	Moderate	Unrelated	Unknown
RBC sedimentation rate increased	1 (0.5)	Moderate	Unlikely	Unknown

Table 3: Summary of change in intensity and frequency of pain.

Category/ parameters	Baseline (visit 1)	EOT	Change from baseline
Change in mean intensity of pain from baseline to EOT			
VAS score			
N	185	185	185
Mean (SD)	64.8 (17.79)	3.3 (8.50)	-61.5 (19.56)
P value [1]	-	-	<0.0001

Continued.

Category/ parameters	Baseline (visit 1)	EOT	Change from baseline
Mean change in frequency of daily pain episodes from baseline to EOT (Statistics)			
Daily pain episodes[@]			
N	181	178	178
Mean (SD)	5.3 (2.41)	1.7 (1.01)	-3.5 (2.14)
P value [1]	-	-	<0.0001
Change in mean intensity of pain from baseline to EOT for patients with meaningful pain relief* (n=185)			
N	176	176	176
Mean (SD)	66.9 (15.41)	3.1 (8.40)	-63.9 (16.93)
P value [1]	-	-	<0.0001
P value [1]	-	-	<0.0001

*Meaningful pain relief was defined as at least 30-mm decrease in pain intensity from baseline reported on VAS EOT, end of treatment; SD, standard deviation; VAS, visual analog scale.

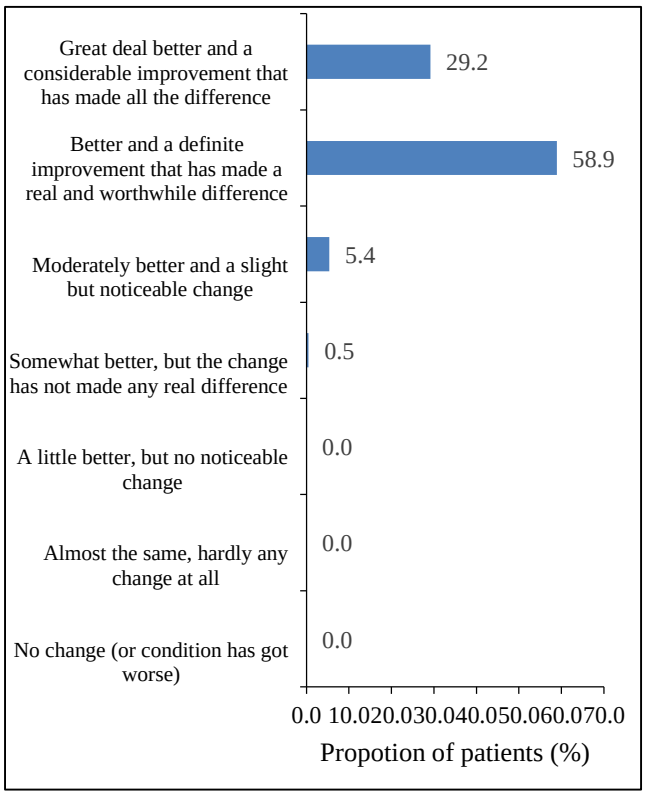

Figure 1: Summary of physicians' global assessment of effectiveness and tolerability at visit 3 (Day 6).

DISCUSSION

The study assessed the safety, tolerability and effectiveness of a fixed dose combination of camylofin dihydrochloride (12.5 mg) and paracetamol (125 mg) in children presented with acute colicky abdominal pain. The results showed that of the 197 patients, 17 subjects (<10% of the study cohort) reported 20 adverse events, which were recorded as treatment emergent. Of the total AEs, >99% of the events were mild or moderate; 1 anemia AE was severe. Rest of the events were non-serious and for majority of them drug-event relationship was recorded as not related. The common adverse events included anemia, vomiting and constipation. The obtained results showed that the reported AEs were comparable to the known side effects of both the drugs.

Camylofin has a dual mode of action, i.e., it causes relaxation of smooth muscle cells by inhibiting the enzyme phosphodiesterase and in turn increasing the concentration of cyclic AMP. It also has a mild atropine-like anticholinergic action, thereby acting as a potent antispasmodic.[21] Camylofin and its combination have been found to be effective in different types of colic like GI colic, menstrual colic, renal colic and biliary colic.[21]

As a measure of effectiveness, significant reduction ($p<0.0001$) in pain intensity was observed as measured through 100-mm VAS scale post 5 days of treatment. Majority of patients (95.1%) of the 185 patients in study cohort) achieved a meaningful change in pain from baseline. Although, most of the published literature has provided evidence on effectiveness of camylofin in obstetrics, only a few studies have reported its effectiveness in abdominal colic. An Indian study on patients with intestinal, renal, and biliary colic demonstrated effective pain relief in more than 94% of study patients when treated with 25 mg camylofin.[13] These findings are consistent with those of an open-label, randomized, comparative study including 50 patients with abdominal spasmodic pain, in which an oral FDC of camylofin 25 mg and paracetamol 300 mg showed significantly higher reduction in VAS scores for pain compared with an FDC of dicyclomine 20 mg and paracetamol 500 mg, following 5 days of treatment, as well as significant improvement in tenderness, abdominal rigidity, and inflammation.[22]

Additionally, in the present study, physicians' global assessment of pain further corroborated the effectiveness of the FDC in reducing pain, wherein approximately more than 85% of the patients demonstrated considerable improvement in pain intensity and majority of the patients felt better after 5 days of treatment. At visit 3, mean change in parent response as rated on a 5-point Likert scale showed significant improvement in patient mood, activity, alertness, oral intake, and comfort. Similar results were obtained in the study by Ali et al where the FDC of camylofin and paracetamol was rated as good to very good by 95.2% patients as against the FDC of dicyclomine and paracetamol by 42.1% patients. With regard to tolerability rating by patients, the FDC of camylofin and paracetamol combination was rated as

good by 81% patients as against dicyclomine-paracetamol by 79% patients.[22]

To our knowledge, this is the first of its kind pan India study to demonstrate current evidence on safety and effectiveness of the FDC of camylofin and paracetamol in pediatric patients with acute colicky abdominal pain. Nevertheless, the main limitation of the study was the use of VAS and physicians' global assessment to assess pain severity, which can be highly subjective and variable from patient to patient, using pain scores alone may not be adequate. Moreover, the study duration being short, it failed to provide insights on the long-term safety outcomes. Further, being an observational study, no comparator analysis was performed.

In summary, among pediatric patients presenting with acute abdominal colicky pain, thrice a day oral treatment with an FDC of camylofin dihydrochloride 12.5 mg and paracetamol 125 mg showed a significant reduction in intensity of pain with a few non-serious side effects. Thus, the study findings suggest that a fixed-dose combination of camylofin dihydrochloride and paracetamol was effective and well tolerated and had a good safety profile in Indian children with acute colicky abdominal pain.

ACKNOWLEDGEMENTS

The authors would like to thanks to JSS medical research Pvt. Ltd. for writing assistance in the development of this manuscript. The authors also thank the study participants without whom this study would not have been accomplished.

Funding: Funded by funded by Abbott Healthcare Pvt. Ltd.
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Spee LAA, Lisman-Van Leeuwen Y, Benninga MA, Bierma-Zeinstra SMA, Berger MY. Prevalence, characteristics, and management of childhood functional abdominal pain in general practice. Scand J Prim Health Care. 2013;31:197-202.
2. Wong C, Lau E, Palozzi L, Campbell F. Pain management in children: Part 1 Pain assessment tools and a brief review of nonpharmacological and pharmacological treatment options. Can Pharm J (Ott). 2012;145:222-5.
3. American Academy of Pediatrics. Committee on Psychosocial Aspects of Child and Family Health; Task Force on Pain in Infants, Children, and Adolescents. The assessment and management of acute pain in infants, children, and adolescents. Pediatrics. 2001;108:793-97.
4. Gabhane M, Braganza L. Preference trends for antispasmodics among Indian healthcare professionals: Results of a cross sectional survey. Indian Practitioner. 2015;68:32-7.
5. Assa A. School attendance in children with functional abdominal pain and inflammatory bowel diseases. J Pediatr Gastroenterol Nutr. 2015;61:553-7.
6. Kim JS. Acute Abdominal pain in children. Pediatr Gastroenterol Hepatol Nutr. 2013;16:219-24.
7. Devanarayana NM, De Silva DGH, De Silva HJ. Recurrent abdominal pain syndrome in children is a significant burden on health care system of Sri Lanka, Proceedings of the Annual Research Symposium 2006, Faculty of Graduate Studies, University of Kelaniya. 2006;88-98.
8. Reust CE, Williams A. Acute abdominal pain in children. Am Fam Physician. 2016;93:830-37.
9. Tytgat GN. Hyoscine butylbromide. Drugs. 2007;67:1343-57.
10. Rathod R, Misra D. SPICE Study: An Indian experience with buscopan plus in spasm and pain. Ind J Clin Prac. 2008;19:21-6.
11. Vinod K M, Ashish D. Oral drotaverine and aceclofenac combination versus aceclofenac alone for postoperative pain relief: A prospective randomized clinical trial. Ind J Pharm Prac. 2013;6:18-21.
12. Warke HS, Chauhan AR, Raut VS, Ingle KM. A randomised double-blind trial-Bombay Hospital Journal. J Clin Diagn Res. 2013;7(9):1897-99.
13. Mayadeo N. Camylofin dihydrochloride injection: a drug monograph review. Int J Reprod Contracept Obstet Gynecol. 2019;8:360-68.
14. Dubey R, Dubey R, Omrey P, Vyas SP, Jain SK. Development and characterization of colon specific drug delivery system bearing 5-ASA and Camylofine dihydrochloride for the treatment of ulcerative colitis. J Drug Target. 2010;18:589-601.
15. De Martino M, Chiarugi. Recent advances in pediatric use of oral paracetamol in fever and pain management. Pain Ther. 2015;4:149-68.
16. Mattia A, Coluzzi F. What anaesthesiologists should know about paracetamol (acetaminophen). Minerva Anestesiol. 2009;75:644-53.
17. Mallet C, Barrière DA, Ermund A, Jönsson BAG, Eschalier A, Zygmunt PM et al. TRPV-1 in brain is involved in acetaminophen-induced antinociception. PLoS ONE. 2010; 5:e12748.
18. Graham GG, Davies MJ, Day RO, Mohamudally A, Scott KF. The modern pharmacology of paracetamol: therapeutic actions, mechanism of action, metabolism, toxicity and recent pharmacological findings. Inflammopharmacology. 2013;21:201-32.
19. de los Santos AR, Zmijanovich R, Pérez Macri S, Martí ML, DiGirolamo G. Antispasmodic/ analgesic associations in primary dysmenorrhea double-blind crossover placebo-controlled clinical trial. Int J Clin Pharmacol Res. 2001;21:21-9.

20. Mueller-Lissner S, Tytgat GN, Paulo LG, Quigley EMM, 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;23:1741-8.
21. Mayadeo N. Role of camylofin and its combinations in obstetrics and gynaecological practice: a review of Indian evidence. Int J Reprod Contracept Obstet Gynecol 2019;8:343-8.
22. Ali M, Naik M. Open, randomized comparative study to evaluate efficacy, safety and tolerability of Anafortan Vs. dicyclomine+paracetamol in treatment of mild to moderate abdominal colic and spasmodic abdominal pain. Indian Med Gazette. 2010;314-21.

Cite this article as: Nagendra K., Sarvanan P., Pandey DC, Bhosale MN, Jindal K, Hanse U. A prospective, single-arm, open-label, multicenter study to determine the safety and effectiveness of a fixed-dose combination of camylofin dihydrochloride and paracetamol in Indian children with acute colicky abdominal pain. Int J Contemp Pediatr 2022;9:706-12.