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Comparison of paracetamol and hyoscine-N-butylbromide in the treatment of abdominal pain and cramps due to acute gastroenteritis

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Abstract

Background and objective: Hyoscine-N-butyl bromide (HBB) and paracetamol (acetaminophen) are widely used in emergency departments for abdominal pain and cramps. However, there is not enough data on the efficacy, safety, and superiority of each other in treating acute gastroenteritis (AGE) related abdominal pain and cramps. In this study HBB and paracetamol were compared for the treatment of abdominal pain and cramps related to acute gastroenteritis.

Materials and methods: The study was conducted in a tertiary university hospital emergency department as a prospective, randomized-controlled, and double-blind study. Intravenous (IV) 1000 mg paracetamol and IV 20 mg hyoscine-N-butyl bromide (HBB) were used to treat abdominal pain and cramps related to AGE. Visual analogue scale (VAS) was used to evaluate the degree of abdominal pain before and after treatment.

Results: HBB and paracetamol groups consisted of 123 and 158 cases respectively. In both groups, it was observed that the VAS score gradually decreased from the 0th hour to the 1st and 2nd hours ($p<0.001$).When comparing each time within itself, it was observed that HBB and paracetamol measurements had similar values ($p>0.05$). No severe side effects were observed in any of the patients.

Conclusion: HBB and paracetamol were used for symptomatic treatment in AGE patients presenting with abdominal pain and cramps. A significant reduction in pain and cramps was achieved in both patient groups. There was no difference between the two drugs in terms of treatment efficacy and side effects.

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Introduction

Acute gastroenteritis (AGE) is a generally self-limiting acute inflammatory condition of the gastrointestinal tract due to infectious or non-infectious causes [1]. Diarrhea is the main finding and may be accompanied by nausea, vomiting, fever, abdominal pain and cramps, bloating, gas, bloody stool, tenesmus, and urgency to defecate [1,2]. Visceral pain, associated with smooth muscle spasm, is a common symptom observed in gastrointestinal pathologies [3]. Although antispasmodic agents are widely used in the symptomatic treatment of abdominal pain and cramps, there is insufficient data on their

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efficacy and safety and is not included in the guidelines [5-7]. Hyoscine N-butylbromide (HBB), frequently used in symptomatic treatment, is a quaternary ammonium derivative that reduces abdominal cramps and pain by reducing smooth muscle tone [5]. On the other hand, paracetamol (acetaminophen), a weak prostaglandin synthesis inhibitor, has been used for many years as an analgesic and antipyretic [8]. Both drugs are widely used in emergency departments and are effective in abdominal pain and cramps [5,6]. However, there is not enough data on the efficacy, safety, and superiority of each other in treating AGE-related symptoms.

In this study, intravenous 1000 mg paracetamol and IV 20 mg HBB were used to treat abdominal pain and cramps related to AGE. The effectiveness of drugs, their superiority to each other, and their side effects were compared to find the safest and most effective treatment method that can be used in the emergency room.

Materials and Methods

Ethics committee approval was obtained from Bolu Abant İzzet Baysal University for the study (Decision no: 2020/268; Date: 24/11/2020). The study was conducted in a tertiary university hospital emergency department as a prospective, randomized-controlled, and double-blind study. The emergency department receives approximately 75,000 patient admissions per year. Written informed consent was obtained from all participants prior to the enrollement in the study.

Study population, inclusion and exclusion criteria: Patients aged 18 years and over who presented to the emergency department with symptoms of AGE and had abdominal pain and cramps were included in the study. Patients who were allergic to the drugs to be given, had acute surgical abdominal findings in physical and radiological examinations, known to have GIS disease (liver dysfunction, mega colon, gastrointestinal ulceration, history of chronic inflammatory bowel disease), renal dysfunction, history of bleeding diathesis, with a heart rate of more than 120/minute, systolic blood pressure below 90 mmHg, use of analgesics or antispasmotic in the last 24 hours, and who were pregnant were not included in the study.

Randomization and blinding: Anamnesis was taken from the patients in the triage room, and after written informed consent was obtained, they were sent to the examination room. Patients were informed about both treatments to be given. Consecutive numbers were given for each treatment with a simple randomization program (https://tr.rakko.tools). The researchers who administered the treatment and the researchers who filled the form were different. Patients and researchers who filled out the forms were unaware of the treatment the patient was receiving.

Intervention and measurement: Before the treatment, direct abdominal X-rays and abdominal ultra sonogram (USG) were performed in all patients. Patients with acute surgical abdominal findings in the physical and radiological examinations were excluded from the study. Visual Analogue Scale (VAS) was used to evaluate the degree of abdominal pain before treatment. "Little pain" and "more pain" were written on both ends of a 10 cm line, and the patient was asked to mark where his condition was appropriate on this line (1-10). After keeping the patient's VAS score before the treatment (0 h), a non-working nurse began administering the treatment.

Two different patient groups were formed. One group was called HBB, and the other group was called the paracetamol group. In the HBB group, 20 mg HBB in 100 ml 0.9% NaCl was administered by slow infusion over 15 minutes. One gram (1g) of paracetamol in 100 ml 0.9% NaCl package was administered to the paracetamol group by slow infusion within 15 minutes (there are 1g vials of paracetamol in our country). However, to double-blind the study, the drugs in the vials were applied in 100 ml 0.9% NaCl packages.

After the treatment, the patients were asked to mark the 1st and 2nd-hour VAS scores again. Patients' age, gender, first presentation symptoms, first admission examination findings, comorbidities, vital signs [fever (high fever >38^0 C was accepted), systolic and diastolic pressure], VAS scores at 0,1 and 2 hours, and side effects if developed were recorded.

Post-treatment follow-up: All patients were informed that they should inform again or call the phone number given to them if their pain increased or changed in character. All patients were called back 24 hours after the treatment, and the presence and nature of pain were questioned. Patients with severe abdominal pain and suspected acute abdomen were called to the hospital. After treatment, 22 patients were re-evaluated in the first 24 hours. No acute surgical abdomen was detected in any of them.

Calculating sample size: In proportional data where the sample universe is unknown, the minimum sample size required for the research was determined by power analysis. Accordingly,a minimum of 255 samples was found with an effect size of 0.5, an error level of 0.05, and a confidence interval of 0.95.

Statistical analysis: The conformity of the data to the normal distribution was tested with Shapiro Wilks, and Student's t-test was used to compare the customarily distributed features in two independent groups. Mann Whitney U test was used to compare the non-normally distributed features in 2 separate groups. Two-way Repeated ANOVA and Bonferroni post hoc test was used to examine the pain measurements of the paracetamol and HBB groups, which had normal distribution at recurrent times. As descriptive statistics, mean ± standard deviation, median, min-max for numerical variables, and number and % values for categorical variables are given. SPSS Windows version 23.0 package program was used for statistical analysis, and $p<0.05$ was considered statistically significant.

Results

A total of 281 cases were enrolled in the study of which 123 were in HBB and 158 were in paracetamol group. Gender distribution, age and comorborbidities of HBB and paracetamol groups were not different ($p>0.05$) from each other (Table-1). Systolic and diastolic pressures, complaints in first presentation, physical examination findings and post-treatment side effects were not different from each other in both groups ($p>0.05$) (Table-2).

Table-1:*Distribution of age, gender and comorbitities of study population*

Parameters	HBB group (n=123)	Paracetamol group (n=158)	Total (n=281)	p
Male n (%)	79 (64.2)	105 (66.5)	184 (65.5)	0.697
Age (mean±sd)	37.98±14.67	36.23±13.98	37.00±14.29	0.309
Comorbidities, n (%)				
None	97 (78.9)	126(79.7)	223 (79.4)	0.141
Yes	26 (21.1)	32 (20.3)	58 (20.6)	
Asthma	*2 (7.7)*	*2 (6.3)*	*4 (6.9)*	
DM	*7 (26.9)*	*2 (6.3)*	*9 (15.5)*	
DM, HT	*4 (15.4)*	*4 (12.5)*	*8 (13.8)*	
HBV	*0 (0)*	*3 (9.4)*	*3 (5.2)*	
HT	*3 (11.5)*	*12 (37.5)*	*15 (25.9)*	
HT, CVE	*2 (7.7)*	*0 (0)*	*2 (3.4)*	
CAD	*4 (15.4)*	*3 (9.4)*	*7 (12.1)*	
CAD, HT	*2 (7.7)*	*2 (6.3)*	*4 (6.9)*	
COPD	*1 (3.8)*	*2 (6.3)*	*3 (5.2)*	
CVE	*1 (3.8)*	*2 (6.3)*	*3 (5.2)*	

** More than one complaint was recorded in some patients. DM: diabete smellitus; HT: hypertension; HBV: hepatitis B virüs infection; CVE: cerebrovascular events; CAD: coronary artery disease; COPD: chronic obstructive pulmonarydisease.*

Table-2: *Clinical findings and post treatment adverse effects observed in HBB and paracetamol groups*

Parameters	HBB group (n=123)	Paracetamol group (n=158)	Total (n=281)	p
SBP (mean±sd)	110.46±12.08	110.37±12.34	110.41±12.20	0.958
DBP (mean±sd)	68.04±9.05	68.14±8.82	68.10±8.91	0.930
Complaint in first admission* n (%)				
Nausea	100 (81.3)	131 (82.9)	231 (82.2)	0.726
Vomiting	50 (40.7)	82 (51.9)	132 (47)	0.061
Fever	14 (11.4)	35 (22.2)	49 (17.4)	0.018
Others	3 (2.4)	3 (1.9)	6 (2.1)	0.694
Examination, n (%)				
Epigastric discomfort	5 (4.0)	7 (4.4)	12 (4.3)	0.665
Wide spread tenderness	15 (12.2)	32 (20.3)	47 (16.7)	
Tenderness in both lower quadrants	1 (0.8)	4 (2.5)	5 (1.8)	
Normal	102(83.0)	115(72.8)	217 (77.2)	
Post treatment advers effects, n (%)				
Blurred vision	2 (1.6)	0 (0)	2 (0.7)	0.143
Skin eruption	0 (0)	2 (1.3)	2 (0.7)	
Tachycardia	1 (0.8)	0 (0)	1 (0.4)	

** More than one complaint was recorded in some patients.*

Table-3: *Comparison of VAS scores of HBB and paracetamol Groups*

Group	Pain 0 h mean±sd (M)	Pain 1h mean±sd (M)	Pain 2 h mean±sd (M)	p*
HBB	7.04±2.30 (7)	2.77±2.18 (2)	0.60±1.41 (0)	**<0.001**
Paracetamol	6.65±2.36 (7)	2.58±1.77 (3)	0.87±1.04 (1)	
p**	0.168	0.405	0.064	

*Bold values indicate statistically significant p values. M, median, sd,standard deviation; p*two-way repeated ANOVA; P**Student t or Mann Whitney U test.*

It was observed that patients with high fever were more common in the paracetamol group [n= 35 (22.2%); p=0.018].

In both groups, VAS score gradually decreased from the 0th hour to the 1st and 2nd hours (p<0.001). Although the initial VAS score of the HBB group was higher than the paracetamol group and the 2nd-hour VAS score was lower than the paracetamol group, no significant difference was found when the groups' VAS scores at 0, 1 and 2 hours were compared (p>0.05; Table-3). When comparing each time within itself, it was observed that HBB and paracetamol measurements had similar values (p>0.05) (Figure-1).

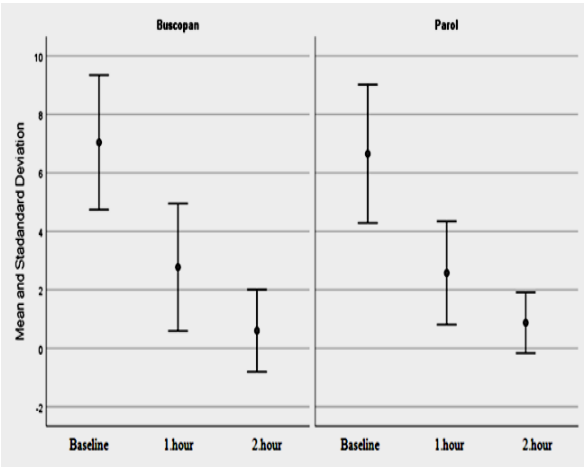

Figure-1:*Variation of VAS scores over time. Buscopan – HBB, Parol - paracetamol*

Discussion

HBB is a frequently preferred agent, especially in pain and cramps of gastrointestinal and genitourinary systems (GUS). It is known that smooth muscles reduce the frequency and severity of pain by lowering tone and mobility [3,5]. Paracetamol. which has a weak anti-inflammatory effect, is considered a safer choice and is frequently used for similar conditions [5,6,8]. It has been shown that 20 mg IV HBB reduces smooth muscle mechanical motility index by 50.9% and electrical motility by 36.5% [9]. It has been observed that HBB reduces pain after 30 minutes in 90% of patients with renal colic and similarly a pain reduction of 42-78% was observed in patients with biliary colic [6]. In the study where Kumar et al. compared the effects of diclofenac and HBB on colic pain, a reduction in pain was found in 69.4% of the patients who used HBB [10]. In their study with 132 patients, Remington-Hobbs et al. showed that oral paracetamol was at least as effective as IV HBB or paracetamol-HBB combination in treating abdominal pain [11]. While similar analgesia levels were observed in all groups at the 30th minute, it was observed that at the 60th minute, the pain scores of the patients who took oral paracetamol decreased more than those who received IV paracetamol + HBB In the study conducted by Poonai et al in 236 patients aged 8-17 years with nonspecific colic pain, no significant difference was found between HBB and paracetamol regarding pain reduction and side effects [12]. In the study of Mueller-Lissner et al., 1637 patients with recurrent cramps and abdominal pain were treated with HBB, paracetamol and HBB-paracetamol combination. A significant reduction in pain intensity and pain frequency was achieved in intervention groups compared to placebo [5].. In the study of Schäfer et al which included 712 patients with irritable bowel syndrome, were given HBB+paracetamol, HBB, paracetamol,or placebo. After four weeks of treatment, pain relief was detected in more than 75% of the patients in the HBB groups [8]. Esmaeili et al used HBB in acute appendicitis in a study of 70 patients; they found a significant decrease in pain and sensitivity [13]. Mousavi et al compared paracetamol and placebo in 107 patients diagnosed with acute appendicitis and found that the pain was significantly lower in the paracetamol group at 30 minutes, 1 hour, and 4 hours compared to placebo [14]. In our study, a significant reduction in pain and cramps was detected in both patient groups. It has been found that both drugs have a similar effect on reducing pain. While the initial (0 hour) median pain score of both groups was 7, the second-hour median pain score was lower in the HBB group, but this was not statistically significant (p=0.064). This p-value may give us an idea that HBB may provide a more effective reduction of pain in many patients.

Anticholinergic side effects such as nausea, blurred vision, palpitations, dry mouth, and urinary retention may be observed after HBB treatment [15]. Intravenous paracetamol is almost as tolerable as a placebo. During treatment, adverse effects like discomfort, hypersensitivity, hypotension, increase in liver enzymes and thrombocytopenia can rarely be seen [16]. A previous study reported adverse effects in 16% (0.2% severe side effects) cases in the HBB group and 14% (0.7% severe side effects) in the paracetamol group [5]. In the study of Schäfer et al. conducted with HBB, HBB + paracetamol, paracetamol, and placebo, no difference was observed among the groups in terms of side effects [8]. Poonai et al [12] reported no significant difference of adverse effects between HBB and paracetamol groups (27.6% in the HBB group vs. 24.3% in the paracetamol group). In our study, side effects were observed in 3 (2.4%) patients in the HBB group and 2 (1.3%) patients in the paracetamol group. There was no significant difference between the groups in terms of side effects. No severe side effects were observed in any of the patients.

Conclusion

HBB and paracetamol were used for symptomatic treatment in AGE patients presenting with abdominal pain and cramps. A significant reduction in pain and cramps was achieved in both patient groups. There was no difference between the two drugs in terms of treatment efficacy and side effects. No severe side effects were observed in any of the patients in either group. These showed that both drugs are effective in the symptomatic treatment of AGE patients with abdominal pain and

cramp and can be used safely with a 15-minute IV infusion.

Authors' contributions

HS, MB: Conceptualization, methodology, software; HS, MB, YS: Data curation, writing- original draft preparation; HS,MED: Visualization, investigation; MB, HBA: Supervision; MB, MCD: Validation, formal analysis; HS, MB,MED: Writing, reviewing and editing MED: Project administration.

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