

Evaluation of Prochlorperazine Buccal Tablets (Bukatel) and Metoclopramide Oral Tablets in the Treatment of Acute Emesis

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The dizziness associated with vertiginous disorders is often accompanied with nausea and/or vomiting. Anti-emetic effect of prochlorperazine (PCZ) is diminished by its low bioavailability owing to a significant gastric and hepatic first pass effect. This effect could be further diminished by likelihood of regurgitation of nauseating patients further limiting the therapeutic effect of oral PCZ. A buccal preparation achieves higher plasma concentrations through direct systemic absorption. In this study buccal prochlorperazine (Bukatel) was compared/or its efficacy and tolerability with commonly used metoclopramide. Bukatel was well tolerated and well rated by both patients and investigators with no adverse effects on buccal mucosa and causing less drowsiness and sedation. Results indicate that Bukatel is safe and effective for the treatment of nausea and/or vomiting in patients suffering from vertiginous disorders and could be safely and strongly recommended as an alternative to less bioavailable and indiscriminately used oral metoclopramide tablets.

Introduction

Retention of the administered antiemetic oral dose and its subsequent absorption during antiemetic therapy is critically effected by recurrent emesis, a process coordinated by vomiting centre in the lateral reticular formation of the medulla receiving inputs from the chemoreceptor trigger zone and other neural sites'. Vomiting induced by physiological processes like impaired gastric emptying and other GI disturbances will also effect drug retention and absorption^{2,3}. Retention of oral dose is therefore, a prerequisite for absorption to prevent emesis. For drugs with low oral bioavailability, partial drug loss by emesis will result in therapeutic failure. One such antiemetic drug, prochlorperazine (PCZ) after oral dosing undergoes extensive gastric and hepatic first pass effect resulting in low bioavailability which therefore, will not minimise the rate of vomiting.

Buccal tablets of prochlorperazine are designed for rapid and complete absorption in the body and for achieving therapeutic success. The objective of the present study, was to evaluate comparative efficacy and safety of prochlorperazine maleate (PCZ) buccal tablets and metoclopramide oral tablets in the treatment of postoperative vomiting.

Study design

Fifty patients who underwent cholecystectomy for gallstone under general anaesthesia between the age group of 15 and 75 years and consisting of 8 males and 42 females were assessed in an open labelled manner and were divided into 25 subjects each in PCZ and metoclopramide groups (Tables 1 & 2).

Inpatients or outpatients of emesis associated with symptoms from postanaesthesia, drug induced, alcoholism, gastroenteritis, peptic ulcer, cholecystitis, gastroenteritis, peptic ulcer, and chemotherapy induced were included in the study. Written informed consent was obtained from the patients prior to their inclusion in the study. Patients allergic to any of these drugs, pregnant or nursing mothers, patients suffering from coronary artery disease, peripheral venous disease, seizure disorder, those with abnormal screening neurological examinations, hepatitis and intestinal obstruction were excluded. In addition, patients taking concomitant medication with antiemetic and antidepressants were also excluded from the study.

Age (years)	Male	Female
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	Metoclopramide group	Bukatel group	Metoclopramide group	Bukatel group
15-30	2	-	9	8
>30-45	1	5	10	9
>45-60	-	-	2	2
>60-75	-	-	1	1

Time (minutes)	No of patients	
	Metoclopramide group	Bukatel group
0-30	-	-
>30-60	5	6
>60-90	9	6
>90-120	9	12
>120-150	1	-
>150-180	1	-

One group of patients received PCZ (3mg) huccal tablets. Bukatel, (Panacea Biotec Ltd) and the other group received metoclopramide oral tablets. Bukatel was placed high up along top of the gum on either side of the mouth where it was left to be dissolved. No other antiemetic therapy was given within 1 hour of taking either of the study drugs during the study period in the event of recurrence of vomiting. If the vomiting occurred after one hour, an additional dose of the study drug was administered.

Baseline general health was obtained by asking patients to complete a written health status questionnaire. The severity of the vomiting was scored as None (0), mild nausea only (1), moderate/ vomited once (2), severe vomiting repeatedly (3), very severe / incapacitating (4). Patients' buccal mucosa was examined before and after the treatment using a scale: None (0), slight erythema (1), well defined erythema (2), severe erythema (3), severe erythema with ulceration(4). Relief from vomiting after drug intake was scored as none (0), slight (1), moderate (2), good (3) and complete relief (4). Unwanted effects were analysed through interview by use of open questions and patients were asked to score the case of using the buccal tablets: Very easy (0), easy (1), satisfactory (2), difficult (3) and very difficult (4).

Results

In metoclopramide group, 21 patients experienced a single count of vomiting and 3 patients experienced 2 counts of vomiting before drug administration. In PCZ group 22 patients experienced one count of vomiting while 2 patients experienced more than 1 count of vomiting. The severity of vomiting was rated by patients as depicted in Table 3.

Scale	Metoclopramide group	Bukatel group
0	-	-
1	-	-
2	21	22
3	3	2
4	-	-

Relief with single dose of drug was obtained in 23 patients in metoclopramide group and 21 patients in the PCZ group. Two patients in metoclopramide group and 4 patients in PCZ group needed a second dose of the drug for control of emesis. The onset of relief of symptoms in metoclopramide

group ranged from 30 minutes to 60 minutes and in the PCZ group it ranged from 15 to 60 minutes.

Eighteen of the 25 patients had no difficulty in taking PCZ buccal tablets (Table 4). Seventeen patients experienced no local irritation while 2 patients experienced slight erythema on buccal mucosa while on PCZ therapy (Table 5).

Table 4 - Ease of administration of PCZ Buccal Tablets

Scale	Bukatel group
0	18
1	3
2	2
3	1
4	-

Table 5 - Effect of PCZ Tablets on Buccal Mucosa

Scale	Bukatel group
0	17
1	2
2	-
3	-
4	-

None of the patients experienced recurrence of vomiting on follow-up and no other therapy to control vomiting was given. The global quality of life at the end of 24 hours was found to be comparatively better by 17 patients in metoclopramide group and by 19 patients in PCZ group (Table 6)

Table 6 - Global Quality of Life as Evaluated by the Doctor. Overall Change in Symptoms is Defined as 7- Very Much Better, 6-Much Better. 5-Better. 4-Satisfactory. 3-No Difference, 2-Worse and 1-Very Much Worse

Scale (years)	2 hours		24 hours	
	Metoclopramide group	Bukatel group	Metoclopramide group	Bukatel group
7	3	3	17	19
6	3	3	2	1
5	8	4	-	-
4	9	13	-	-
3	-	1	-	-
2	-	-	-	-
1	-	-	-	-

Discussion

Oral antiemetics often get vomited out before systemic absorption compelling parenteral administration which results in hyper adverse effects like sedation, akathisia and hypotension, thereby, raising safety issues. Buccal formulation of PCZ, Bukalel, was developed to increase the extent of absorption through by-pass of hepatic first pass metabolism and also as a strong alternative antiemetic therapy to metoclopramide which has a highly variable oral bioavailability and could be as low as 32%⁴. Pharmacokinetic studies have shown bioavailability of PCZ was greater after buccal administration⁵. In our study, relief from nausea and vomiting with both drugs were comparable. However, the onset of relief was faster with Bukatel tablets than oral metoclopramide therapy which may be rationalised on the basis of higher bioavailability after by-pass of hepatic first pass effect which is missing in metoclopramide therapy. Bukatel tablets were well tolerated by all patients and therapy edges the side-effect profile of parenteral route.

Our findings assume importance by providing evidence on alternative antiemetic therapy with buccal

PCZ tablets Bukatel, which controls emesis to a greater extent than oral PCZ and would be more effective and less toxic in lower buccal dose than oral dose and in comparison to more toxic oral metoclopramide. These results are in agreement with studies conducted by Bond⁵.

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