Impact of Intracanal Medicaments on Interappointment Flare-up and Post Treatment Pain in Immunocompromised Patients

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ABSTRACT:

Background: Interappointment flare-up and postoperative pain remain important complications in endodontic therapy, particularly in immunocompromised patients. Intracanal medicaments may reduce microbial load and inflammatory response between appointments. This study aimed to evaluate the effect of different intracanal medicaments on interappointment flare-up and post-treatment pain in immunocompromised patients undergoing root canal treatment. Methods: This study included 76 immunocompromised patients undergoing multirooted root canal treatment. Patients were equally assigned to four groups (n=19): no medicament, calcium hydroxide, triple antibiotic paste, or Ledermix paste as intra canal medicaments. Pain, swelling, and interappointment flare-ups were assessed after standardized treatment, and data were analyzed using chi-square tests ($p<0.05$). Results: Baseline characteristics were comparable among groups. Interappointment flare-up was highest in the no medicament group (21.1%), followed by calcium hydroxide and triple antibiotic paste groups (5.3% each), with no flare-up observed in the Ledermix group. Although the overall difference was not statistically significant, age showed a significant association with flare-up occurrence ($p=0.043$). Post-treatment pain progressively decreased in all groups, and all patients were asymptomatic by 7 days. No significant associations were found between systemic comorbidities and flare-up. Conclusion: Intracanal medicaments, particularly Ledermix paste, demonstrated a favorable clinical trend in reducing interappointment flare-up and early postoperative pain in

immunocompromised patients, although differences among groups were not statistically significant. Age was the only significant factor associated with flare-up. Larger randomized studies are required to confirm these findings.

Keywords: Interappointment flare-up; intracanal medicament; Ledermix; calcium hydroxide; triple antibiotic paste; immunocompromised patients; postoperative pain; endodontics.

Introduction:

Successful endodontic treatment depends on the effective elimination of microorganisms, necrotic tissue remnants, and their byproducts from the root canal system. However, the complex anatomy of the root canal system, including lateral canals, isthmuses, and apical ramifications, may harbor persistent microbial biofilms that are difficult to eliminate completely through instrumentation and irrigation alone [1]. These residual microorganisms can contribute to postoperative complications, including interappointment flare-up, characterized by severe pain and/or swelling requiring unscheduled intervention [2].

The management of endodontic infections is particularly challenging in immunocompromised patients. Individuals with diabetes mellitus, chronic kidney disease, and malignancy often exhibit impaired immune responses and compromised healing capacity, making them more susceptible to persistent infection and inflammatory complications. Diabetes mellitus has been associated with impaired neutrophil function and delayed tissue repair, whereas chronic kidney disease and malignancy may adversely affect periapical healing and treatment outcomes [3-5].

To improve root canal disinfection between appointments, intracanal medicaments are commonly used as adjuncts to mechanical preparation and irrigation [6]. Calcium hydroxide remains the most widely used medicament because of its antimicrobial properties, although its effectiveness against resistant microorganisms has been questioned [7-9]. Triple antibiotic paste provides broad-spectrum antimicrobial activity against polymicrobial endodontic infections [10,11], while Ledermix paste combines antimicrobial and anti-inflammatory effects that may reduce postoperative pain and flare-up [12,13].

Despite the widespread use of these medicaments, evidence regarding their effectiveness in immunocompromised patients remains limited. Most previous studies have been conducted in healthy populations, leaving a significant knowledge gap in the management of medically compromised individuals. Therefore, this study was undertaken to evaluate the impact of different intracanal medicaments on interappointment flare-up and post-treatment pain in immunocompromised patients undergoing root canal treatment.

Materials and methods:

Present study was conducted over 12 months in the Department of Conservative Dentistry and Endodontics, Bangladesh Medical University (BMU), Dhaka. Immunocompromised patients requiring root canal treatment of multirooted teeth with periapical lesions were included. Teeth with immature apices, resorption, mobility, or pregnancy cases were excluded.

A total of 76 patients were enrolled using purposive sampling and allocated into four equal groups (n=19). Root canal treatment was performed under a standardized multi-visit protocol using crown-down preparation and irrigation with sodium hypochlorite, EDTA, and saline.

Following canal preparation, intracanal medicaments were assigned sequentially (Fig 1):

- Group I: No medicament
- Group II: Calcium hydroxide
- Group III: Triple antibiotic paste
- Group IV: Ledermix paste

Calcium hydroxide $Ca(OH)_2$ | Triple Antibiotic Paste (TAP) | Ledermix paste

Fig 1: Intracanal medicaments.

On the second visit & third visit, consecutively after 7& 14 days of the first visit patients was recalled. The root canals were evaluated for any kind of discharge or tenderness, swelling related to the same region of the oral cavity and subsequently, cleaned and irrigated with 2.5% sodium hypochlorite, 17% EDTA, with intermittent use of normal saline. When the patient was asymptomatic, and root canals were clean, obturation was done, using gutta-percha points and sealer using lateral compaction technique. (Fig2) Post operative radiograph was taken to ensure standard obturation. (Fig 3,4,5,6)

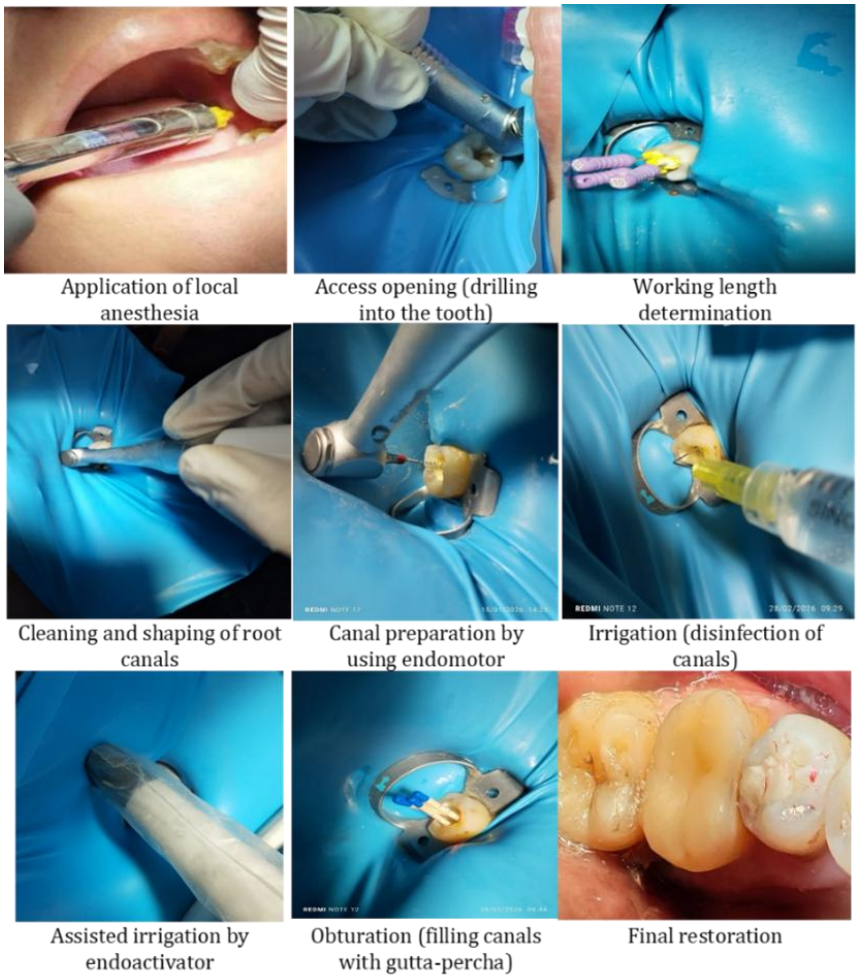
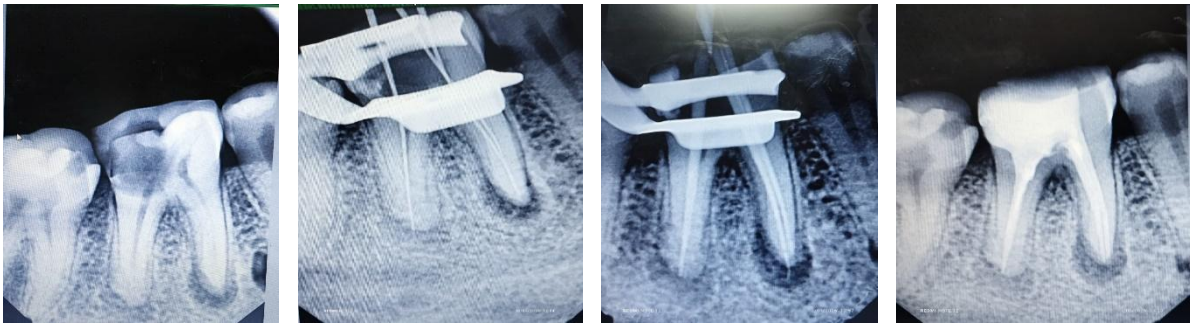


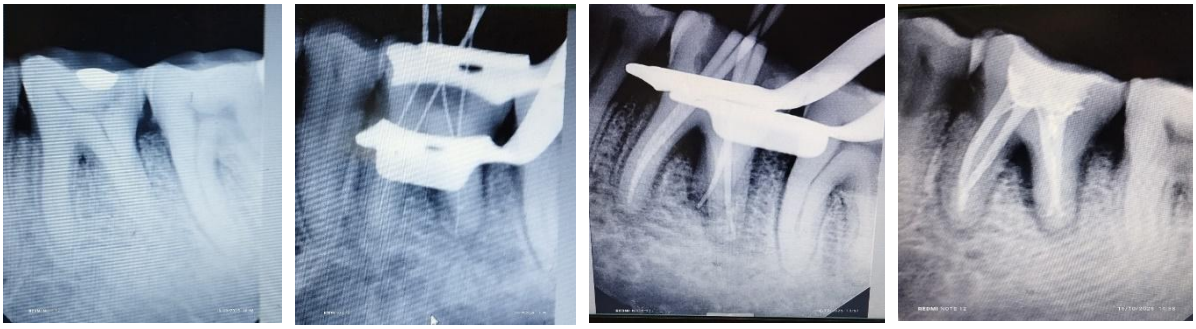
Fig 2: Steps of Root Canal Treatment.

Fig 3: Group I- No Medicament



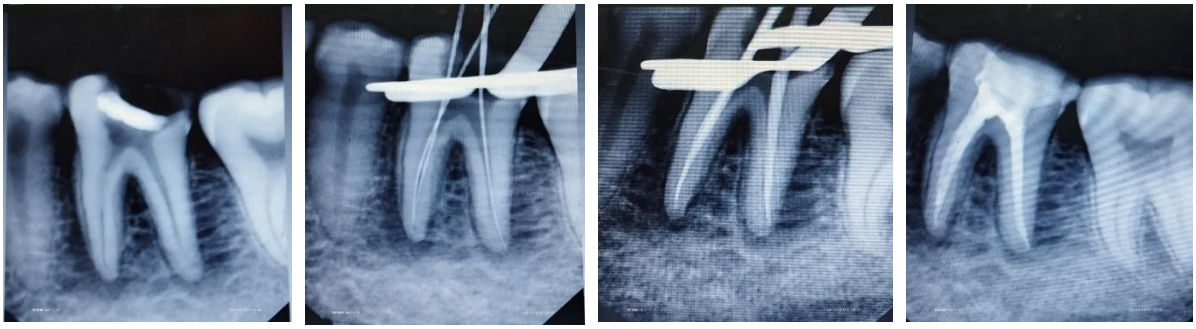
Pre-operative WLD Pre-seal Post operative

Fig 4: Group II- Calcium Hydroxide



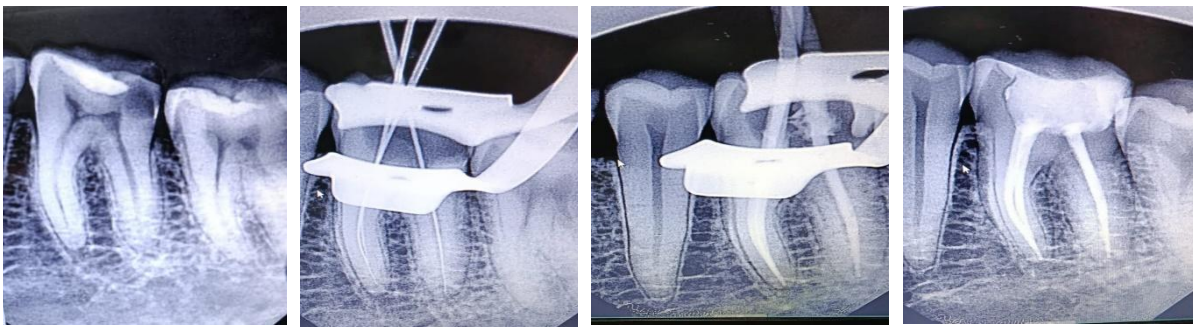
Pre-operative WLD Pre-seal Post operative

Fig 5: Group III- Triple Antibiotic Paste



Pre-operative WLD Pre-seal Post operative

Fig 6: Group IV- Ledermix paste



Pre-operative WLD Pre-seal Post operative

Results

A total of 76 patients were included in the study, equally distributed into four groups (n = 19 per group).

Baseline characteristics

Table 1 shows baseline demographic and clinical characteristics were comparable among the groups. There was no statistically significant difference among the groups regarding sex distribution (p = 0.291, Table 1). Male patients ranged from 36.8% to 63.2%, while female patients ranged from 36.8% to 63.2% across the groups. Diabetes mellitus was the most prevalent systemic condition, followed by chronic kidney disease and cancer; however, no significant differences were observed among the groups for any comorbidity (p > 0.05, Table 1).

TABLE 1: Baseline demographic and clinical characteristics of study participants (N = 76)

Variable	Group I (n=19), n (%)	Group II (n=19), n (%)	Group III (n=19), n (%)	Group IV (n=19), n (%)	p-value
Sex (Male)	9 (47.4)	12 (63.2)	7 (36.8)	9 (47.4)	0.291
Sex (Female)	10 (52.6)	7 (36.8)	12 (63.2)	10 (52.6)	
DM	15 (78.9)	16 (84.2)	18 (94.7)	15 (78.9)	0.498
CKD	2 (10.5)	2 (10.5)	1 (5.3)	2 (10.5)	0.925
Cancer	2 (10.5)	1 (5.3)	0 (0.0)	2 (10.5)	0.502

Pain during follow-up after initial treatment

Table 2 presents the distribution of pain with or without swelling after initial treatment. A progressive reduction in pain was observed across all groups over time. On Day 1, most patients reported no pain (68.4%–84.2%). By Day 7, nearly all patients were pain-free in all groups. During the second follow-up visit, all patients were pain-free by Day 3 and remained so at Day 7. No statistically significant differences were observed among the groups at any time point (p > 0.05)

TABLE 2: Pain with or without swelling during follow-up after initial treatment (Visit 1 & Visit 2 combined)

Time point	Group I,n(%)	Group II,n(%)	Group III,n(%)	Group IV,n(%)	p-value
Day 1 (No pain)	13 (68.4)	13 (68.4)	13 (68.4)	16 (84.2)	0.678
Day 2 (No pain)	16 (84.2)	17 (89.5)	18 (94.7)	19 (100)	0.606
Day 3 (No pain)	16 (84.2)	18 (94.7)	18 (94.7)	19 (100)	0.506
Day 7 (No pain)	17 (89.5)	17 (89.5)	18 (94.7)	19 (100)	0.621
Visit 2 Day 1 (No pain)	17 (89.5)	18 (94.7)	18 (94.7)	19 (100)	0.549
Visit 2 Day 2 (No pain)	18 (94.7)	19 (100)	19 (100)	19 (100)	0.386
Visit 2 Day 3 (No pain)	19 (100)	19 (100)	19 (100)	19 (100)	—
Visit 2 Day 7 (No pain)	19 (100)	19 (100)	19 (100)	19 (100)	—

Post-obturation pain

Table 3 shows at 6 hours, the highest proportion of pain-free patients was observed in Group IV (94.7%), while Group I showed the lowest (52.6%). Mild to moderate pain was more frequently observed in Group I and Group II at early time points. However, pain reduced significantly in all groups over time, and by 7 days, all patients were completely pain-free. No statistically significant differences were observed among the groups at any time point ($p > 0.05$).

TABLE 3: Post-obturation pain at different time intervals (Visit 3)

Time	Group I,n(%)	Group II,n(%)	Group III,n(%)	Group IV,n(%)	p-value
6 hours (No pain)	10 (52.6)	13 (68.4)	15 (78.9)	18 (94.7)	0.105
6 hours (Any pain)	9 (47.4)	6 (31.6)	4 (21.1)	1 (5.3)	
12 hours (No pain)	15 (78.9)	16 (84.2)	19 (100)	19 (100)	0.228
24 hours (No pain)	17 (89.5)	18 (94.7)	19 (100)	19 (100)	0.292
7 days (No pain)	19 (100)	19 (100)	19 (100)	19 (100)	—

Interappointment flare-up and associated factors

Table 4 shows the incidence of interappointment flare-up. The highest flare-up rate was observed in Group I (21.1%), followed by Group II and Group III (5.3% each), while no flare-up was observed in Group IV. Although a decreasing trend was observed across the groups, the difference was not statistically significant ($p = 0.089$) A higher proportion of flare-up was observed in males (11.4%) compared to females (4.9%), although this difference was not statistically significant ($p = 0.291$). Age was significantly associated with interappointment flare-up ($p = 0.043$) with higher occurrence in younger age groups (20–40 years). No significant association was found between comorbid conditions and flare-up occurrence, including diabetes mellitus, chronic kidney disease, and cancer ($p > 0.05$)

TABLE 4: Interappointment flare-up and its association with demographic and clinical factors among study participants (N = 76)

Variable	Category	Flare-up Yes,n(%)	Flare-up No,n(%)	Total	p-value
Study Group	Group I	4 (21.1)	15 (78.9)	19	0.089
	Group II	1 (5.3)	18 (94.7)	19	
	Group III	1 (5.3)	18 (94.7)	19	
	Group IV	0 (0.0)	19 (100)	19	
Sex	Male	4 (11.4)	31 (88.6)	35	0.291
	Female	2 (4.9)	39 (95.1)	41	
Age group (years)	20–30	1 (20.0)	4 (80.0)	5	0.043*
	31–40	2 (16.7)	10 (83.3)	12	
	41–50	1 (5.3)	18 (94.7)	19	
	51–60	1 (4.2)	23 (95.8)	24	
	61–70	1 (4.8)	20 (95.2)	21	
Comorbidity	DM	5 (83.3)	59 (84.3)	64	0.951
	CKD	0 (0.0)	7 (10.0)	7	0.416
	Cancer	1 (16.7)	4 (5.7)	5	0.299

Overall, pain decreased progressively over time in all groups, with complete resolution by 7 days. Although Group IV showed the lowest incidence of interappointment flare-up, the difference among groups was not statistically significant. Age was the only factor significantly associated with flare-up occurrence, whereas sex and systemic comorbidities showed no significant association.

Discussion:

This study demonstrated a lower incidence of interappointment flare-up and early postoperative pain in groups receiving intracanal medicaments compared to no medicament, with the most favorable outcomes observed in the Ledermix group.

The reduction in flare-up can be attributed to enhanced microbial control between appointments. In the absence of intracanal medicaments, residual bacteria may persist and proliferate, triggering periapical inflammation [6,14]. Although overall differences were not statistically significant, pairwise trends suggested a clinically meaningful benefit of medicament use, particularly Ledermix.

Ledermix paste demonstrated superior clinical outcomes, likely due to its combined antimicrobial and anti-inflammatory effects. The presence of triamcinolone reduces inflammatory mediators, while demeclocycline provides antimicrobial action, which may explain reduced early postoperative pain and flare-up [7,12,15].

Calcium hydroxide and triple antibiotic paste also reduced flare-up compared to no medicament, consistent with their antimicrobial properties [8–10]. However, their lack of anti-inflammatory action and possible microbial resistance may explain residual flare-up cases.

Post-obturation pain decreased significantly over time in all groups, aligning with established evidence that post-endodontic pain is self-limiting following adequate debridement [16]. Intracanal medicaments may accelerate symptom resolution by reducing microbial load and inflammatory response [6].

Although diabetic patients showed a higher proportion of flare-up, no statistically significant association was observed between systemic disease and outcomes. This may be due to sample size limitations and effective chemomechanical disinfection reducing systemic influence on treatment response [3–5,17].

Overall, intracanal medicaments—particularly those with combined antimicrobial and anti-inflammatory effects—appear beneficial in reducing early endodontic complications in immunocompromised patients.

Conclusion:

Within the limitations of this quasi-experimental study, intracanal medicaments showed a clinically beneficial effect in reducing interappointment flare-up and early postoperative pain in immunocompromised patients undergoing root canal treatment. The lowest incidence of flare-up and the most favorable pain outcomes were observed with Ledermix paste, followed by calcium hydroxide and triple antibiotic paste, compared to no medicament. However, these differences were not statistically significant. Age was found to be significantly associated with flare-up occurrence, while systemic comorbidities showed no significant influence. Overall, the use of intracanal medicaments—particularly those with combined antimicrobial and anti-inflammatory properties—may improve clinical outcomes, although further large-scale randomized controlled trials are needed for definitive evidence.

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