

Original Research

## The antimicrobial efficacy of 0.1 % Octenidine dihydrochloride and 0.2% Chlorhexidine gluconate mouthwash in children undergoing chemotherapy for Acute Lymphoblastic Leukemia

Jain A, Pandey RK, Mishra A

**Abstract:** *Background:* Hypo-salivation is one of the chief complications of children undergoing chemotherapy. This promotes the growth of cariogenic flora and increases the incidence of dental caries. *Objective:* To compare the anti-microbial efficacy, taste perception, odour and post rinse sensation of 0.1 % Octenidine dihydrochloride (OCT) and 0.2% Chlorhexidine gluconate (CHX) mouthwash in children. *Material & Methods:* Children of age group 6 to 12 years were selected from two independent sources, which includes patients reporting to the outpatient department (control group) and children in the indoor ward after being diagnosed with acute lymphocytic leukemia (test group). Total 84 children were selected and each test and control group was further divided into two groups (one receiving OCT mouth wash and another CHX mouthwash). Saliva samples were collected at 1, 3 and 5 days intervals and were assessed for microbial load of Mutans streptococcus (MS) and Lactobacillus. After 5<sup>th</sup> day children were asked to fill a questionnaire assessing the taste, odour and sensation post rinse. *Results:* Statistically significant ( $p < 0.001$ ) decrease in bacterial colony count at post rinse was observed in all groups and at all periods. <sup>2</sup> test revealed significant difference and higher liking of taste of OCT as compared to CHX. However, no significant difference was found between OCT and CHX rinse for prolonged mouth sensation. *Conclusion:* OCT was found to be the most effective mouth rinse in reducing the salivary microbial load when compared to CHX mouth rinse.

Keyword: Chlorhexidine; Leukemia; Mouth Wash; Octenidine.

### INTRODUCTION

Acute lymphoblastic leukemia is the most common malignancy in children.<sup>1,2</sup> The late effects of anti-neoplastic drugs have gained an increasingly important importance today.<sup>3</sup> Reduced salivary flow rate favors the cariogenic micro-flora in oral cavity.<sup>4</sup> Chlorhexidine gluconate is the most effective anti-plaque agent.<sup>5,6,7</sup> Unfortunately, it has side effects, unpleasant taste and tooth staining.<sup>8</sup> Octenidine dihydrochloride is a broad spectrum topical anti-microbial agent.<sup>9</sup> It inhibits plaque formation and dental caries in rats, primates and human.<sup>10,11,12</sup> So, the present study was undertaken to evaluate the efficacy of Octenidine mouth wash against Mutans streptococci and Lactobacillus compared to Chlorhexidine and its acceptance among children.

### MATERIAL AND METHOD

The present study was conducted in the department of Paediatric and preventive dentistry, in collaboration with the department of Paediatrics and department of Microbiology. The study design was approved by the institutional ethical committee. Children of age group 6 to 12

years were selected from two independent sources, which includes patients reporting to the outpatient department of Paediatric and preventive dentistry (control group) and children admitted in the indoor ward of the department of Paediatrics after being diagnosed with acute lymphocytic leukemia (ALL) (test group). A written consent was obtained from the parents of the children participated in the present study.

### Inclusion criteria:

#### Control Group:

- The child patients of both the sex, screened for moderate to high caries risk as per American Academy of Paediatric Dentistry (AAPD) guidelines 2014.
- Child with poor oral hygiene as per Oral Hygiene Index Simplified by Greene and Vermillion.

#### Test group:

- Children diagnosed with acute lymphocytic leukemia and undergoing induction chemotherapy.

**Exclusion criteria:****Control Group:**

- Physically or medically compromised child.
- Child with a history of systemic antibiotics medication within past one month.
- Child with acute infections such as acute abscess, cellulitis, herpes etc.

**Test group:**

- Child receiving any radiotherapy in neck and head region.
- Child having active oral infection, trauma to oral mucosa/ulceration prior to chemotherapy.
- Child suffering from diabetes or major cardiovascular disorder.

The patients selected were randomly allotted to one of the four groups as per lottery system. Eighty four chits were prepared (21 for each group) and color code of each group was printed on them and was kept in a sealed opaque envelope. The child was instructed to pick any chit randomly and was then allocated mouth rinse in opaque bottle, whose color code was inscribed within the chit, was delivered to the patient and written instructions were given to the parents accompanying them regarding saliva sample collection and rinsing of mouth with the requisite drug.

- **Control group: Group 1-** 21 subjects received 0.2% Chlorhexidine mouth rinse.
- **Control group: Group 2-** 21 subjects received 0.1% Octenidine mouth rinse.
- **Test group: Group 3-** 21 subjects received 0.2% Chlorhexidine mouth rinse.
- **Test group: Group 4-** 21 subjects received 0.1% Octenidine mouth rinse.

Chlorhexidine gluconate 0.2% mouthwash (CHX) (ICPA Health Products Ltd., India) and Octenidine Dihydrochloride 0.1% mouthwash (OCT) (Octenidol, Schulke and Mayr GmbH, Norderstedt, Germany) were used in the present study.

**Sampling Procedure:**

- Pre rinse sample- Collected before child performs oral rinsing on first, third and fifth day.
- Post rinse sample- Collected 15 mins later after the child performs oral rinsing on first, third and fifth day.

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Each patient was asked to sit in an upright position and was instructed to swallow any residual saliva present in mouth. Thereafter patient was instructed to lean forward for 2 minutes and spit the saliva collected in the floor of mouth in a pre- weighed sterile container. Thus 2-3 ml of unstimulated saliva sample was collected as a baseline sample. The children were then instructed to rinse his/her mouth with the drug allocated to him as per randomization. The subjects were required to swish 10 ml of mouth rinse in their mouth for 1 minute before rinsing it out. Then, 15 minutes after the rinsing, the saliva sample was collected again. Children were instructed to use 10 ml of the mouth rinse for 1 minute twice a day for 5 days.

The saliva collection was repeated on third and fifth day. The subjects were asked to brush only teeth after dinner without any toothpaste and were also asked to refrain from breakfast during the course of the study i.e. until the end of fifth day. Since, the present study was a double blind, it was mandatory to ask all participants to use mouth rinses with same instructions. However, parallel amount and duration of mouth rinse administration was followed in a study by Axelsson and Lindhe.<sup>[13]</sup> They were then instructed not to rinse their mouth with water or eat anything for half an hour because the retention of CHX in the oral cavity is dependent on a number of factors as stated by Walton and Thompson<sup>[14]</sup>, and the food ingestion significantly decreased salivary CHX.

The sample was collected between 9 am to 10 am to eliminate any effect of diurnal variation. The saliva samples collected were immediately streaked on Mitis Salivarius Bacitracin agar (MSB) and Lactobacillus MRS agar (MRS) for the identification of Mutans Streptococci and lactobacillus respectively followed by Gram's staining and Catalase test. The plates were incubated at 37 degree Celsius for 24-48 hours in

anaerobic conditions. After incubation the total colony forming units CFU on each plate was counted. A questionnaire was given to children regarding the assessment of taste, odour and prolonged sensation of the mouth rinse.

**RESULTS**

Total two dropouts were reported, one each in group 1 and 3. The basic characteristics viz. age and sex distribution of all the four groups at the time of admission (enrollment)

Characteristics	Control CHX (n=20) (%)	Control OCT (n=21) (%)	Test CHX (n=20) (%)	Test OCT (n=21) (%)	F/ <sup>2</sup> value	p value
Age (years): Mean ± SD	8.30 ± 1.81	8.19 ± 1.66	8.25 ± 1.71	8.38 ± 1.69	0.05	0.987
Sex:						
Male	12 (60.0)	14 (66.7)	14 (70.0)	15 (71.4)	0.71	0.870
Female	8 (40.0)	7 (33.3)	6 (30.0)	6 (28.6)		

**Table 1:** Basic characteristics of four groups.

Comparisons	Day 1	Day 3	Day 5
Control CHX vs. Control OCT	0.981	0.976	0.056
Control CHX vs. Test CHX	0.587	1.000	1.000
Control CHX vs. Test OCT	1.000	0.749	0.128
Control OCT vs. Test CHX	0.999	0.998	0.052
Control OCT vs. Test OCT	0.9427	1.000	1.000
Test CHX vs. Test OCT	0.430	0.916	0.121

**Table 2:** Comparison (p value) of mean change (pre-post) in bacterial colony count of Mutans streptococci for each day among the groups by Tukey test.

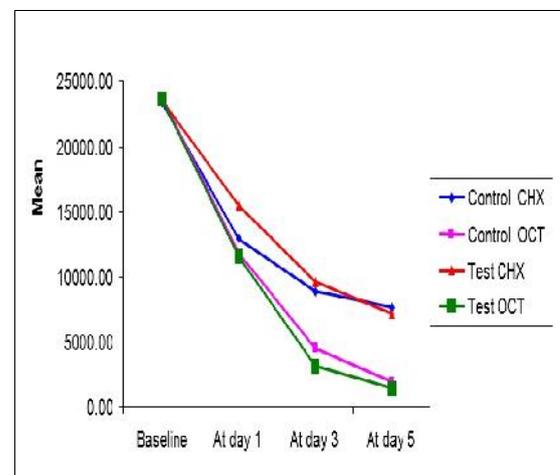
Comparisons	Day 1	Day 3	Day 5
Control CHX vs. Control OCT	0.850	0.813	0.348
Control CHX vs. Test CHX	0.990	0.997	1.000
Control CHX vs. Test OCT	0.818	0.119	0.723
Control OCT vs. Test CHX	1.000	1.000	0.350
Control OCT vs. Test OCT	1.000	0.991	1.000
Test CHX vs. Test OCT	1.000	0.743	0.725

**Table 3:** Comparison (p value) of mean change (pre-post) in bacterial colony counts of Lactobacilli on each day amongst the various groups by Tukey test.

Comparing the pre and post rinse mean bacterial colony counts of MS and

are summarized in Table I. The pre and post bacterial colony counts of Mutans streptococci (MS) and Lactobacillus of four groups over the periods (day 1, day 3 and day 5) are summarized in Table II and Table III respectively. The mean bacterial colony count of MS and Lactobacillus decreases after use of mouth rinses and the decrease wastime dependent i.e. the count decreases over the time and higher decrease was observed in OCT than CHX.

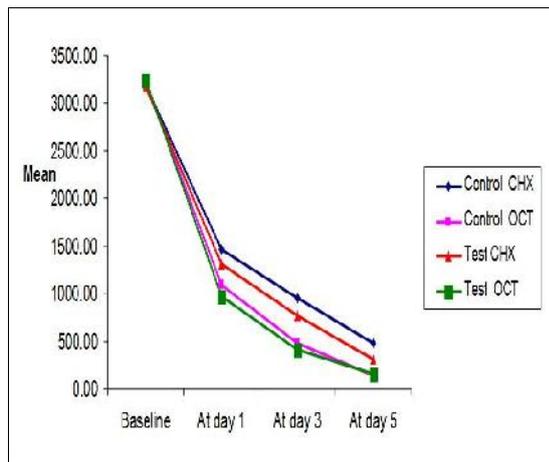
lactobacillus in each group, the Wilcoxon signed rank test revealed significant (p<0.001) decrease in bacterial colony count of MS and lactobacillus at post rinse was observed as compared to pre rinse in all groups and at all periods. (Graph 1 and 2)



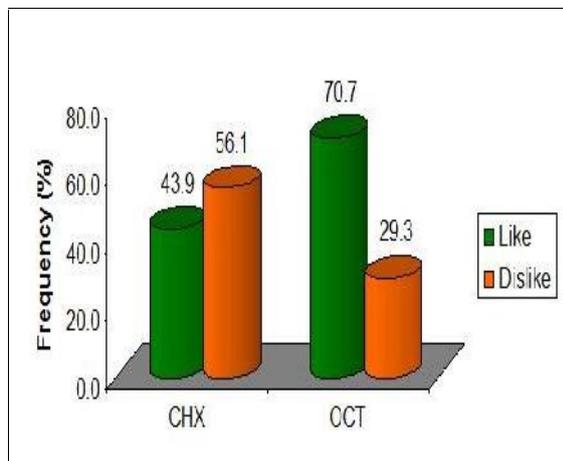
**Graph 1:** Post treatment mean bacterial colony counts of Mutans streptococci of different groups as compared to pretreatment (baseline).

The acceptance of taste of mouth rinses in patients is depicted graphically in Graph 3. Comparing the frequency (%) of likings of taste of rinses, <sup>2</sup> test revealed significantly different and higher liking of taste of OCT as compared to CHX among patients. The acceptance of odour of mouth rinses amongst patients is depicted graphically in Graph 4. Comparing the frequency (%) of

odour of rinses, <sup>2</sup> test revealed significantly different and more liking of odour of OCT as compared to CHX among patients (34.1% vs. 56.1%, <sup>2</sup>=3.99; p=0.046). The any oral systemic sensation in mouth after using mouth rinses in patients is depicted graphically in Graph 5. Comparing the frequency (%) of sensation of rinses, <sup>2</sup> test revealed similar feeling of sensation in mouth after using rinses (41.5% vs. 31.7%, <sup>2</sup>=0.84; p=0.359) i.e. not differed statistically.



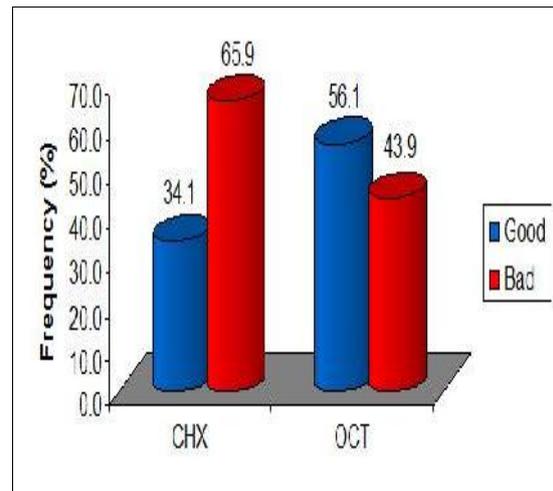
**Graph 2:** Post treatment mean bacterial colony counts of Lactobacilli of different groups as compared to pretreatment (baseline).



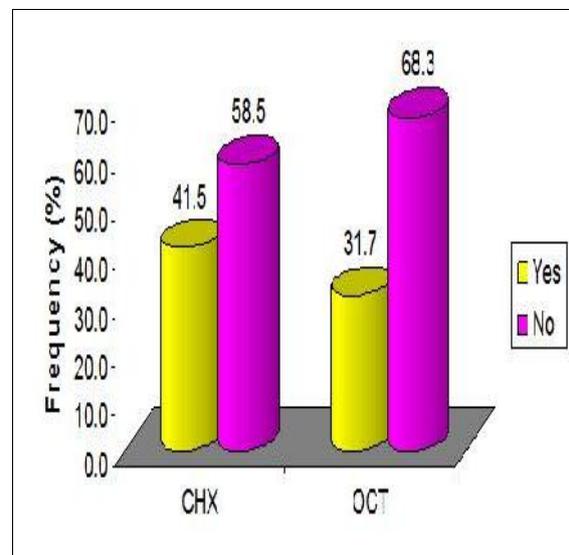
**Graph 3:** Distribution of liking of taste of mouth rinses amongst patients.

Continuous data were summarized as Mean ± SD while discrete (categorical) in no. or %. The pre and post bacterial counts were compared by Wilcoxon matched pairs signed rank (W) test. The change in (pre-post) in bacterial counts of four groups over the periods were compared by repeated measures analysis of variance (ANOVA)

using general liner models (GLM) and the significance of mean difference within and between the groups was done by Tukey post hoc test after transforming data to log10 transformation. The age of four groups were compared by ANOVA followed by Tukey post hoc test. Categorical groups were compared by chi-square (<sup>2</sup>) test. A two-sided ( =2) p value less than 0.05 (p<0.05) was considered statistically significant.



**Graph 4:** Distribution of acceptance of odour of mouth rinses amongst patients.



**Graph 5:** Frequency distribution of any oral systemic sensation in mouth after rinsing.

**DISCUSSION**

The present study showed decrease in mean bacterial colony counts of Mutans streptococci and lactobacillus after use of mouth rinses and this decrease time dependent i.e. it decrease over the time and higher decrease was observed in OCT than

CHX. These results were similar to that observed by Kocak et al.,<sup>15</sup> Dogan et al.<sup>16</sup> and Decker et al.<sup>17</sup> The method to collect salivary sample was of utmost importance. Navazesh and Christensen<sup>18</sup> concluded that stimulatory potential of suction technique and uneven saliva collection in various parts of the mouth makes it highly unreliable method compared to spitting and draining method. Hence, in the present study salivary sample was collected by spitting method as it is superior, simple and has greater reproducibility of flow rates as compared to other methods. Unstimulated saliva is believed to represent an equilibrated condition and thus it was opted for collection of bacterial sample. Any stimulation procedure (chewing, citric acid stimulation or stimulation with medicaments) was not used in the present study.

To prevent or reduce plaque formation chlorhexidine gluconate has been among the most effective of all antiseptics tested so far and can be regarded as the best agent to be used as a positive control. In the present study, CHX had significantly reduced the Mutans streptococci and Lactobacilli levels in saliva samples. However, it was observed that its efficiency was lower than Octenidol over 5 days follow up period.

Robrish et al.<sup>19</sup> also reported that OCT had a more persistent antimicrobial effect on the organisms in plaque than that obtained by CHX. Dogan et al.<sup>16</sup> in their in vitro and in vivo study compared the short-term relative antibacterial effects of OCT and CHX. Their results were in concurrence with the present study, as OCT was found more effective than CHX in its antibacterial activity. Although, the initial antimicrobial activities of OCT and CHX are comparable, but because of better persistent antimicrobial activity of octenidine, we may suggest that OCT has promising effect on Mutans streptococci and Lactobacilli. Therefore, octenidine can be a better alternative for mouth rinse in comparison to chlorhexidine.

The acceptance of medications by the child patients depends largely upon the taste, colour, odour, appearance and mode of delivery. The children generally have great aversion to any medication having bitter

taste. Therefore, it is important especially in pediatric patients to make consumption of medicaments pleasant by also considering these mentioned aspects. The results of the questionnaire used in the present study revealed that the taste of octenidine was appealing compared to CHX mouth rinse and was easily accepted by the children. However, the prolong sensation post rinse was similar to that of CHX mouth rinse and was not pleasant for children. More long term studies in future should be undertaken to study organoleptic effects and bio compatibility of Octenidine.

**CONCLUSION:** Within the limitations of the present study, it can be concluded that during 5 days of usage, OCT was the most effective mouth rinse than CHX mouth rinse as, a substantial reduction in microbial load in saliva and better taste perception was observed.

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