ORIGINAL RESEARCH

Comparing the Effectiveness of Octenidine Hydrochloride and Chlorhexidine Gluconate Mouthrinses in Reducing Plaque and Oxidative Stress in Institutionalized Children with Down Syndrome

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Abstract

Background and objectives: Due to decreased manual dexterity, a lack of motivation, and difficulty on the part of the caregiver conducting efficient oral hygiene measures at home, patients with Down syndrome (DS) are badly affected. The objective of this study is to compare the efficacy of 0.1% octenidine (OCT) hydrochloride and 0.12% chlorhexidine (CHX) gluconate on plaque control and oxidative stress in institutionalized children with DS.

Materials and methods: In 20 children, salivary samples were collected for analysis of the inflammatory marker high-sensitive C-reactive protein (hsCRP) and oxidative stress markers, specifically malondialdehyde (MDA). Plaque index (PII) and gingival index (GI) were scored. After oral prophylaxis, the participants were randomly assigned to two groups, each consisting of 10 individuals (octenidol and CHX). Salivary oxidative stress marker assays were carried out using a modified version of Yagi's (1984) method, and absorbance was measured at 540 nm using an ultraviolet-visible spectrophotometer at 535 nm. hsCRP assays were conducted *via* latex turbidimetric immunoassay.

Results: On comparison between the two groups, the OCT group showed a statistically significant reduction in GI, PII, and MDA values ($p < 0.05$).

Conclusion: It was seen that the use of 0.1% OCT hydrochloride could facilitate the maintenance of good oral hygiene and periodontal status, especially in patients with motor difficulties.

Clinical trial registration: PMS/IEC/2016/02.

Keywords: Chlorhexidine gluconate, Down syndrome, Gingival index, High-sensitive C-reactive protein, Malondialdehyde, Octenidine hydrochloride, Oxidative stress marker, Periodontal disease, Plaque index.

International Journal of Clinical Pediatric Dentistry (2024): 10.5005/jp-journals-10005-2816

Introduction

Maintaining good oral health is a particular challenge for children with special healthcare needs (CSHCN) because of increased medically based oral health risks. It is found that 8% of CSHCN nationally have unmet dental needs.[1] Children with Down syndrome (DS) are more susceptible to oxidative stress due to the overexpression of the antioxidant enzyme superoxide dismutase, which is encoded on chromosome 21. The elevated levels of superoxide dismutase induce oxidative stress by elevating reactive oxygen species. The oxidative stress leads to the breakdown of deoxyribonucleic acid, lipids, and proteins, of which the main breakdown products of lipids are highly reactive malondialdehyde (MDA). Increased levels of lipid peroxidation may play a role in inflammation and destruction of the periodontium.[2]

Children with DS are often further disadvantaged by poor preventive dental health practices. Poor periodontal health and prognosis are associated with individual age, intelligence quotient level, and parental education. However, supervised brushing, good dental care, and preventive measures tend to improve the periodontal status.[3–5] This has led to the use of chemical antibacterial agents as an important aid or adjuvant to mechanical procedures in home oral hygiene regimens used in children with physical or mental disabilities.

Chlorhexidine (CHX) gluconate 0.12% (PerioGard® Colgate-Palmolive India Ltd) is the most studied and effective antiseptic for plaque inhibition and prevention of gingivitis. Meanwhile, octenidine (OCT) hydrochloride 0.1% (Octenidol® mouthwash solution, Schulke India Pvt. Ltd., New Delhi) exerts beneficial clinical effects upon plaque accumulation and gingivitis and was shown to be efficacious when compared with CHX with respect to antiplaque activity.[6]

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How to cite this article: Raj AS, George S, S A, *et al.* Comparing the Effectiveness of Octenidine Hydrochloride and Chlorhexidine Gluconate Mouthrinses in Reducing Plaque and Oxidative Stress in Institutionalized Children with Down Syndrome. Int J Clin Pediatr Dent 2024;17(4):437–441.

Source of support: Nil

Conflict of interest: None

Literature shows that there are very limited studies comparing the antimicrobial and antiplaque efficacy of 0.1% OCT mouthwash over 0.12% CHX gluconate mouthwash. Hence, this study is conducted to assess the efficacy of these mouthwashes by evaluating the difference in gingival and plaque index (PII), salivary oxidative stress markers (MDA), and salivary inflammatory markers [high-sensitive C-reactive protein (hsCRP)] before and after treatment with these chemical plaque control agents in institutionalized children with DS between the age-group of 9 and 15 years.

Materials and Methods

Due permission was obtained from the head of the institutions, and ethical clearance was obtained from the Institutional Review Board (IEC No-PMS/IEC/2016/02). Written consent was obtained from the parents/guardians of all children and the director of the respective institution of the children. All patient information was kept confidential and was not revealed to anyone under any circumstances.

Inclusion Criteria

- Down syndrome children between the age-group of 9 and 15 years.
- Down syndrome children with a mild-to-moderate degree of mental disability (Stanford-Binet Intelligence Scale or Wechsler's Intelligence Scale) so that they can maintain oral cleanliness unaided.
- Down syndrome children who do not show any allergic reactions to mouthrinses.
- Down syndrome children with no periodontal treatment received in the previous 6 months.
- Parents and children willing to participate in the study.

Exclusion Criteria

- Down syndrome children with any systemic diseases like coronary heart disease and nephrotic syndrome.
- Subjects who have been on systemic/topical steroidal and nonsteroidal anti-inflammatory drugs or antibiotics during the past 3 months.
- Diabetes mellitus or any other chronic inflammatory disease or infection.
- Parents or children are not willing to participate.

Study Design

A total of 20 children who met the selection criteria were examined by the principal investigator. Salivary samples were collected for the analysis of inflammatory and oxidative stress markers. PII and gingival index (GI) were scored. Supragingival scaling was performed for the children. The principal investigator instructed the children on the use of mouthrinse. Then, the participants were divided into two groups, each consisting of 10 individuals (OCT group and CHX group) using a lottery method by the second examiner (Fig. 1). The first examiner (principal investigator) was blinded with respect to this. The allocation was known only to the second examiner, who checked it and sealed it in an envelope with the child's name on it. The participants were not informed whether they belonged to the OCT or CHX group. Sufficient amounts of the products needed by a single participant for the 2-week study duration were provided to each child in an opaque bottle labeled with the child's name. Children were instructed to rinse for 1 minute using 10 mL of mouthrinse twice daily, in the morning and evening, for 2 weeks (Fig. 2). Rinsing was done under the supervision of the principal investigator in the institutions. After 2 weeks, the children were revisited, and GI and PII were assessed (Fig. 3). Salivary samples were collected for the analysis of marker values. The samples were transported to the laboratory using dry ice. GI, PII, oxidative stress markers (MDA), and inflammatory markers (hsCRP) before and after treatment were evaluated. Salivary oxidative stress marker assays were conducted using a modified version of Yagi's (1984) method, and absorbance was measured at 540 nm using an ultraviolet-visible spectrophotometer at 535 nm (Fig. 4). The hsCRP assay was carried out by latex turbidimetric immunoassay (Fig. 5).

Salivary Oxidative Stress Marker Assay (MDA)

First, 0.25 N hydrochloric acid (HCl) is prepared by diluting 4.16 mL of concentrated HCl to 200 mL. Reagent 1 is thiobarbituric acid (TBA) 0.375% (0.375 gm of TBA powder mixed in 100 mL of 0.25 N HCl), and reagent 2 is trichloroacetic acid (TCA) 15% (15 gm of TCA powder mixed in 100 mL of 0.25 N HCl). Around 50 µL of saliva samples were taken as the test solution and added to 500 µL of 70% alcohol, followed by the

Fig. 1: 0.1% OCT hydrochloride and 0.12% CHX gluconate mouthrinses

addition of 1 mL of TBA and TCA. Then, all the tubes were placed in a boiling water bath for 20 minutes. After cooling to room temperature, 50 µL of acetone was added and cooled, and the absorbance was read at 535 nm in a spectrophotometer, yielding the optical density reading. The concentration of MDA was calculated using this optical density and expressed in nanomoles per liter (nmol/L).

Fig. 2: Saliva collection—passive drooling performed by the child

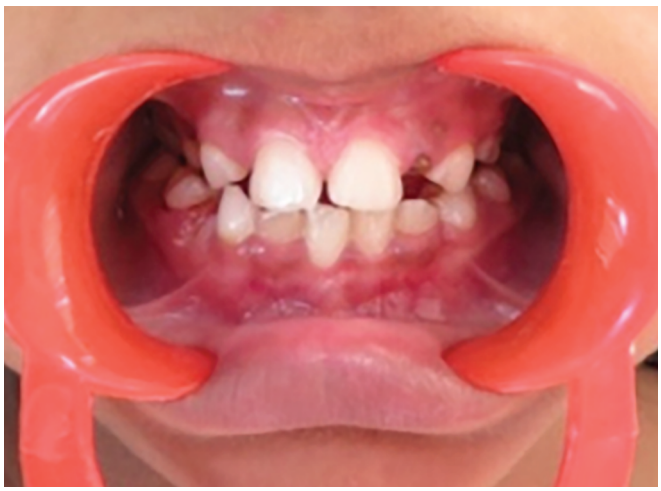

Fig. 3: Pre-examination and scoring of indices

Salivary Inflammatory Marker Assay (hsCRP)

Salivary samples were centrifuged at 3000 rpm for 10 minutes. The clear supernatant was used for the assay. First, the photometer (cuvette holder) was brought to a temperature of 37°C, with a wavelength set to 540 nm (530–550 nm), and the cuvette light path was adjusted to 1 cm. The instrument was then zeroed with distilled water. The working reagents were mixed (0.8 mL of R1 mixed with 0.2 mL of R2 and 10 µL of calibrator), and the Ablank value was calculated. Then, 0.8 mL of R1 and 0.2 mL of R2 were pipetted into a cuvette, followed by the addition of 10 µL of supernatant saliva sample. Finally, mixing was performed, and absorbance was read after 4 minutes (A2) of the calibrator addition.

Calculations

The absorbance difference (A2-Ablank) of each point on the calibration curve was calculated, and the values obtained against the CRP concentration of each calibrator dilution were plotted. The CRP concentration in the sample was calculated by interpolation of its (A2-Ablank) in the calibration curve and expressed in nanograms per milliliter (ng/mL).

Results

For comparison, either parametric or nonparametric tests were used depending on the variable type. The outcome variables considered were GI, PII, MDA, and hsCRP. GI and PII were compared with nonparametric tests, while MDA and hsCRP were compared

Fig. 4: Ultraviolet-visible spectrophotometer

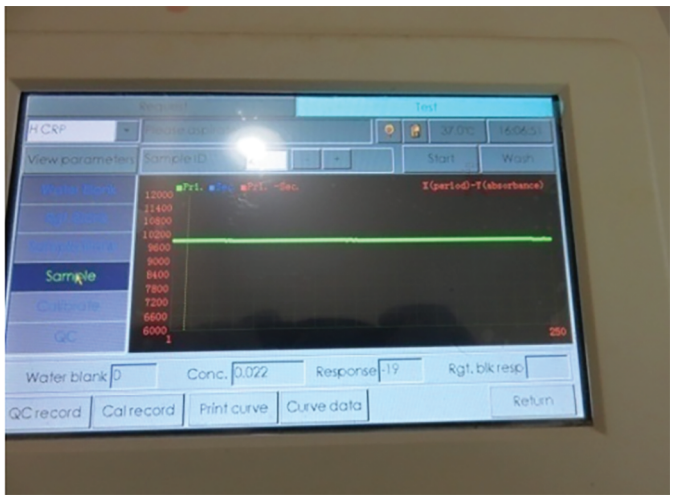

Fig. 5: Mispa—neo latex turbidimeter

with parametric tests. For all statistical evaluations, a two-tailed probability value of <0.05 was considered significant.

Distribution According to Age

Children from age-group 9 to 15 years were selected for the study (Table 1). The comparability of both groups with respect to age showed that there was no significant difference in age between the groups, with a *p*-value of 0.888 (Table 2).

Baseline Data of Patients

Pretreatment values of GI, PII, MDA, and hsCRP from both groups were tabulated (Tables 3 and 4).

Distribution of Outcomes with Respect to Group Status before and after Treatment

Posttreatment values in OCT and CHX were shown in Tables 5 and 6, respectively.

Table 1: Distribution of patients according to age

Age	*Frequency*	*Percentage*
A. OCT group		
9	4	40%
10	1	10%
11	1	10%
12	1	10%
13	3	30%
Total	10	100%
B. CHX group		
9	2	20%
10	2	20%
11	1	10%
12	5	50%
13	–	–
Total	10	100%

Table 2: Comparability of groups with respect to age

Variable	*Group*	*Mean*	*SD*	*Test used*	*p-value*
Age	OCT	10.8	1.814	Chi-squared test 0.142	0.888
	CHX	10.9	1.287		

Table 3: Pretreatment values of OCT group

Serial number	*Age*	*Sex*	*ID*	*Pre-GI*	*Pre-PII*	*Pre-MDA*	*Pre-hsCRP*
1	9	F	Mild	1.67	1.87	0.541	0.36
2	11	M	Moderate	2.76	2.92	0.563	0.85
3	13	F	Moderate	2.42	2.62	0.465	0.71
4	10	M	Mild	1.95	2.08	0.546	0.45
5	9	M	Mild	1.81	1.62	0.314	0.39
6	13	F	Moderate	2.37	2.58	0.621	0.54
7	12	F	Mild	2.12	2.29	0.428	0.71
8	9	F	Mild	1.71	2.26	0.415	0.37
9	9	F	Moderate	1.87	1.79	0.351	0.52
10	13	F	Moderate	2.32	2.79	0.517	0.65

For GI, the mean reduction in scores for OCT and CHX were shown from 2.100 to 1.234 and 2.233 to 1.806, respectively. For PII, the mean reduction in scores for OCT and CHX were shown from 2.282 to 1.298 and 2.235 to 1.928, respectively.

For MDA, OCT shows a mean reduction in score from 0.476 to 0.167, while CHX shows a reduction from 0.472 to 0.256. For hsCRP, OCT shows a mean reduction in score from 0.555 to 0.158, and CHX shows a reduction from 0.532 to 0.209.

Discussion

Children with special healthcare needs are at a greater risk of developing dental and oral diseases than their typically developing peers.[7] Research has shown that this increased risk is due to a

Table 4: Pretreatment values of the CHX group

Serial number	*Age*	*Sex*	*ID*	*Pre-GI*	*Pre-PII*	*Pre-MDA*	*Pre-hsCRP*
1	12	M	Mild	2.5	2.5	0.474	0.56
2	12	F	Moderate	2.7	2.8	0.456	0.76
3	12	F	Mild	2.02	2.4	0.562	0.45
4	12	M	Mild	2.27	2.7	0.498	0.61
5	9	F	Moderate	2.27	2.5	0.439	0.36
6	9	F	Mild	1.9	2.0	0.425	0.44
7	10	F	Mild	2.5	1.7	0.521	0.67
8	10	M	Moderate	1.82	2.4	0.417	0.34
9	11	F	Moderate	2.32	2.0	0.514	0.62
10	12	F	Mild	2.03	2.3	0.417	0.51

Table 5: Postintervention values of OCT group

Serial number	*Age*	*Sex*	*ID*	*Pre-GI*	*Pre-PII*	*Pre-MDA*	*Pre-hsCRP*
1	9	F	Mild	1.02	0.76	0.125	0.145
2	11	M	Moderate	1.36	1.31	0.168	0.137
3	13	F	Moderate	1.08	1.41	0.245	0.125
4	10	M	Mild	1.29	1.58	0.146	0.122
5	9	M	Mild	1.02	1.1	0.191	0.104
6	13	F	Moderate	1.33	1.54	0.147	0.12
7	12	F	Mild	1.29	1.16	0.139	0.314
8	9	F	Mild	1.3	1.12	0.185	0.136
9	9	F	Moderate	1.2	1.25	0.135	0.165
10	13	F	Moderate	1.45	1.75	0.195	0.216

Table 6: Table showing postintervention values of the CHX group

Serial number	*Age*	*Sex*	*ID*	*Pre-GI*	*Pre-PII*	*Pre-MDA*	*Pre-hsCRP*
1	12	M	Mild	1.7	2	0.297	0.213
2	12	F	Moderate	1.96	2.12	0.254	0.121
3	12	F	Mild	1.75	1.7	0.359	0.29
4	12	M	Mild	1.7	2	0.255	0.254
5	9	F	Moderate	2	2.12	0.241	0.135
6	9	F	Mild	1.73	1.97	0.132	0.125
7	10	F	Mild	1.95	1.72	0.312	0.249
8	10	M	Moderate	1.75	1.56	0.201	0.254
9	11	F	Moderate	1.83	2.0	0.215	0.24
10	12	F	Mild	1.69	2.03	0.297	0.214

combination of factors, including the effects of their underlying health conditions and reduced appropriate dental care. These conditions can have a direct and negative impact on the quality of life of the child and their family, causing pain, discomfort, difficulty eating and speaking, and even affecting their social interactions and self-esteem.[8]

Antimicrobial mouthrinses play a synergistic effect in conjunction with mechanical debridement. Stabholz et al.[9] in 1991 used CHX as an adjunct to mechanical plaque removal in institutionalized children with DS. A study by Teitelbaum et al.[10] in 2009 also provided similar findings on CHX, indicating that the dentifrice containing CHX is useful in controlling biofilm and in reducing gingival bleeding. Chlorhexidine gluconate (CHX) is considered as the gold standard mouthrinse in oral antiseptic therapy. This is why CHX was used in this study. Allergic reactions are usually noticed if CHX is applied in concentrations of >4%, and serious anaphylactic reactions have been described.[11] The antimicrobial effect of CHX is primarily bacteriostatic, rather than killing bacteria outright. In contrast, OCT hydrochloride has been shown to remain highly effective even when highly diluted, while CHX loses its effectiveness when diluted below 10% of its original concentration.[12]

On comparison of pre-post scores of GI and PII between both groups using Student's *t*-test, the OCT group showed a significantly greater reduction in both GI and PII compared to the CHX group. These results are in accordance with studies by Patters et al.[13] in 1983, who showed that 0.1% of OCT patients had significantly less plaque and gingivitis after a 7-day use without performing any mechanical tooth cleaning measures. Beiswanger et al.[14] in 1990 also showed similar results in a 3-month clinical trial that mouthrinses containing 0.1% OCT are effective in significantly reducing dental plaque by 30% and gingivitis by 50%.

In our study, levels of MDA were evaluated for assessing oxidative stress before and after treatment. There was a significant reduction in MDA level after treatment in both groups, of which the MDA levels in the CHX group were found to be significantly higher ($p < 0.002$) (0.25 ± 0.06) compared to the OCT group (0.16 ± 0.03). Thus, the OCT group showed a greater reduction than the CHX group.

In this study, CRP levels in the CHX group were found to be significantly higher ($p < 0.001$) in the preintervention phase (0.53 ± 0.13) compared to the postintervention phase (0.20 ± 0.06). Similarly, CRP levels in the OCT group were found to be significantly higher ($p < 0.001$) in the preintervention phase (0.55 ± 0.16) compared to the postintervention phase (0.15 ± 0.06). Although there was a greater reduction in hsCRP levels in the OCT group postintervention, there was no significant difference ($p = 0.082$) in CRP levels between the CHX group and the OCT group after the treatment.

Despite advances in oral healthcare, children with disabilities have a higher burden of oral diseases due to factors such as lack of manual dexterity, limited understanding, and restricted access to dental care and preventive treatments. Saliva was used as the diagnostic tool to determine the influence of these mouthrinses on gingival and PII, as well as to analyze the expressions of the oxidative stress marker (MDA) and inflammatory marker (hsCRP) postintervention. In the present study, both mouthrinses were found to be effective adjuncts to tooth brushing for improving oral hygiene and periodontal status in children with DS, with comparatively fewer side effects. Octenidine is an excellent antimicrobial mouthrinse capable of exerting beneficial clinical effects on plaque accumulation and gingivitis development. However, future long-term studies need to be carried out in this risk group for further evaluation and more promising results.

Conclusion

According to the presented results, 0.1% OCT hydrochloride mouthrinse, when compared with 0.12% CHX gluconate mouthrinse, revealed better efficacy as an antibacterial and antiplaque agent to reduce gingivitis and oxidative stress in children with DS. Thus, OCT hydrochloride mouthrinse may become an alternative to commercially available 0.12% CHX gluconate mouthrinse in children with special healthcare needs. However, further clinical studies are needed to evaluate its safety and efficacy in long-term use.

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