ORIGINAL RESEARCH PAPER

Dental Science

KEY WORDS:

PROSPECTIVE, SINGLE-CENTRE, NON-RANDOMIZED, OPEN-LABEL, SINGLE-ARM, POST MARKETING STUDY TO EVALUATE SAFETY AND EFFICACY OF DENTE91® MOM TOOTHPASTE AND DENTE91® MOM MOUTHWASH IN PREGNANT FEMALES

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INTRODUCTION

Oral and dental health problems in pregnancy are of special importance. Pregnancy-related hormonal changes can lead to hyperemia, inflammation, bleeding, increased gingival sensitivity and an increased risk of bacterial infection all of which can worsen gum disease. Between 30 % and 98.8 % of pregnant women experience oral and dental health issues. However, pregnant women typically put off getting treatment because they think getting dental treatment while pregnant is detrimental for the baby. According to scientific studies, even when they believe they require dental care around 50% of pregnant women do not attend the dentist[1,2].

Neglecting oral and dental health during pregnancy does not only cause problems such as tooth decay and tooth loss but may also lead to problems such as premature birth, low birth weight infant and pre-eclampsia. Therefore, the present study was planned to study the efficacy and safety of novel formulation DENTE91® Mom Mouthwash and DENTE91® Mom Toothpaste in pregnant subjects [3].

AIMS AND OBJECTIVES

To demonstrate efficacy and safety of DENTE91® Mom Toothpaste and DENTE91® Mom Mouthwash in Pregnant subjects.

MATERIAL AND METHODS

This was a prospective, single-centre, non-randomized, open-label, clinical study. Subjects with positive urine/serum pregnancy tests, extrinsic dental stains and bad oral hygiene, one or more dental cavities, history of dental caries/tooth decay, at least one sensitive teeth (buccal aspect with recession, abrasion, erosion) with a score of >3 cm using air blast on the Visual Analogue Scale (VAS 10 cm, ranging 0 = no pain, 10 = extreme pain) and provided with written informed consent and agreed to comply with study instructions were included in this study.

Subjects with known hypersensitivity to any tooth paste, use of any antibiotics, antimicrobial, analgesic medications, mouthwash or desensitizing toothpaste 1 month prior to screening, any history of periodontal therapy by surgical interventions, dentine hypersensitivity treatment, orthodontic treatment with fixed appliances, intrinsic dental stains, abnormal frenum attachment, severe level of calculus and tartar, who had presence of any fixed appliance, large or defective restorations, cracked enamel, or caries on the history hypersensitive tooth and any removable device such as a removable partial denture or orthodontic retainer were excluded. The subjects participated in the study were given verbal information regarding the study. The Ethics review committee assessed and approved the subject consent form and study protocol prior to the study initiation.

Subjects were instructed to use rinse DENTE91® Mom Mouthwash (undiluted 15 mL) twice a day for 30 seconds and expel and brush DENTE91 Mom Toothpaste at least twice daily for 2 minutes with a soft toothbrush for 60 days.

Clinical And Safety Evaluation

Antimicrobial effectiveness as assessed by mean plaque index score and dental caries between different caries risk category were assessed using the Tureskey-Gilmore-Glickman modification of Quigley Hein Plaque Index test, was compared between baseline and Day 60 using T test. Difference in plaque reduction mean scores within group was expressed as reduction from baseline Mean ± SD of plaque reduction score as compared to Day 60 using t test.

Digital image collection software was used to compare dental remineralization. It was measured by Microscopic Evaluation and compared images from Day 60 to baseline.

Reduction in hypersensitivity score was assessed by Tactile Test, Airblast Test and Cold Water Test with VAS scale. Day 60 scores were compared with baseline (Timeframe: Baseline and Day 60) and were analyzed using descriptive statistics and t tests.

Incidence of dental stains and cavities were assessed through dental X-ray at each visit and difference in incidences of nausea and vomiting within group as reduction from baseline mean ± SD of incidences of nausea and vomiting to Day 60 which was analyzed using t test.

Safety evaluation was based on physical examination, vital signs (blood pressure, pulse rate, respiratory rate, and body temperature), laboratory investigations and treatment emergent adverse events (TEAEs).

OBSERVATIONS AND RESULTS

Out Of the 35 pregnant subjects screened, 30 were enrolled and received at least one dose of test treatment and were included in the safety population and mITT population (30 at Site). Mean ± standard deviation (SD) age was 24.2 ± 2.93 years (standard deviation: 2.93), mean ± SD body weight was 56.72 ± 4.16 kgs, mean ± SD height 157.06 ± 5.72 cms and mean ± SD BMI of 23.08± 1.85 kg/m^2.

Antimicrobial effectiveness based on mean plaque index scores with Turseky–Gilmore–Glickman modification of Quingley Hein plaque index for high risk, medium risk, and low risk shows statistically significant improvement with a p value of <0.001.

Mean ± SD reduction from baseline to Day 60 in whole mouth plaque score was 0.41 ± 0.26, proximal plaque score was 0.29 ± 0.35, and gingival plaque score was 0.44 ± 0.21.

Test products (DENTE91® Mom Toothpaste and DENTE91® Mom Mouthwash) demonstrated highly statistically significant reductions in mean whole mouth, proximal and gingival plaque scores post 60 days of daily brushing and mouth rinse versus baseline ($p < 0.001$) (Table 1).

A SEM with a 15 or 20 kV accelerating voltage was used to analyse teeth. Digital image acquisition software was used to capture the images (PrinterfaceTM). The field width was calculated using a calibration standard Agar with 10-meter intervals. Except when the buccal surfaces (tooth surfaces facing the cheeks or lips) were damaged or dirty, in which case the lingual/palatal surfaces (tooth surfaces facing the tongue or palate) were checked. The cervical root, mid-root, and apical root surfaces were photographed at high magnifications (500 and 1000). The buccal or lingual/palatal surfaces of both the mesial and distal roots of multirooted teeth were investigated. The average diameter of cementum fibres and cementocyte lacunae were measured using a calibration standard used in the microscope.The enamel was assessed in 60 teeth at baseline, day 30 and day 60. In all cases, the surface was primarily smooth and featureless, with no evidence of perikymata or features associated with the external ends of enamel prisms (rods).

There was no significant improvement shown in mineralization as assessed by Microscopic Evaluation on Day 60 as compared with baseline due to short duration of treatment.

Mean ± SD change in hypersensitivity score as assessed by Tactile Test (VAS) at Day 60 was 4.47 ± 0.57, Mean ± SD change in hypersensitivity score as assessed by Cold water test (VAS) at Day 60 was 4.43 ± 0.82, and Mean ± SD change in hypersensitivity score as assessed by Airblast test (VAS) at Day 60 was 4.10 ± 0.71.

There was significant reduction in hypersensitivity score as assessed by Tactile Test (VAS) ($p<0.05$, Table 2 and Figure 1), Cold water test (VAS) ($p<0.05$, Table 3, Figure 2) and Airblast test (VAS) ($p<0.05$, Table 4 and Figure 3) on Day 60 as compared with baseline.

96.67% (29) subjects had dental cavities and 3.33% (1) subject had dental stains as assessed by dental X ray at baseline. Post use of DENTE91® Mom Toothpaste and DENTE91® Mom Mouthwash at Day 60, 80% (24) subjects had shown improvement in dental cavities and stain and showed normal Dental X ray and 20% (6) subjects had dental cavities as assessed by dental X ray which indicated significant improvement (Table 05) in dental cavities and dental stain compared to baseline (Table 5 and Figure 4).

Reduction in incidences of nausea from baseline to Day 60 was 0.03 ± 0.29 and reduction in incidences of vomiting from baseline to Day 60 was 0.28 ± 0.35 which were statistically non-significant values compared to baseline. (Table 6).

No TEAEs were reported in this study and no safety concern was observed with respect to physical examination, vital signs (blood pressure, pulse rate, respiratory rate, and body temperature) and laboratory investigations.

Table 1: Mean Reduction in Plaque Score from Baseline to Day 60

Parameter	N	Baseline Mean ± SD Plaque Score	EOT/EOS: Visit 4 Mean ± SD Plaque Score	Mean ± SD Reduction FromBase-line to Day 60	p-value
Whole Mouth	30	2.57 ± 0.37	2.16 ± 0.42	0.41 ± 0.26	<0.001
Lingual Proximal	30	2.25 ± 0.29	1.96 ± 0.31	0.29 ± 0.35	<0.001
Gingival	30	3.11 ± 0.42	2.67 ± 0.33	0.44 ± 0.21	<0.001
SD = standard deviation.					

Table 2: Hypersensitivity score as assessed by Tactile Test with VAS scale at Each Visit

Summary	Screening: Visit 1	Baseline: Visit 2	Follow-up: Visit 3	EOT/EOS: Visit 4
Mean Tactile VAS Score (VASSCR)	5.90	5.90	5.07	4.47
Standard Deviation	0.84	0.84	0.64	0.57
Confidence Level (95.0%)	0.32	0.32	0.24	0.21

Statistical Analysis: t-Test			
	Baseline: Visit 2	Follow-up: Visit 3	EOT/EOS: Visit 4
Mean Tactile VAS Score (VASSCR)	5.9	5.06	4.47
P Significance (T<=t) one-tail *		< 0.000	< 0.000
t Critical one-tail		1.69	1.69
P Significance (T<=t) two-tail *		< 0.000	< 0.000
t Critical two-tail		2.04	2.04
EOS = End of study; EOT = End of treatment; VAS =visual analogue scale.			

Table 3: Hypersensitivity Score as assessed by Cold Water Test with VAS scale at Each Visit

Summary	Screening: Visit 1	Baseline: Visit 2	Follow-up: Visit 3	EOT/EOS: Visit 4
Mean Cold Water VAS Score (VASSCR)	5.83	5.83	4.97	4.43
Standard Deviation	0.87	0.87	0.67	0.82
Confidence Level (95.0%)	0.33	0.33	0.25	0.31
Statistical Analysis: t-Test:				
	Baseline: Visit 2	Follow-up: Visit 3	EOT/EOS: Visit 4	
P(T<=t) one-tail		0.00	0.00	
t Critical one-tail		1.70	1.70	
P(T<=t) two-tail		0.00	0.00	
t Critical two-tail		2.05	2.05	
EOS = End of study; EOT = End of treatment; VAS =visual analogue scale.				

Table 4: Hypersensitivity Score as assessed by Air Blast Test with VAS scale at Each Visit

Mean Airblast VAS Score (VASSCR)	Screening: Visit 1	Baseline: Visit 2	Follow-up: Visit 3	EOT/EOS: Visit 4
Mean	5.87	5.87	5.07	4.10
Standard Deviation	0.78	0.78	0.74	0.71
Confidence Level(95.0%)	0.29	0.29	0.28	0.27
Statistical Analysis: t-Test:				
	Baseline: Visit 2	Follow-up: Visit 3	EOT/EOS: Visit 4	
P Significance (T<=t) one-tail		0.00	0.00	
t Critical one-tail		1.70	1.70	
P Significance (T<=t) two-tail		0.00	0.00	
t Critical two-tail		2.05	2.05	
EOS = End of study; EOT = End of treatment; VAS =visual analogue scale.				

Table 5: Change in Dental X-Ray Assessment at Each Visit as Compared With Baseline

Dental X-ray Assessment	Screening: Visit 1	Baseline: Visit 2	Follow-up: Visit 3	EOT/EOS: Visit 4
Dental Cavities	96.67% (N=29)	93.10% (N=27)	43.33% (N=13)	20.00% (N=6)
Dental Stain	3.33% (N=1)	3.45% (N=1)	16.67% (N=5)	0.00% (N=0)
Normal	0.00% (N=0)	3.45% (N=1)	40.00% (N=12)	80.00% (N=24)
EOS = End of study; EOT = End of treatment				

Table 6: Reduction in Incidences of Nausea and Vomiting at Day 60 as Compared With Baseline

Incidences	N	Baseline Mean number of daily incidences	EOT/EOS: Visit 4	Reduction From Baseline	p-value
Nausea	30	3.86 + 0.77	3.83 + 0.68	0.03 + 0.29	>0.05
Vomiting	30	2.73 + 0.43	2.45 + 0.49	0.28 + 0.35	>0.05

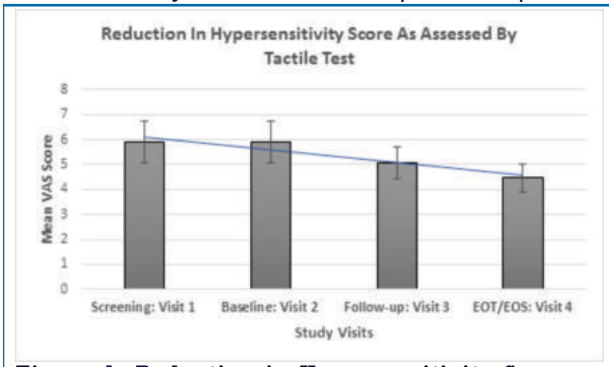

Figure 1: Reduction in Hypersensitivity Score as Assessed by Tactile Test at Each Visit as Compared With Baseline (Timeframe: Baseline and Day 60).

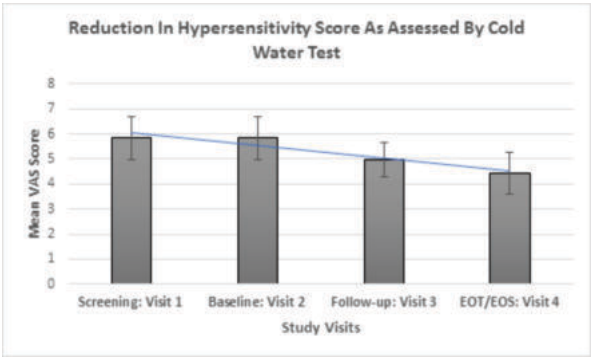

Figure 2: Reduction in Hypersensitivity Score as Assessed by Cold Water Test at Each Visit as Compared With Baseline

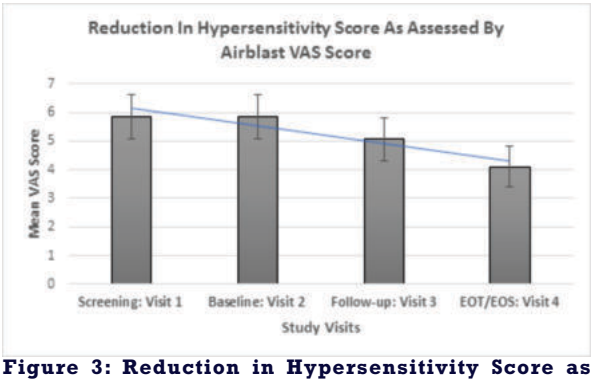

Figure 3: Reduction in Hypersensitivity Score as Assessed by Airblast Test at Each Visit as Compared With Baseline

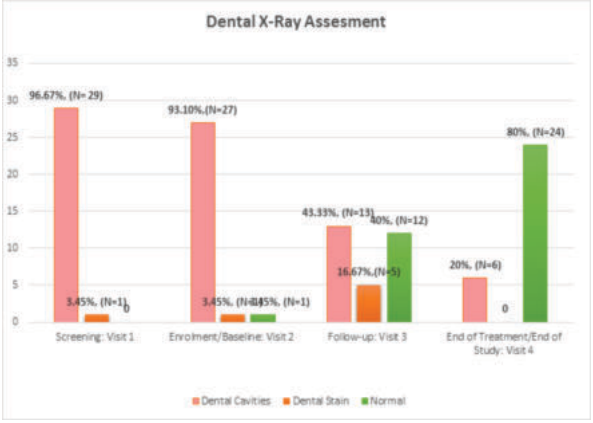

Figure 4: Change in Dental X-Ray Assessment at Each Visit as Compared With Baseline

DISCUSSION

Experts have different opinions with regards to using mouthwash while pregnant as most brands of mouthwash contain alcohol. According to the American Pregnancy Association, alcohol affects human development and can cause irreparable cognitive, physical and neurological birth defects.[3] Since many mouthwashes are alcohol based, it is best not to use them during pregnancy. American Dental Association recommends fluoride based toothpaste in pregnancy. However, fluoridated toothpaste has certain anti-caries effects, excessive intake may cause some adverse effects such as skeletal fluorosis and dental fluorosis.[4] The study product Dente91 Mom Mouthwash provides a novel approach to augmenting oral health and hygiene during pregnancy. It primarily preserves oral homeostasis by supplementing saliva's natural protective mechanisms. This way it not only maintains oral health naturally but also protects the oral Eco-flora. Dente91 Mom Toothpaste offers a unique approach to protect as well as augment oral health during pregnancy. Dente91 Mom toothpaste contains lactoferrin which has multifunctional protein with antibacterial, antifungal, antiviral and anti-inflammatory properties. Nano-hydroxyapatite helps to remineralize (rebuild) tooth structure without any known side effects, prevent hypersensitivity and also reduces plaque and gum irritation caused due to mild gingivitis. It further addresses the oral bacteria that can contribute to dental decay and gum degradation. Cetylpyridinium chloride (CPC) which is a broad spectrum antibacterial/antimicrobial ingredient and has substantial antiviral effects against certain viruses, prevents plaque and gingivitis. Xylitol which reduces the levels of mutans streptococci in plaque and saliva by disrupting their energy production processes leading to futile energy cycle and cell death. It reduces the adhesion of these micro-organisms to the teeth surface and also reduces their acid production potential. Xylitol like any other sweetener, promotes mineralization by increasing the salivary flow. Xylitol is considered safe in pregnancy and during breast-feeding according to the United States Food and Drug Administration.[5] Dente91 Mom Toothpaste also contains Vitamin B9, Vitamin B6, Vitamin E and Vitamin D[6].

OUR STUDY DEMONSTRATED:

- Statistically significant reduction in mean plaque index and dental caries between different caries risk category using the Tureskey-Gilmore-Glickman modification of Quigley Hein Plaque Index test.
- Statistically significant reductions in mean Whole mouth, Proximal and Gingival plaque scores after 8 weeks of daily brushing and mouth rinse versus baseline.
- Statistically significant reductions in hypersensitivity score as assessed by Tactile Test, Airblast Test and Cold Water Test with VAS scale at each visit from baseline in pregnant subjects.

Improvement in mineralization as assessed by Microscopic Evaluation on Day 60 as compared with baseline was comparable. According to dental X-rays, 96.67 % (29 subject) had dental cavities and 3.33 % (1 subject) had tooth stains at baseline. At Day 60 after using DENTE91® Mom Toothpaste and DENTE91® Mom Mouthwash, 80 % (24 subject) had improved dental cavities and stain and had a normal dental X-ray, while only 20% (6 subjects) had dental cavities as determined by dental X-ray which indicated significant improvement. Reduction in incidence of nausea and vomiting was comparable at each visit when compared to baseline.

CONCLUSION

Study demonstrated that the DENTE91® Mom Mouthwash and DENTE91® Mom Toothpaste reduce and control plaque accumulation compared to baseline and thereby show their antimicrobial effectiveness.

DENTE91® Mom Mouthwash and DENTE91® Mom Toothpaste also reduces hypersensitivity, dental cavities and reduces stains compared to baseline.

Nausea with or without vomiting is common in early

pregnancy. However, study showed statistically non-significant reductions in incidences of nausea, vomiting and remineralization of teeth. Study showed no clinically significant change in physical examination and vital signs. In absence of any treatment emergent adverse event, DENTE91® Mom Mouthwash and DENTE91® Mom Toothpaste are found to be safe for use by pregnant females. There is a need for large scale prospective study to examine relative remineralization effect and effectiveness of the DENTE91® Mom Mouthwash and DENTE91® Mom Toothpaste for incidences of nausea and vomiting in pregnant females.

Conflict of Interest:

The authors certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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