A Study of the Effects of Stabilized Chlorine-Dioxide Gel in the Treatment of Oral Aphthous Ulcerative Conditions in Children

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Abstract

A test of the relative efficacy of Durafresh® (chlorine dioxide) gel (test) versus hexetidine rinse (control) in the treatment of oral aphthous ulcers in children was conducted in a clinical setting. Twenty seven subjects were randomly assigned as test or control subjects under a regimen of chlorine dioxide gel and hexitidine, respectively. Metric of the test was the recorded size of the lesion; first, at the time subject patients sought treatment (base size) and, second, at recall of subject patients. The test group showed statistically significant improvement in the reduction of size of ulcerative lesions relative to the control group. Interviews further revealed marked improvement in the alleviation of acute symptoms in all test group subjects on recall appointment. Control group subjects, on the other hand, reported pain symptoms at recall appointment. Test group subjects also reported acceptable palatability of chlorine dioxide gel regimen. Control group subjects, on the other hand, reported stinging taste of hexetidine. The aforementioned results indicate the relatively better efficacy of chlorine dioxide gel than hexetidine rinse in the treatment of aphthous ulcerative conditions in children.

Introduction

Aphthous ulcers are round or oval recurrent painful ulcers found on the tongue, vestibular mucosa, floor of the mouth, and faucial pillars. Ulcers of this type are differentiated from other ulcerative conditions in that they are neither preceded by vesicles nor are found on skin, vermillion, attached gingiva or hard palate. The etiology is unknown, but an immune defect mediated by T-cells is probable. It is not caused by virus but may be caused by stress and trauma. Like reactive lesions, aphthous ulcers are also symptomatic and medications contain either steroid or tetracycline. The disease is not debilitating but is a painful nuisance that recurs often.

The purpose of this study is to clinically determine and document the efficacy of Durafresh® (chlorine dioxide) gel in the treatment of aphthous conditions in children that consult at the Philippine Children's Medical Center, Pediatric Dentistry Department. The chlorine dioxide gel regimen was compared to a commercially available hexetidine mouth rinse regimen approved for commercial use by the Philippine Bureau of Food and Drugs.

Metrics considered are the size of lesion reduction, the amount of reduction of acute symptoms, and the acceptability of the taste of the medication.

Materials and Methods

Twenty seven (27) children, with ages 3 years to 11 years, mean age of 5.66 years, were randomly assigned into two groups as "test", using the stabilized chlorine dioxide regimen, or "control" using a hexetidine regimen. Subjects were all outpatient and normal children classified as either American Society

of Anesthesiologists I (ASA I) or ASA II presenting and seeking treatment for an aphthous ulcer.

The study excluded patients with the following conditions.

- significant cardiac histories, esp. endocarditis
- active cancer therapy
- compromised renal function
- infectious disease
- systemic diseases such as diabetes, hepatitis, lupus
- oral candidiasis
- autoimmune/mucocutaneous diseases
- systemic conditions within the last 3 months
- NSAIDS within the last 3 months chlorhexidine or sanguinaria based products in the last 3 months

To assess clinical improvement of ulcerative lesions, test and control subjects were clinically examined. Oral lesion location (relative to tooth location FDI system and vestibular area) and size were recorded. Medical histories of subjects were taken by way of a structured questionnaire. Test and control groups were given respective regimens and instructions for home use during the entire duration of the study until the lesions healed. Initial application of each regimen was given at the Pediatric Dentistry Department clinic following manufacturer recommendations. The same measurements were taken 3 to 7 days after initial appointment to assess improvement of oral condition. Further recall appointments were encouraged until lesions were unremarkable.

Results

All patients complied and were reexamined on the recall appointment. Marked improvements in reduction and lesion size were recorded and preliminary and post-treatment digital photographs were taken.

Mean age of all subjects was 5.66. The mean age for test and control subjects was 5.53 and 5.83, respectively. Age range of all subjects is 3 years to 11 years.

The following table summarizes, among others, the mean and variance of the changes in lesion sizes in both the test group and the control group.

Before testing the (null) hypothesis of equality of means, a test of the hypothesis of equality of test group and control group variances was conducted. The variance test indicated that test group and control group variances of changes in lesion sizes are equal. The following table summarizes the aforementioned test.

As the variances of the test group and control group changes in lesion sizes are equal, the t-test may be used for testing the hypothesis that the test group's mean change in lesion sizes is statistically greater than the control group's mean change in lesion sizes.

	No. Of Subjects	Change in lesion Size	
		Mean (mm)	Variance (mm^2)
Test Group	15	1.55	1.25
Control Group	12	0.63	0.49

The t-test that was conducted indicates that the mean change in lesion sizes in the test group is statistically greater than the mean change in lesion sizes in the control group. The following table summarizes the aforementioned test.

Hypothesis Test on Equality of Variance of Sizes of Relative Changes

Null hypothesis	$\sigma_T^2 \leq \sigma_C^2$	
Alternative hypothesis	$\sigma_T^2 > \sigma_C^2$	
Level of significance	1%	5%
Degrees of Freedom 1	14	14
Degrees of Freedom 2	11	11
F-Statistic	2.535	2.535
Critical F-Statistic	4.293	4.739
Conclusion	Accept Null	Accept Null

Note: $\sigma_T^2 \leq \sigma_C^2$ test and control group variances

Poor compliance for successive recall was encountered. Of the subjects that returned until the ulcerations were unremarkable, the mean lesion durations were 6.45 days est subjects reported subjective acceptable palatability of regimen compared to control subjects who all reported stinging taste of the mouth rinse. All patients claimed reduction of acute symptoms in at least 2 days after application of chlorine dioxide gel. Control subjects did not report any symptomatic relief in at least 2 days.

Discussion

Hexetidine was used for the control group as it is readily available in the Philippine market. Therapeutically, hexetidine is mainly used as a 0.1% w/v solution in mouthwash formulations for the prevention and treatment of minor local infections, gingivitis, and mouth ulcers. Hexetidine is a non-antibiotic antimicrobial agent that possesses broad-spectrum antimicrobial activity against Gram-positive and Gram-negative bacteria and fungi. It reduces bacteria in the affected

Hypothesis Test on Equality of Mean of Sizes of Relative Changes

Null hypothesis	$\mu_T - \mu_C = 0$	
Alternative hypothesis	$\mu_T - \mu_C = 0$	
Level of significance	5%	1%
Degrees of Freedom	25	25
Pooled Variance	0.920	0.920
F-Statistic	2.499	2.499
Critical T-Statistic	1.708	2.485
Conclusion	Reject Null	Reject Null

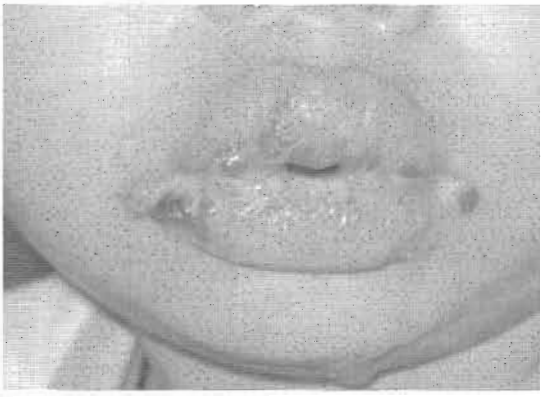
Note: μ_T and μ_C test and control group means

areas to prevent and relieve soreness. It also adheres to mucosal lesions for an extended period for a longer lasting action.

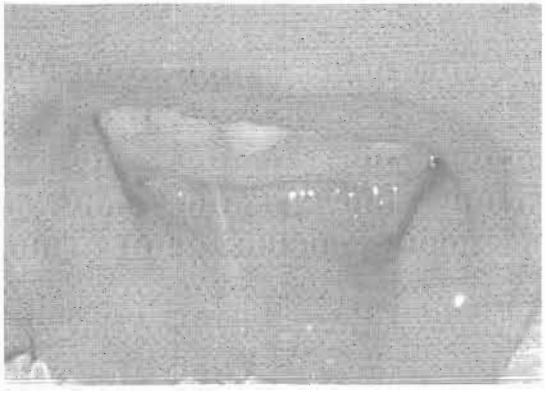
While hexetidine provided relief from ulceration and reduced the size of ulceration, majority of control subjects reported a stinging sensation with the use of this regimen. This may be attributable to the 9% alcohol content of the formulation.

Test group subjects that were treated with Durafresh® oral gel, on the other hand, noted the acceptability of taste besides symptomatic relief from the treatment. Being non-alcohol based, no stinging sensation was reported. The experimental gel contained 2% stabilized chlorine dioxide. The antibacterial property of chlorine dioxide may be contributory to preventing super-infection of the ulcerations and thereby promoting the natural healing process. In addition, the aloe powder (0.05%) contained in the gel provided the soothing effect that was appreciated by the test group subjects.

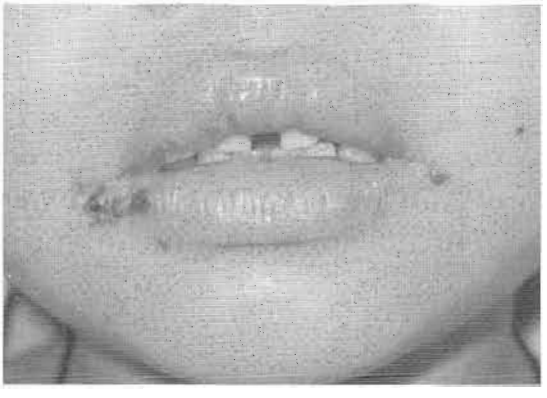
Fig, 1: December 16, 2005, 7.9 mm.



Fig, 3: February 14, 2006, multiple lesions.



Fig, 2: December 19, 2005, unremarkable.



Fig, 4: February 16, 2006, reduced lesions.

Conclusion

The results of the study indicate that stabilized chlorine dioxide is a viable and relatively more effective regimen for the treatment of acute aphthous lesions of the oral cavity than hexetidine. However, the small sample size of this study points to the need for a study with a larger number of subjects. A double blind study of the use of the Durafesh® gel versus a placebo or similar gel formulation is also suggested to derive a more compelling comparative conclusion.

References

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