Research Article
Volume 16:4, 2022

Journal of Molecular and Genetic Medicine

ISSN: 1747-0862 Open Access

Pain Comparison with Visual Analog Scale (EVA) in Patients with Acute Necrotizing Ulcerative Gingivitis (ANUG) and Wisdom Pericoronitis during Chlorine Dioxide Treatments

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Abstract

Introduction: The aim of this article is to analyze the amount of pain during 4 days treatment with Chlorine dioxide in patients with oral inflammation (pericoronitis and acute necrotizing ulcerative gingivitis).

Methods: A visual analogue scale for pain (EVA scale) during a period of 4 days of treatment with Chlorine dioxide was given to patients. The scale used for this study measures from 0-10 the intensity of the pain with a series of "faces" that show the intensity in the pain experimentation.

Results and Discussion: A total of 172 patients were analyzed, 101 males and 71 females, aged between 14 and 28 years (mean 19 years). Patients were divided in 2 groups according to the pathology. The first group with 140 patients presented wisdom pericoronitis and were divided in 2 subgroups of 83 males and 57 females. The second group presented with ANUG with a total of 32 patients (18 males and 14 females). 83 males with pericoronitis had an average pain at the beginning of treatment of 9.7 (SD 0.5) and the 57 females 9.8 (SD 0.5). The 32 patients with ANUG (18 males and 14 females) had an average initial pain score of 10.0. By the end of the first day, pain had reduced in male patients with pericoronitis to 3.9 (SD 0.4) and in females to 4.0 (SD 0,4). On the second day it dropped to 2.9 (SD 0.4) and 3.0 (SD 0.4) respectively, on the third day to 1.0 (SD 0.3) and 1.1 (SD 0,3) in females, and on the last day 0.0 and 0.1.

Patients with ANUG had a higher pain score at baseline 10.0 for both men and women. At the end of the first day, the pain dropped to 4.7 (SD 0.9) in male and 4.9 (SD 0.9) in female. On the second day the pain dropped to 3.4 (SD 0.5) and 3.6 (SD 0.5) respectively. On the third day the pain was 2.3 (SD 0.5) and 1.3 (SD 0.5) respectively and on the last day 0.3 and 0.2.

No medications such as analgesics, anti-inflammatory or antibiotics drugs were prescribed during the follow-up period. The biggest change occurs on the first day with a very significant decrease in pain, going from worst to moderate.

Conclusion: This study demonstrates a high level of efficacy of Chlorine dioxide in the treatment of pericoronitis and ANUG where the pain was reduced from worst to mild in 2 days.

Keywords: Chlorine dioxide • ANUG • Pericoronitis • EVA scale

Introduction

Chlorine dioxide (ClO_2) is a water-soluble yellow gas at room temperature with a powerful disinfectant action, and it is known to inactivate both viruses and bacteria. It was discovered in 1814 by Humphry Davy [1]. These aqueous solutions have been used since 1944 in the treatment of drinking water due to its biocidal power, as well as in most bottled waters suitable for human consumption due to its almost zero lack of toxicity in an aqueous solution. It is being used systematically in the disinfection and conservation of blood transfusion bags [2-3].

Mechanism of action and safety

His strong oxidizing activity against microbes is due to the denaturation of the viral capsids specific proteins [2]. The action of Chlorine dioxide is given by its selectivity for pH and by the area or size where it generates its action. It means that this molecule dissociates and releases oxygen when it comes into contact with another acid [2].

It is safe for use in humans in adequate concentrations [2,4-6]. It is a size-selective antimicrobial agent that can neutralize microorganisms rapidly but cannot cause real harm to much larger organisms such as animals or humans, as it cannot penetrate deep into their tissues. According to Noszticzius [6], the multicellular tissue has the highest capacity to dissipate electrical charges and therefore is not affected in the same way by the voltages of the Oxidation-reduction Process (ORP) as is the case of unicellular organisms and therefore there is biochemically speaking, a greater cell protection because of size. Furthermore, it can be used in animals and humans without adverse effects in proper concentrations because of its incapability to penetrate the tissues [7]. The great advantage of the possible therapeutic use of Chlorine dioxide in infections is the impossibility of a bacterial or viral resistance to ClO_2 since it has an oxidation mechanism unlike Chlorine (Cl_2) which acts by chlorination. Chlorine dioxide reacts rapidly with phenols and thiols essential for bacterial life. In phenols, the mechanism consists in the attack of the benzene ring, eliminating odor, taste and other intermediate compounds [8]. Chlorine dioxide kills viruses effectively and is up to 10 times more effective than sodium hypochlorite. It was also shown to be very effective against small parasites [9].

Chlorine dioxide (ClO_2) was used for different purposes during decades, and multiple patents for use in different treatments can be find apoptosis induction cancer treatment (CN 103720709 A) [10] tumor treatment (US 10, 105, 389 B1) Sinusitis antiviral treatment (US 2o16/0074432 A1), system stimulation immunological (US 5,830,511), stem cell initiation and differentiation (WO2014082514A1), vaginal treatment method (US 6280716B1), skin treatment against viruses and bacteria (US 4,737,307), Human amoebiasis treatment method (US 4,296,102), treatment against candidiasis infections (

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Received: 30-March-2022, Manuscript No: jmgm-22-58843; **Editor assigned:** 31-March-2022, PreQC No. P-58843; **Reviewed:** 14- April -2022, QC No. Q-58843; **Revised:** 20- April -2022, Manuscript No. R-58843; **Published:** 27-April -2022, DOI: 10.37421/1747-0862.22.16.547

US 2015/0320794 A1), wound treatment (US 87.3106), Oral cavity treatment (US 100015251), (US4689215), against inflammations (US53841134), nail fungus treatments (US 20100159031) and Swiss patent pending/11136-CH.[1]

Different applications of ClO_2

Its virucidal potential against influenza virus caused by oxidating tryptophan 153 residue in the receptor-binding site and SARS-CoV-[2] has recently been suggested [11-17]. According to the SARS-CoV-2 spike protein composition (12 tryptophan, 54 tyrosine, and 40 cysteine residues), it can be assumed that ClO_2 also has the potential to inactivate this virus. Chlorine dioxide in spray has been reported to be effective for SARS-coV-2 due to the inactivation of the binding of the variant spike proteins to the human ACE2 receptor protein. This strategy may be useful in blocking the transmission of variant SARS-CoV-2 viruses. Other studies showed the efficacy of ClO_2 against SARS-CoV-2 showing that patients who receive a solution of Chlorine dioxide have a reduced probability of developing sequelae. Furthermore, the incidence of long-term effects is lower in individuals treated exclusively with ClO_2 [18,19].

Chlorine dioxide has been used in the dental care, for different applications: disinfection of the air of dental offices, disinfection of dental instruments, in endodontic and periodontics to reduce bacteria population [20,21].

One of the sources of the dental stem cells with capacity for multipotent differentiation in vitro and ability to repair tooth-related tissues or bone in vivo, is periodontal ligament (PDL). Chlorhexidine (CHX) and hydrogen peroxide (H_2O_2) routinely applied as disinfectants in dentistry and endodontic procedures frequently disturbed the integrity of these cells[22].

Orsolya L, et al. compared the H_2O_2, CHX to ClO_2 regarding the viability of periodontal ligament stem cells and concluded: "while the active ingredients of mouthwash (H_2O_2, CHX) applied in endodontic or periodontitis management have a serious toxic effect on PDLSCs, the hyper pure ClO_2 is less toxic providing an environment favoring dental structure regenerations during disinfectant interventions" [23].

ClO_2 is less toxic for humans and is still effective against the microbes according to Lubbers JR, et al. [4] who have shown in 1982 that Chlorine dioxide is "the ideal biocide" [23]. In 2006 the system to make a hyper pure and more stable ClO_2 solutions was described and commercialized in Hungary since 2008 for dental care like periodontal treatments and oral rinse, with 1:10 dilution of the hyper pure ClO_2 solution [24,25].

Their favorable antimicrobial efficacy was demonstrated against oral pathogen bacteria. ClO_2 can be also used as intracanal bleaching substance. The selectivity of the ClO_2 is based not on their different biochemistry, but because of a size-selective antimicrobial agent which explains theoretically why ClO_2 solutions are not harmful to humans and are lethal for microbes [6,26-28].

The effectiveness of Chlorine dioxide in periodontal disease was reported by Spindler and Spindler in 1998 [29]. Chlorine dioxide has an antibacterial effect, is easy to use, and is widely available. Various companies have used Chlorine dioxide as the main ingredient in oral medicine, especially in the treatment of periodontal disease [30].

Komara I, et al., applied gel of Chlorine dioxide as an adjunct to scaling and root planning (SRP) in the treatment of chronic periodontitis during 30 days and found better clinical improvement in pocket depth reduction and bleeding index compared to SRP alone [31,32].

Thuy Anh, et al. found a significantly reducing plaque index, tongue coating score, oral malodor, and the amounts of F. nucleatum, S. moorei, T. denticola, and T. forsythia in the whole saliva, after 2 weeks mouthwash with 0,1% Chlorine dioxide compared with those at baseline [33].

Chlorine dioxide, when stabilized in water and used in a low concentration effectively, will neutralize volatile sulfur compounds in the oral cavity [34]. It has the ability to inhibit Enterobacter faecalis bacteria; this makes this material effective as an endodontic irrigant [35]. Previous studies have shown the positive effects of Chlorine dioxide in the inhibition of volatile sulfur compound formation [36-38].

Materials and Methods

Patients with a degree of pain intensity above 8 (intense and worst) were admitted to the study. A total of 172 patients were analyzed, 101 males and 71 females, aged between 14 and 28 years (mean 19 years).

Patients were divided in 2 groups according to the pathology. The first group with 140 patients presented wisdom pericoronitis and were divided in 2 subgroups of 83 males and 57 females. The second group presented with ANUG with a total of 32 patients (18 males and 14 females).

No medications such as analgesics, anti-inflammatory or antibiotics drugs were prescribed during the follow-up period. This protocol was designed according to our experience of 14 years using ClO_2 and more than 6 thousand patients treated.

Since 2007 we are using Chlorine dioxide in our clinic for equipment disinfections, and for different oral problems such as aphtha, herpes, gingivitis, periodontitis, acute necrotizing ulcerative gingivitis, aphthous stomatitis, wisdom pericoronitis, acute pulpitis, peri implantitis, gingival graft necrosis and toothache.

In this study, CLO_2 was prepared in our clinic and given to patients to ensure that all the patients have the same concentration and to reduce errors in preparation.

ClO_2 can be produced in several ways. The chemical process is adding some acid (citric or 4% hydrochloric) to sodium chlorite ($NaClO_2$) because $NaClO_2$ dissociates into ClO_2 and Cl ion in acidic medium. However, to achieve a hyper pure CLO_2 a generator should be used (and in this case the acid is not necessary).

A CLO_2 generator was used to produce an ultra-pure gas from the precursor sodium chlorite (24.5% solution), using a membrane electrolysis method[3]. The purity of ClO_2 produced by this generator exceeds 99.99%. It is practically impossible to achieve such a purity using any chemical method. The purity of ClO_2 from this generator is as much as 100 times higher than ClO_2 produced chemically. Double distilled water was used for saturation.

After reaching 3000 PPM saturation, the solution is stored in an amber glass bottle in the refrigerator.

Each patient received every day a half-liter water bottle prepared with 40ml of this hyper pure CLO_2 solution at 3000 PPM.

The protocol includes a mouthwash for 1 mn every 15 mn of interval during the first 3 hours, followed by mouthwashes every hour until the end of the day, repeating the same protocol for another 3 days (4 in total).

Patients were informed of the benefits and possible side effects of ClO_2 mouthwash, before starting treatment and they had signed the informed consent form.

Results and Discussion

Comparative evaluation of the discomfort or pain in patients with acute necrotizing ulcerative gingivitis (ANUG) or wisdom pericoronitis was determined every day of the protocol (4 days) with Visual Analog Scale for pain, which is a psychometric measuring instrument designed to assess the pain intensity experienced by each patient individually. Was employed for first time in 1921 and referred as a "graphical rating method", which has the characteristic of being able to achieve a rapid classification (statistically measurable and reproducible) of the severity of pain experience.

The analogous visual scale used for this study measures from 0-10 the intensity of the pain with a series of "faces" that show the intensity in the pain experimentation with categories like "No pain" approximately 0-1, mild in number 2, moderate in number 4, severe in number 6, very severe in number 8 and worst possible in number 10 (Figure 1).

Among the 172 patients analyzed, 83 males with pericoronitis had an

average pain at the beginning of treatment of 9.7 (SD 0.5) and the 57 females 9.8 (SD 0.5). The 32 patients with ANUG (18 males and 14 females) had an average initial pain score of 10.0.

By the end of the first day, pain had reduced in male patients with pericoronitis to 3.9 (SD 0.4) and in females to 4.0 (SD 0.4). On the second day it dropped to 2.9 (SD 0.4) and 3.0 (SD 0.4) respectively, on the third day to 1.0 (SD 0.3) and 1.1 (SD 0.3) in females, and on the last day 0.0 and 0.1 (Table 1) (Figure 2).

There is no significant difference between men and women. The biggest change occurs on the first day with a very significant decrease in pain, going from worst to moderate. Considering that the patients were not taking analgesics, this protocol shows a big potential against this type of inflammation (Figure 3).

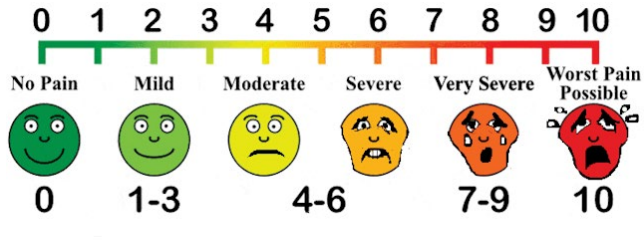

Figure 1. The analogous visual scale used for this study measures from 0-10 the intensity of the pain with a series of "faces" that show the intensity in the pain experimentation with categories like "No pain" approximately 0-1, mild in number 2, moderate in number 4, severe in number 6, very severe in number 8 and worst possible in number 10.

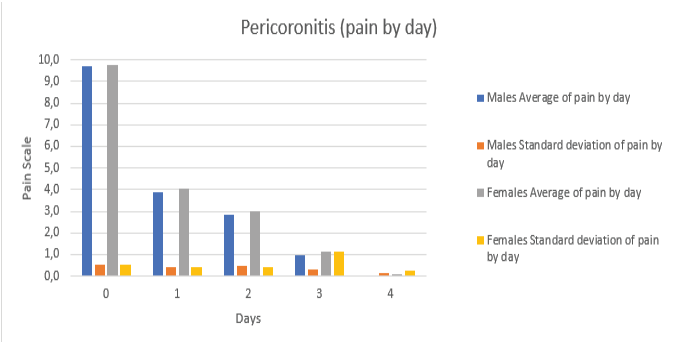

Figure 2. Pericoronitis (pain by day).

Patients with ANUG had a higher pain score at baseline 10.0 for both men and women. At the end of the first day, the pain dropped to 4.7 (SD 0.9) in male and 4.9 (SD 0.9) in female. On the second day the pain dropped to 3.4 (SD 0.5) and 3.6 (SD 0.5) respectively. On the third day the pain was 2.3 (SD 0.5) and 1.3 (SD 0.5) respectively and on the last day 0.3 and 0.2 (Table 2) (Figure 2).

As usual, ANUG cases are always more difficult to treat, take longer, and are much more uncomfortable for the patient. Even so, the decrease in pain to a moderate high level on the first day and mild on the second day is very significant considering that the patients did not take analgesics, antibiotics and anti-inflammatories, drugs that are usually prescribed in these cases.

Table 1. Reduced pain in male patients with pericoronitis from 9.7 to 3.9 (SD 0.4) and in females to 4.0 (SD 0,4) at the end of first day. On the second day it dropped to 2.9 (SD 0.4) and 3.0 (SD 0.4) respectively, on the third day to 1.0 (SD 0.3) and 1.1 (SD 0.3) in females, and on the last day 0.0 and 0.1.

Day	Males		Females	
	Average of Pain by Day	Standard Deviation of Pain by Day	Average of Pain by Day	Standard Deviation of Pain by Day
0	9.7	0.5	9.8	0.5
1	3.9	0.4	4.0	0.4
2	2.9	0.4	3.0	0.4
3	1.0	0.3	1.1	1.1
4	0.0	0.2	0.1	0.3

Table 2. At the end of the first day, the pain dropped from 10 to 4.7 (SD 0.9) in male and 4.9 (SD 0.9) in female. On the second day the pain dropped to 3.4 (SD 0.5) and 3.6 (SD 0.5) respectively. On the third day the pain was 2.3 (SD 0.5) and 1.3 (SD 0.5) respectively and on the last day 0.3 and 0.2.

Day	Males		Females	
	Average of Pain by Day	Standard Deviation of Pain by Day	Average of Pain by Day	Standard Deviation of Pain by Day
0	10.0	0.0	10.0	0.0
1	4.7	0.9	4.9	0.9
2	3.4	0.5	3.6	0.5
3	2.3	0.5	1.3	0.5
4	0.3	0.5	0.2	0.4

Figure 3. Patient with wisdom pericoronitis at the beginning (A) and after 4 days of ClO_2 protocol (B).

Conclusion

Chlorine dioxide is a size selective antimicrobial agent which can kill micron sized organisms rapidly.

Our findings indicate that when used correctly, Chlorine dioxide as a solution for mouthwash is safe for human at the appropriate concentration and dosage. This study demonstrates that Chlorine dioxide can be used with a high level of efficacy in the treatment of pericoronitis and ANUG to reduce pain from worst to mild in 2 days. After 4 days protocol the patients are free of pain.

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How to cite this article: Ritto, Korrodi. "Pain Comparison with Visual Analog Scale (EVA) in Patients with Acute Necrotizing Ulcerative Gingivitis (ANUG) and Wisdom Pericoronitis during Chlorine Dioxide Treatment." *J Mol Genet Med* 16 (2022): 547.