## LOCAL EFFECTS OF USAGE OF OROPHARYNGEAL ANTISEPTICS (CETYLPYRIDINIUM CHLORIDE) IN ORAL INFLAMMATORY CONDITIONS AND ORAL SURGICAL INTERVENTIONS

## ЛОКАЛНИ ЕФЕКТИ ПРИ УПОТРЕБА НА ОРОФАРИНГЕАЛНИ АНТИСЕПТИЦИ (CETYLPYRI-DINIUM CHLORIDE) ПРИ ОРАЛНИ ИНФЛАМАТОРНИ СОСТОЈБИ И ОРАЛНОХИРУРШКИ ИНТЕРВЕНЦИИ

# Veleska-Stevkovska D.¹, Peeva-Petreska M.¹, Gjurcheski J.², Trajchuleski S.³, Nedelkovska I.⁴, Lameski M.⁵

<sup>1</sup>Department of Implantology, Ss. Cyril and Methodius University in Skopje Faculty of Dentistry – Skopje; <sup>2</sup>Faculty of Dentistry – European University; PHO "UDCC Prof. Dr. Bojo Andreski" – Skopje; <sup>3</sup>Clinic of Oral Surgery, UDCC "St. Pantelejmon" - Skopje, <sup>4</sup>Clinic of Oral and Periodontal Diseases, UDCC "St. Pantelejmon" Skopje; <sup>5</sup>PHO Apolonia – Dent – Kavadarci.

#### Abstract

Cetylpyridinium Chloride belongs to a group of cationic quaternary ammonium compounds. Its properties are widely used for local treatment of inflammatory conditions in the oral cavity, as well as for a complementary treatment after oral surgical interventions to ease the postoperative pain and reduce the postoperative inflammation. The examined sample consisted of sixty patients divided into two main groups. The first group consisted of examinees in which an oral surgery with cumulative soft tissue and bone trauma was indicated, while the second group included examinees with symptoms of pericoronitis. During the study, the parameters we examined were: pain, inflammation, index of gingival bleeding, index for determining the depth of the pericoronary pocket and we compared the values obtained at the first, second and third visit. During that period, solutions based on cetylpyridinium were used for rinsing. The results were statistically processed and on that basis, a definite standpoint was taken for the therapeutic efficacy and safety in treated patients. Clinically verified results from this study confirm the properties of cetilpyridine and its ability to reduce pain in the postoperative period and reduce local tissue inflammation. These data encouraged us to propose topical application of antiseptic solutions in the preoperative period for conditioning oral tissues and reducing microbial load and plaque control as well as its prolonged use 7 days after oral surgery. **Keywords**: local treatment, inflammation, antiseptics, perioperative management.

#### Апстракт

Цетилпиридин хлоридот (Cetylpyridinium Chloride) припаѓа на групата катјонски квартерни амониумски соединенија. Неговите својства се широко применети за локален третман на воспалителни процеси во оралната празнина и како комплементарен третман по оралнохируршка интервенција за ублажување на постоперативната болка и намалување на постоперативната инфламацијата. Во истражувачкиот примерок беа опфатени вкупно шеесетина пациенти и истиот беше поделен на две групи испитаници. Првата група се состоеше од испитаници со индицирана оралнохируршка интервенција со кумулирана ткивна траума на меки ткива и коска, додека втората група се состоеше од испитаници со индицирана оралнохируршка интервенција со кумулирана ткивна траума на меки ткива и коска, додека втората група се состоеше од испитаници со индицирана оралнохируршка интервенција со кумулирана ткивна траума на меки ткива и коска, додека втората група се состоеше од испитаници со индицирана оралнохируршка интервенција со кумулирана ткивна траума на меки ткива и коска, додека втората пурпа се состоеше од испитаници со индицирана оралнохируршка интервенција со кумулирана ткивна траума на меки ткива и коска, додека втората пурпа се состоеше од испитаници со индицирана оралнохируршка интервенција со кумиранате параметри: болка, инфламација, индекс на крварење на пингивата, индекси за одредување длабочина на перикоронарен џеб и нивна компарација со вредностите за истите добиени на првата, втората и третата визита при континуирана употреба на препарати на база на цетил пиридин.. Резултати беа статистички обработени врз основа на што се донесе дефинитивен став за тераписката ефикасност и безбедност кај третираните пациенти. Клинички верифицираните резултати од оваа студија ги потврдуваат својствата на цетилпиридинот во способноста за намалување на болката во постоперативниот период и редукцијата на локалната ткивна инфламација. Овие податоци ни даваат за право да сугерираме локална примена на антисептички растори во предоперативниот период за кондиционирање н

## Introduction

According to the ADA, mouthwashes are an additional tool in standard oral hygiene or support in the perioperative period and/or conservative initial treatment of periodontal/peri-implant diseases. It is not recommended to use them immediately after using fluoride paste because they can eliminate the effect of fluoride. It is recommended to use them passively by rinsing during the postoperative period (in oral surgery, implantology, augmentation procedures) or actively rinsing the mouth through contraction of the perioral muscles as well as for hygiene of the peritonsillar and pharyngeal region (gargle).

Generally, mouthwashes, depending on their compounds, can have:

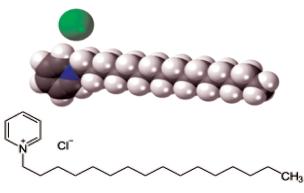
- antiseptic effect (reduction of microbial load) and antifungal effect. They control the formation of Volatile Sulfur Compound (VSC) by anaerobes (halitosis);
- anti-inflammatory effect (act on the production of proinflammatory cytokines);
- analgesic effect;
- effect as artificial saliva (in xerostomia, chemotherapy, radiotherapy) with enzymes lactoperoxidase, lysozyme, and lactoferrin.

Examples of previously known oral hygiene products are: benzydamine, chlorhexidine digluconate, essential oils (phenol, thymol, and eugenol), triclosan, fluoride, povidone/iodine, hydrogen peroxide, sodium bicarbonate, sodium chloride, etc.

There are a number of studies investigating the effect of mouthwashes on oral biofilm (chlorhexidine, cetylpyridinium chloride and antiseptics of plant origin eucalyptus, menthol, and thymol)<sup>1,2,3</sup>.

However, in addition to therapeutic effects, oral hygiene mouthwashes can also have side effects, such as: transient disturbance of the sense of taste, tooth discoloration, dry mouth sensations<sup>4</sup>. Alcoholic solutions dry the oral mucosa.

Cetylpyridinium chloride (CPC) is a cationic quaternary ammonium compound<sup>5</sup> containing the cetyl group (derived from cetyl alcohol initially isolated from whale's fat) and the pyridine cation [CsH5NH] +, which is a conjugated acid of pyridine (Picture 1).



**Picture 1.** Chemical formula of cetylpyridinium chloride (CPC)

CPC has a direct effect on the bilayer lipid membrane, leading to bacterial cell lysis and releasing cytoplasmic contents (bacteria, fungi, viruses with viral envelope). The ability to bind to the bacterial membrane depends on the positive electric charge of the CPC cationic surface. Some anionic compounds can reduce the antiseptic effect by inactivating the positive electric charge of the CPC, so a brake of 30 min is recommended between mechanical brushing of teeth with toothpaste and the use of CPC-based solutions.

Oral antiseptics containing CPC in concentrations 0.05% -0.07% (cationic surface agent, reduces surface tension, bacterial surface tension - cationic surfaceactive agent) have a wide range of antimicrobial and fungicidal effects. CPC in concentrations 0.05% -0.07% is effective in the control of dental plaque (acts on gram + and gram in view of bacteria and fungi) and gingivitis<sup>6</sup>.

Haps and Slot in their literature review state that "CPC-containing mouthwashes provide a small but significant benefit in reducing plaque and gingivitis, compared with groups that used only mechanical brushing or brushing and rinsing with placebo solution."<sup>7</sup>. In the study by Rao D. et al.,<sup>8</sup> the effect of 0.075% CPC solution on the biofilm was described, and was found that the number of damaged biofilm cells after using the solution was significant, compared to other tested antiseptics.

CPC solutions act on periodontopathogenic bacteria: Actinomyces, Campylobacter, Moraxella, Veillonella, Eikenella corrodens, Porphyromonas gingivalis, Prevotella intermedia and Prevotella nigrescens, Aggregatibacter, Candida and Streptococci<sup>9</sup>. In higher concentrations it is effective against Pseudomonas aeruginosa and Escherichia coli. The 0.1 and 0.2% CPC have also been shown to be extremely effective in eliminating Enterococcus faecalis, used as an irrigation agent in endodontic treatments<sup>10</sup>.

In a study by PopkinL.D.et al.,<sup>11</sup>, antiviral activity against influenza virus was demonstrated by targeting and disintegrating the viral envelope. CPC also reduces influenza-associated morbidity in vivo.

Recent studies on the effects of oral antimicrobials (especially CPC and povidone-iodine) on SARS-CoV-2, related to the degree of COVID 19 symptoms and the severity of the clinical picture are described in the work of Hererra et al.<sup>12</sup>. Oral viral load with SARS-CoV-2 is associated with the severity of COVID 19. Similarly, reducing viral load in the mouth significantly reduces the amount of viral units released from the mouth, thereby reducing the risk of disease transmission. According to them, during the first 10 days, the virus mainly accumulates in the nasal, oral, and pharyngeal areas. The number of angiotensin-converting enzyme (ACE 2) receptors is higher in the salivary glands compared to the lungs, so

saliva droplets are thought to be the most likely route of transmission. Use of antiseptic solutions is recommended in order to reduce viral load in the oral cavity<sup>12</sup>.

Based on the current knowledge on the mechanism of action of CPC-based antiseptic solutions, we can suggest its clinical application:

- Reduction of the incidence of postoperative complications (alveolitis, alveolar osteitis). Alveolar osteitis is a postoperative complication that most often is a result of disintegration of the fibrin clot, which, according to some theories, occurs due to increased bacterial load (microbal load), which in turn affects the stability of the clot;
- Use in cases of halitosis. As a result of the antimicrobial action of CPC-based antiseptic solutions, the production of sulfur compounds (volatile sulfur compounds VSCs, hydrogen sulfide, methyl mercaptan, dimethyl sulfide) by the anaerobic bacteria degrades the sulfur containing aminoacids cistein and methionine. Sulfur compounds are responsible for the condition called halitosis, which is an alarm for disbalance in the oral microbiome;
- Achieving a high degree of plaque control through the formation of a so-called 24-hour protective shield that has effect in the prevention of soft tissue diseases (gingivitis, periodontitis, and pericoronitis). The antiseptic solution also has an anticariogenic effect;
- By reducing the microbial load, the painful conditions caused by oral infections are regulated (analgesic effect);
- New therapeutic approach in the treatment of periimplant disease;
- Prevention of more serious diseases and more severe clinical pictures in patients infected with Sars-Cov-2 (as well as other viral upper respiratory diseases), and reduced transmission of the disease between people.

In the study of De Waal Y.,<sup>13</sup> the effectiveness of 0.05% CPC in the surgical treatment of periimplantitis (resective method with apically repositioned flap, surgical soft tissue debridement, bone remodeling, debridement of the implant surface and its decontamination) is emphasized. The efficacy of implant surface decontamination (immediate suppression of anaerobic bacterial flora) is proved by the long-term effect of CPC on stabilization of clinical parameters: peri-implant mucosal bleeding, suppuration, depth of the peri-implant pocket, reducing the level of radiographical loss of peri-implant marginal bone (marginal bone loss).

Osteoclasts are responsible for bone resorption in diseases such as osteoporosis, periodontitis, and rheumatoid arthritis. Antiseptic solutions are more often affirmed as potential preventive and therapeutic agents. Zhen Ting's study<sup>14</sup> described the effect of CPC on osteoclast formation from a cell colony (mouse bone marrow-derived macrophages - BMMs). CPC inhibits the activator of the receptor of NF- $\kappa$ B ligand (RANKL-induced osteoclast formation) without causing cytotoxic effects. CPC inhibits osteoclast differentiation via NF- $\kappa$ B and reduces COX-2 (cyclooxygenase) expression. The study's author highlights the possibility of CPC being perceived in the future as a preventative measure in preventing bone loss.

## **Pharmacokinetics**

Cetylpyridinium chloride in concentrations from 0.03% to 0.1% has therapeutic effects but no toxic effects. CPC is generally safe for patients at concentrations up to 1000  $\mu$ g/mL. Prolonged exposure on the CPC solutions, above the permissible upper limit of safe concentration, is expected to raise the question of the toxicity of preparations. The fatal dose of ingested cationic detergents is 1 to 3 g. Thus, 4000 single doses are required, taking into account that the products for use have a CPC concentration of an average of 0.25 mg per single dose<sup>15,16,17</sup>.

## Aim

The aim of the study was to determine the antiinflammatory effect of CPC on the soft tissues through reducing de novo plaque formation as well as the beneficial effect on the postoperative discomfort of the patients and the reduction of the degree of postoperative complications.

### Material and methods

The research sample included a total of 60 patients and it was divided into two main groups of patients (30 patients) with two subgroups of 15 patients each.

**Group I (30 patients).** This group included subjects with indication for oral surgery with cumulative soft tissue and bone trauma (atypical tooth extractions and surgical extractions by creating a mucoperiosteal flap).

1. Subgroup A. Each subject was advised to apply CPC solution at home for two days preoperatively (active rinsing and gargling), perioperative rinsing with CPC solution, as well as postoperative rinsing for 7 days (passive rinsing of the operative wound), with control of the predicted parameters on the first, third and seventh day after the intervention.

- 2. **Subgroup B.** (control group). Patients were not advised to rinse with any oral antiseptic solution, but only to maintain proper oral hygiene and rinse with saline.
- **Group II (30 patients).** This group included patients with symptoms of pericoronitis.
- Subgroup A. Each subject underwent standard conservative treatment (saline rinsing and 3% hydrogen) combined with additional local rinsing with CPC solution and application of drain soaked in CPC solution. Each subject was advised to apply CPC solution at home for 7 days with control of the predicted parameters on the first, third and seventh day after the first examination.
- 2. Subgroup B. (control group) Each subject underwent standard conservative treatment of acute pericoronitis (rinsing with saline, 3% hydrogen and application of iodoform drain).

#### Inclusion criteria:

The study included patients who met the following criteria: signing an informed consent and agreeing to cooperate, i.e. respect and follow the recommendations and come back for control on the specified days.

#### **Exclusion criteria:**

- For female patients, if they pregnant or lactating;
- Hypersensitivity to any of the components of the drug;
- Cardiovascular diseases: severe uncontrolled hypertension, decompensated heart failure, unstable angina pectoris, myocardial infarction in the period of 6 months before the clinical examination or clinically significant history of arrhythmia or disorder in the ECG examination 6 months before the examination;
- Other diseases with serious pathology (brain strokes, hemodialysis patients, organ transplants, etc.);
- Application of antibiotic therapy in the previous 2 months;
- Mental dementia, reluctance or language barrier that would prevent understanding and cooperation within the examination;
- Patients under 18 years.

The dosage was according to the recommended doses, as follows: CPC 0.07% solution for mouth and throat rinsing 2-3 times a day with 15ml (1 tablespoon) pure solution.

During the study we examined the following parameters (variables):

## a) Pain

We monitored the pain through a visual analogue pain scale (VAS) analysis in which patients themselves noted the level of pain from painlessness to very severe pain according to the subjective assessment of pain intensity, on a horizontal or vertical line of 10cm (100mm) with placement on a perpendicular line (dash) according to the subjective feeling of pain, but they did not have insight into the numerical part of the scale which was used exclusively by the therapist (researcher) for numerical objectification of the subjective assessment of patients. Patients described the pain as: absence (0-4mm), mild pain (5-44mm), moderate pain (45-74mm), and very strong pain (75-100mm) (18).

#### b) Gingival Inflammation Index by Muhleman and Cowell

We observed both parameters of this index, the color of the gingiva and bleeding from the gingival sulcus. Both parameters were measured on the gingiva and gingival sulcus of the tooth, mesially on the third molar around which there is acute pericoronitis. Regarding the color of the gingiva, the following parameters were observed: 0pink, healthy gingiva; 1-inflamed, red marginal gingiva; 2-inflamed, red interdental papilla and marginal gingiva; 3-dark-red papilla and generalized redness of the gingiva. To examine the gingival bleeding, gingival sulcus was probed with a periodontal, graduated probe. The following parameters were observed: 0-no bleeding is observed after probing; 1-bleeding in one point in the gingival sulcus after a few seconds; 2-filling the interdental triangular space with blood after probing; 3-profuse bleeding that fills the interdental space and the gingival sulcus.

Index	of gingi	ival color	
0	1	2	3
Index	of gingi	val bleeding	
0	1	2	3

## c) Presence of postoperative trismus according to Ngyene et al.

We measured the interincisal distance and noted the following degrees:

0 -> 40mm - no trismus 1 - <40mm - has trismus

#### d) Postoperative edema and inflammation

For this purpose, evaluation of inflammation, we used the modified index of local gingival inflammation by Gonzalez-Santana et al.<sup>19</sup> where there are 4 degrees of local inflammation ranging from absence of inflammation to severe extraoral swelling postoperatively.

- 1. no/absence of inflammation
- 2. mild inflammation (swelling intraorally in the operated area)
- 3. moderate inflammation (extraoral swelling in the operated area)
- 4. severe inflammation (extraoral swelling outside the surgical zone)

# e) Depth of the pericoronary pocket in patients with pericoronitis (expressed in mm)

A graduated periodontal probe with a blunt tip was used to measure the pericoronal pocket. The depths of several probing paths around the crown of the tooth were measured, and the deepest value was taken as the relevant value.

The study was performed at the Clinic of Oral Surgery at the PHI University Clinical Center "St. Pantelejmon" in Skopje, as well as at the Dental Clinical Center at the European University-Skopje. We explained to the examinees the nature, duration and goals of the study, as well as any side effects that may occur as a result of the use of the test product. Then, before continuing any study-related activities, examinees who met the inclusion criteria signed an informed consent form to participate in the study (Declaration of Helsinki, Hong Kong Amendment, 1989).

The examination was performed in the following order:

### First visit (day 1, start of treatment):

The patients were diagnosed after the examination by taking anamnesis, extraoral, intraoral examination and Xray analysis. Appropriate treatment was performed (oral surgery or conservative treatment of pericoronitis). Examinees were advised to continue with regular oral hygiene.

#### Second visit (3 days from the start of treatment):

Examinees were asked if they experienced any adverse reactions to the solution they were using. During this visit, the researched parameters were re-noted.

#### *Third visit (7 days from the start of treatment):*

Examinees were asked if they experienced any adverse reactions to the solution they were using. An oral examination was performed, with special reference to determining the established parameters and comparing the values for the same obtained at the first, second and third visit. The parameters were noted before the sutures were removed in the same visit.

## **Results and discussion**

The data entered in the test lists were statistically processed (Microsoft Office Excel and Statistica<sup>7</sup>). We present the obtained results in tables and graphs, comparing them with relevant authors from the literature. The mean value of the obtained values was performed and a statistical correlation was made between the two subgroups (A and B) in different visits. It must be emphasized that we have not come across a study similarly designed to this one, that is, a study that follows the same parameters as ours, so the comparison with other literary reviews will be empirical, i.e. indirect.

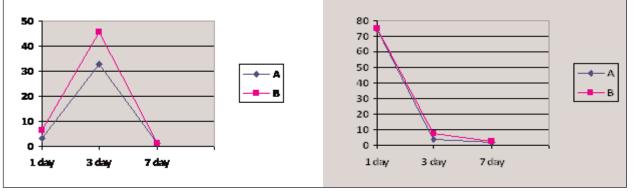
Table 1 and Graph 1 show the values for the Visual Analogue Scale (VAS) for pain expressed in mm (100 mm) for the two large groups and their subgroups, and they were compared in the three different visits. A statistical correlation of the obtained values was made and it a statistically significant difference (t - test; p < 0.05) was noted between the examined group A and the control group B on the first and third day in group I patients (those who underwent oral surgery). On the first day, the difference is due to the different pathology diagnosed in these patients, and hence the different symptomatology. The statistical significance of the difference in pain on the first day (day of intervention) cannot be due to the use of CPC because there is not enough time for its action. On the third day, in the stage of surgical wound healing, there is a statistically significant difference in pain, i.e. patients who have used CPC solution have expressed less symptomatology compared to the control group. Most likely, it is due to the reduced microbial load, the reduced plaque formation on the surrounding teeth, and thus the reduced local immune response.

Results in Group II (acute pericoronitis) showed a statistically significant difference (t-test; p < 0.05) at the second visit, which also indicates the importance of microbial load and plaque accumulation on the local immune response and release of proinflammatory mediators. It is important to say that there was no statistically significant difference on the 7<sup>th</sup> day, which indicates that for permanent relief of the symptoms of acute pericoronitis, mechanical debridement of the pericoronal space (curettage, use of H<sub>2</sub>O<sub>2</sub> with its foaming characteristic), as well as placing a drain and providing a way to eliminate the exudates, it is much more important, regardless of the solutions used for irrigation. This coincides with the study of Parven and al.<sup>20</sup>.

Tables 2 and 3 and Graphs 2 and 3 show the values of gingival inflammation expressed according to the

VAS (expressed in mm/100 mm)												
group (n=30)	I group-Oral surgical intervention						Il group-acute pericoronitis					
visit	1 (1	1 (1 day) 2 (3 day)			3 (7	day)	1 (1 day)		2 (3 day)		3 (7 day)	
subgroup (n=15)	А	В	А	В	А	В	А	В	А	В	А	В
mean value (mean)	3.07	6.53	32.87	45.53	1.13	1.06	74.33	75.13	3.87	7.8	2.2	2.6
t- test (<0,05)	0.0004		0.0002 0.85		0.87		0.02		0.45			





Graph 1. VAS (Visual analogue scale) for pain

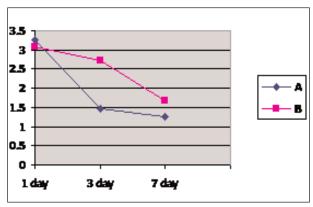
Muhleman and Cowell index of gingival color and gingival bleeding in patients with acute pericoronitis.

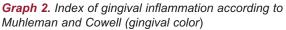
In group II (acute periocoronitis), a statistically significant difference was noted between groups A and B on the

COWELL – index for gingival color										
group (n=30)		Il group-acute pericoronitis								
visit	1 (1	day)	2 (3	day)	3 (7 day)					
subgroup (n=15)	А	В	А	В	А	В				
mean value (mean)	3.27 3.07		1.47	2.73	1.27	1.67				
t- test (<0,05)	0.	57	0.0	006	0.33					

Table 2. Index of gingival inflammation according toMuhleman and Cowell (gingival color)

third day after treatment for the color of the gingiva, but not for the gingival bleeding. This difference was not noted on the seventh day, which also indicates the importance and advantage of mechanical debridement of the periocoronary pocket.

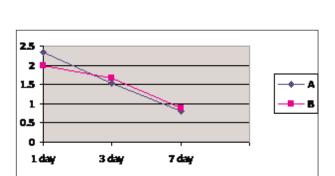




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Table 3. Index of gingival inflammation according toMuhleman and Cowell (gingival bleeding)

COWELL -	index	for gi	ngival	color						
group (n=30)		Il group-acute pericoronitis								
visit	1 (1	day)	2 (3	day)	3 (7 day)					
subgroup (n=15)	А	В	A	В	А	В				
mean value (mean)	2.33	2	1.53	1.67	0.8	0.9				
t- test (<0,05)	0.:	29	0.	54	0.8					



**Graph 3.** Index of gingival inflammation according to Muhleman and Cowell (gingival bleeding)

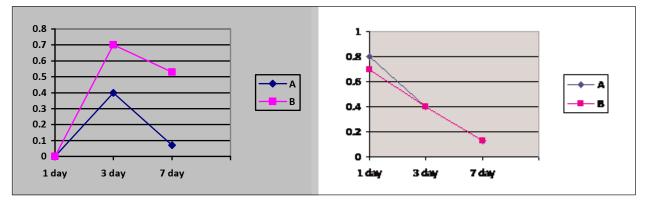
Table 4 and Graph 4 show the results obtained regarding the presence or absence of postoperative trismus (in Group I) and the presence or absence of trismus in patients with acute pericoronitis (in Group II). Trismus, as

Table 4. Presence of trismus according to Ngyene

a postoperative complication, is quite common in posterior oral mandibular surgery. It is defined as a prolonged spasm of the masticatory muscles and is diagnosed as a reduced interincisal distance <40-45mm<sup>21</sup>. Several factors are considered to be the causes of trismus including traumatic inflammation in the pterygomandibular space, infection that spreads to the pterygomandibular space and the masticatory space, traumatic injury of the masticatory muscles during anesthesia, and self-limiting opening due to pain. In postoperative trismus, the most common cause is traumatic inflammation of the surrounding tissues, while in trismus in acute pericoronitis, the cause is usually an extended infection in the above mentioned areas.

In our study, it is vital to note that there is a statistical difference in the presence of trismus between the two subgroups (A and B) only in Group I on the seventh day postoperatively. This means that patients who have used CPC solution have a significantly reduced degree of trismus after 7 days of intervention, indicating the importance of local tissue infection and inflammation on the onset of postoperative trismus. More detailed information can be found in the graphic presentation of this parameter (Graph 4) in our study which indicates an increased occurrence of trismus on the third day postoperatively in Group I (in both subgroups), while on the other hand, in Group II (acute pericoronitis) increased incidence of trismus was observed at the first visit (before treatment) and a sharp decrease in the incidence of trismus on the third and seventh day after treatment in both subgroups. This coincides with our results from the pain parameter, shown in the first table and graph, which goes in addition to the fact that pain as a symptom plays a significant role in the occurrence and course of trismus. This is in line with the results published in Pedersen's study<sup>22</sup>.

Presence of trismus												
group (n=30)	I	group-C	Dral sur	gical int	erventic	on	II group-acute pericoronitis					
visit	1 (1	day)	y) 2 (3 day)			day)	1 (1 day)		2 (3 day)		3 (7 day)	
subgroup (n=15)	A	В	А	В	А	В	А	В	А	В	А	В
mean value (mean)	0	0	0.4	0.7	0.07	0.53	0.8	0.7	0.4	0.4	0.13	0.13
t- test (<0,05)			0.2		0.	01	0.72		1		1	



Graph 4. Presence of trismus according to Ngyene

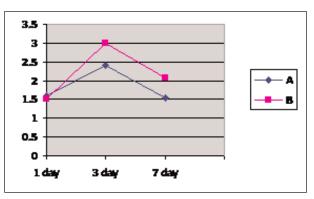
Table 5 and Graph 5 show the values of Gonzales-Santana Inflammation Index. According to this author, the degree of occurrence of tissue inflammation, swelling and the degree of its expansion are numerically expressed<sup>19</sup>.

The results refer to the subjects from the first group (patients in which oral surgeries were performed). Our results showed a statistically significant difference between the two subgroups (examined and control), but only at the second visit (the third day). This points to the fact that local microbial load plays a significant role in the first postoperative days and in the intensity of local tissue inflammation, but does not play a significant role in the definitive healing of the postoperative wound.

The graphic presentation of Graph 5 indicates the greatest local tissue inflammation with extraoral spread in the first postoperative days. This coincides with the results expressed in the graphs above, in terms of the presence of trismus. We can see that the curve for the presence of trismus coincides with the curve for the presence of local tissue inflammation in the operative zone.

Postoperative edema and inflammation according to Gonzales-Santana									
group (n=30) I group-Oral surgical intervention									
visit	1 (1	1 (1 day) 2 (3 day) 3 (7 day)							
subgroup (n=15)	А	В	А	В	А	В			
mean value (mean)	1.6	1.5	2.4	3	1.53	2.07			
t- test (<0,05)	0.	0.54 0.04 0.07							

 
 Table 5. Index of inflammation according to Gonzales-Santana

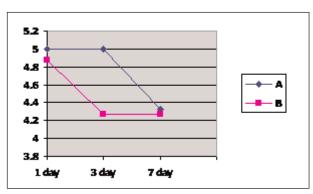


**Graph 5.** Index of inflammation according to Gonzales-Santana

The depth of the pericoronal pocket is an important parameter in patients with acute pericoronitis, which indicates the degree of edema of the pericoronary soft tissue. After conservative treatment of acute pericoronitis, a reduction in the depth of the pericoronal pocket is expected due to a reduction in swelling (volume of pericoronal tissue)<sup>22</sup>. The depth of the pericoronal pocket is taken to be the deepest value measured with a graduated periodontal probe measuring from the edge of the gingiva at the entrance to the pocket to the bottom of the pericoronal pocket.

CPC in combination with 3% hydrogen makes a significant difference in the reduction of inflammatory edema in the first three days of treatment due to the mechanical properties of hydrogen to remove debris from the pericoronal pocket (both antiseptics have a synergistic effect). At the third visit, no statistically significant difference was observed between the two subgroups. This is also consistent with the results of the Parveen and coop study<sup>20</sup>. Table 6. Depth of the pericoronary pocket (only ingroup II – acute pericoronitis)

Depth of pericoronary pocket (expressed in mm)										
group (n=30)		II group-acute pericoronitis								
visit	1 (1	day)	2 (3	day)	3 (7 day)					
subgroup (n=15)	А	В	А	В	А	В				
mean value (mean)	5 4.87		5	5 4.27		4.27				
t- test (<0,05)	0.6	697	0.	01	0.72					



**Graph 6.** Depth of the pericoronary pocket (only in Group II – acute pericoronitis)

### Conclusion

Clinically verified results from this study confirm the antiseptic properties of CPC solutions, particularly their effectiveness in the ability to reduce postoperative pain, microbial load reduction, and reduction of local tissue inflammation. These data encourage us to suggest topical application of CPC solutions in the preoperative period for conditioning oral tissues, intraoperative rinsing as well as prolonged use in the postoperative period. The intention is to turn these recommendations into a mandatory protocol for preoperative preparation and postoperative care of patients after oral surgery, which will minimize postoperative discomfort.

We recommend supplementing the standard protocol for conservative treatment of inflammatory conditions in the oral cavity from an oral surgical point of view, i.e. synergistic use of solutions containing CPC in combination with 3% H2O2 solution, which results in significant and rapid reduction of clinical symptoms of acute pericoronitis. We also suggest the use of mouthwashes containing antiseptic CPC solution in the prevention of respiratory virus infection, their transmission and the severity of the clinical picture caused by the current virus, SARS-CoV-2.

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