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Original article

EFFECTIVENESS OF NSAIDS FOR PAIN MANAGEMENT IN PERIODONTAL SURGERY

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ABSTRACT:

Introduction: The perception of pain is subjective and many factors may affect its power and duration in various oral surgical procedures. An effective treatment suggests a certain volume of knowledge and skills of dental practitioners. A combination of non-pharmacological and pharmacological agents is often used to relieve the pain. There is evidence that non-steroidal anti-inflammatory drugs (NSAIDs) are effective in treating acute pain. Hypotheses suggest that NSAIDs have analgesic and anti-inflammatory effects by reducing the synthesis of arachidonic acid's metabolites - prostaglandins (PGE_2, PGI_2), thromboxane (TxA_2, TxB_2) which are responsible for the occurrence of both - inflammation and pain. With the hyperalgesia initiated by PGE_2 and bradykinin, we can explain the presence of postoperative pain because it reduces the pain threshold and increases susceptibility to available threshold inducements.

Aim: To evaluate the effectiveness of postoperative NSAID administration in order to prevent the production of inflammatory components induced by the surgical treatment.

Material and methods: The study included 15 patients who received surgical therapy. The selective COX-2 inhibitor of the new class Aulin® and the non-selective COX-2 inhibitor Ibuprofen® were taken from the patients as systemic administration postoperatively for a period of 3 days. The VRS-4 scale was used to assess the pain.

Results: The assessment of the mean values for the degree of pain did not show statistically significant differences in the inhibition of pain for the two drugs in the three postsurgical days.

Conclusion: In the absence of a significant difference between the two drugs - Aulin® and Ibuprofen®, we may confirm that according to our study they are both sufficiently effective in controlling postoperative pain in surgical periodontal procedures.

Keywords: non-steroidal anti-inflammatory agents (NSAIDs), prostaglandins (PGE_2, PGI_2), bradykinin, non-selective COX-2, selective COX-2 inhibitors,

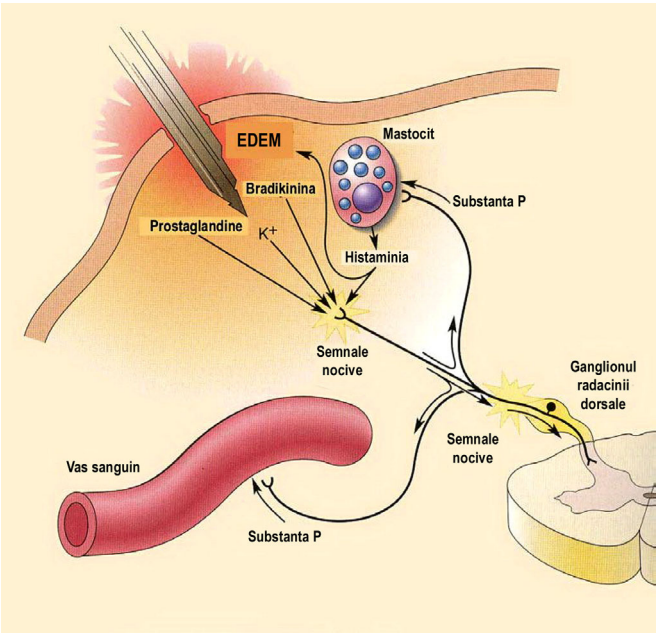
INTRODUCTION:

Pain can be definite as an unpleasant sensation, emotional experience or impact that triggers impulses activating various protective and negative reactions in the body [1, 2]. Unsuccessful treatment of pain during surgical procedures can be the cause of postoperative complications such as: delay of the return of normal sensation; the possibility of physiological changes in the CNS (central nervous system) that lead to a state of chronic pain [3]; as well as the patient's declination to follow the complete treatment plan. [4]

The pain accompanies various diseases - dental, oral and maxillofacial. The perception of pain is subjective and there are many factors affecting its parameters - the duration and volume of the intervention, some psychological aspects: stress and anxiety, as well as the degree of released inflammatory mediators as a result of tissue damage caused by the surgery.

Postoperative pain symptoms are present in patients who have received periodontal surgery and this pain is accordingly associated with the inflammatory processes initiated by the surgical trauma [5, 6].

Fig. 1. Inducement of pain sensitivity.



The sensation of the pain includes:

Pain sensitivity threshold:

- When at the lowest intensity of the pain, the individual stimuli are perceived as pain; and the severe pain in a certain place increases the threshold of pain for the other places (dominance of perceptions);

Pain tolerance threshold:

- This is the susceptibility to the duration or the intensity of the maximum acceptable pain, and the pain tolerance threshold decreases with repeated exposure to pain, in case of fatigue or a sleep disorder.

Data from the literature show that 70% of the patients have experienced pain after periodontal surgery from mild to a moderate degree, 44% have reported moderate pain and 46% - severe pain [7].

Clinical behaviour in the treatment of pain is based on evidence from clinical trials focused predominantly on the efficacy of the use of non-selective COX-2 and selective COX-2 inhibitors. These drugs have been examined for pain control in various types of surgical treatments, periodontal surgery procedures [8, 9].

It is known that mucogingival surgery is associated with pain 3,5 times more than bone surgery, and 6 times more than periodontal flap surgery [10]. A large number of agents have been used to treat pain after surgical interventions with varying degrees of success. Narcotic analgesics have a strong analgesic effect, but also, they possess many side effects. Most often, Codeine is used in a combination with Paracetamol [11, 12].

The other known large group is the group of **non-narcotic analgesics - NSAIDs**, which are shown to combine both analgesic and anti-inflammatory actions [13]. NSAIDs according to their ability to inhibit the enzyme cyclooxygenase (COX-1 and 2) are: **highly selective NSAIDs** (COX-2 inhibitors) - Rofecoxib, Etodolac, Meloxicam, Nimesulid, Celecoxib; **NSAIDs with lower COX selectivity** - Diclofenac, Piroxicam, and **NSAIDs with low COX selectivity** - salicylates [14, 15]. These drugs successfully suppress the mediators of inflammation - mainly prostaglandins (PG), which are important for the occurrence of inflammation and pain: Ibuprofen, Etodolac, Ketoprofen, Ketorolac, Flurbiprofen, Tenoxicam, Meloxicam, Celecoxib and others [16, 17, 18]. Authors suggest that NSAIDs have an analgesic and an anti-inflammatory effect by reducing the synthesis of arachidonic acid metabolites prostaglandins (PGE_2 and PGI_2) and thromboxane's (TxA_2 and TxB_2).

Prostaglandin E_2 is an agent with hyperalgesia action, and it effects on peripheral blood vessels, leading to vasodilation, and is enhanced by the synergistic action of other inflammatory mediators such as bradykinin, complement molecules and histamine [19].

The hyperalgesia initiated by PGE_2 and bradykinin explains the presence of postoperative pain in surgery - it reduces the pain threshold and increases susceptibility to available threshold stimuli [20, 21]. There are studies showing that NSAIDs have other effects besides their analgesic action, such as suppression of free radicals and synthesis of cytokines, which can stimulate signalling chains associated with the inflammatory response [22, 23].

Aim of the study: To evaluate the effectiveness of postoperative NSAID administration in order to prevent the production of inflammatory components induced by the surgical treatment.

MATERIAL AND METHODS:

The study included 15 patients who received a surgical therapy with the technique of free gingival graft (FGG). Standardized conditions of the same surgical procedure presupposed the objectivity of the comparative assessment. The VRS-4 scale was used to assess the pain. Patients self-assessed the degree of pain with a 4-point rating scale (VRS-4) respectively as: severe pain, moderate pain, mild pain(discomfort) and absence of pain [22].

The selective COX-2 inhibitor of the new class Aulin® and the non-selective COX-2 inhibitor Ibuprofen® were taken from the patients as systemic administration postoperatively for a period of 3 days.

The selective COX-2 inhibitor **Aulin®** is a complex-acting anti-inflammatory agent that selectively inhibits the production of proinflammatory prostaglandins and free radicals from active polymorphonuclear leukocytes (PMNs) and other inflammatory cells. Àulin® prevents bradykinin and cytokine-induced hyperalgesia by suppressing tumor necrosis factor-á (TNF-á). Furthermore, it is shown that Aulin® reduces the release of histamine and thromboxane in the blood, as well as platelet activating factor - a powerful mediator leading to an enhanced inflammatory response, including PMNs [14, 15, 24, 25]. There is evidence that Aulin® also successfully inhibits the activity of matrix metalloproteinases (MMPs). Moreover, it is possible that this medical product limits the effect of leukotrienes (LT) due to the fact that their production is influenced by the production of histamine, which is inhibited by Aulin® [13, 14, 22, 26].

The non-selective COX-2 inhibitor **Ibuprofen®** acts mainly on the quinine and histamine systems, which have a proven role in inflammatory processes [16, 17]. Ibuprofen® is rapidly absorbed after oral administration and shows high plasma concentration levels 2 hours after the first dose [10, 18]. It is considered an appropriate tool for long-term analgesic therapy. It has been shown a correlation between Ibuprofen® plasma concentration with its analgesic activity. After taking only 200 mg, the maximum average concentration of the drug is reached in the 4th hour of its administration, but after this period the desired therapeutic effect is lost. When 600 mg Ibuprofen® is taken it reaches its maximum plasma concentration faster, and 50% of patients demonstrate elimination of the pain and the effectiveness of the drug maintained after 4 hours [27].

RESULTS AND DISCUSSION:

Table 1 shows the average values of the pain degree reported on the VRS-4 scale in the groups of patients with Aulun® and Ibuprofen® in the first 8 hours after the

surgical procedure. The analysis did not show statistically significant differences in pain inhibition on the first day after free gingival grafting with the two test-agents.

Table 1. Average values of the pain degree in patients with prescribed Aulin® and Ibuprofen® in the first 8 hours after the intervention.

TIME	AULIN®	IBUPROFEN®	t-coefficient	p-coefficient
1 hour	1.25±0.87	1±0.89	0,53	p>0.10
2 hour	1.25±0.87	0.67 ± 0.82	1,28	p>0.10
3 hour	1.13 ± 0.83	0.67 ± 0.52	1,27	p>0.10
4 hour	1 ± 0.76	0.5 ± 0.55	1,43	p>0.10
5 hour	0.88 ± 0.64	0.5 ± 0.55	1,19	p>0.10
6 hour	0.88 ± 0.64	0.5 ± 0.55	1,19	p>0.10
7 hour	1 ± 0.76	0.67 ± 0.52	0,96	p>0.10
8 hour	0.88 ± 0.64	0.33 ± 0.52	1,77	p=0.10

Table 2 shows the mean pain scores reported on the VRS-4 scale in the Aulun® and Ibuprofen® patient groups for the next three days after the surgical procedure. The assessment of the mean values for the degree of pain again did not show statistically significant differences in the inhibition of pain for the two drugs in the three postsurgical days.

Table 2. Mean pain scores for the patients with prescribed Aulin® and Ibuprofen® in the first 3 days after the intervention.

TIME	AULIN®	IBUPROFEN®	t-coefficient	P-coefficient
1stday, morning	0.5±0.53	0.67±0.82	0.447	p>0.10
1st day, noon	0.38±0.52	0.67±0.82	0.479	p>0.10
1st day, evening	0.5±0.76	1.17±0.75	0.646	p>0.10
2nd day, morning	0.25±0.46	0.67±0.82	1.132	p>0.10
2nd day, noon	0.38±0.52	0.83±0.75	1.327	p>0.10
2nd day, evening	0.63±0.74	1±1.09	0.718	p>0.10
3rd day, morning	0.63±0.74	0.67±0.52	0.353	p>0.10
3rd day, noon	0.5±0.53	0.5±0.55	0	p>0.10
3rd day, evening	0.5±0.76	0.83±0.75	0.810	p>0.10

The assessment of the degree of pain in patients under the medication of NSAIDs Aulin® and Ibuprofen® is presented graphically in diagrams (figures 2-5). Figure 2 shows that in the first 8 hours after the intervention the average values of the registered degree of pain when taking Aulin® were slightly higher (1.25) compared to the Ibuprofen® (range 0.33 to 0.67 to 8 hours) but without statistical differences.

On the **1-st day** after the intervention, the recorded values of the degree of pain with Aulin® administration were lower (up to 0.5) compared to the Ibuprofen® (up to 0.83), but both drugs showed average values next to 1 (discomfort) (fig. 3.).

On **day 2**, morning and noon pain were successfully suppressed with both medications. The reported mean pain levels for Aulin® are again lower - up to 0.36, and for Ibuprofen® they reach 0.83 without the statistical significance of the differences. The reported evening averages were 0.63 for Aulin® and 1.0 for Ibuprofen® (discomfort) (fig. 4.).

On the **3rd day** after the surgical procedure, Ibuprofen® showed a slight increase in mean values – 0.83, while for Aulin® the mean values did not exceed 0.63. For both drugs, the reported pain sensation ranged between discomfort and no pain, and both drugs showed effective analgesia in early postoperative recovery. In all, a successful inhibition of pain was seen during the first three days in both groups (fig. 5.).

Fig. 2. Intensity of pain – first 8 hours.

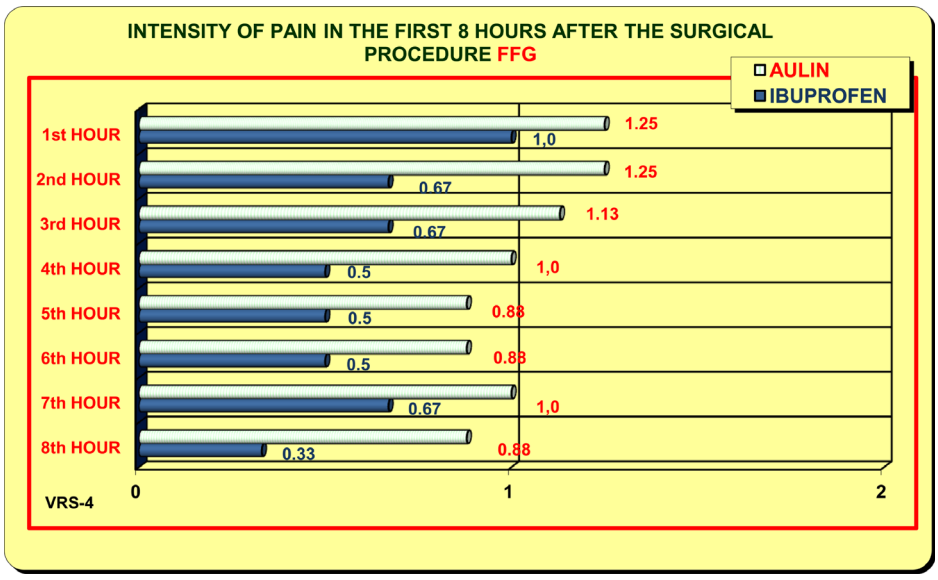


Fig. 3. Intensity of pain – first day.

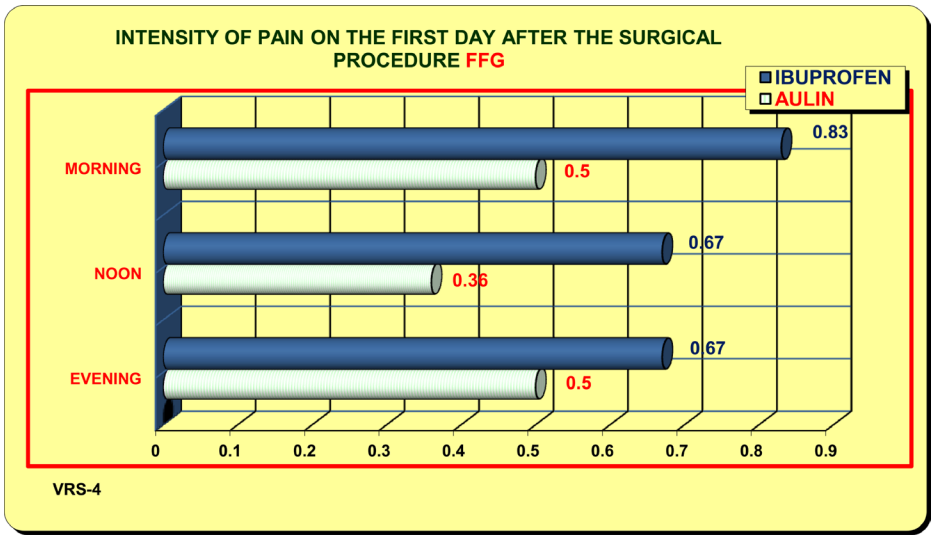


Fig. 4. Intensity of pain – second day.

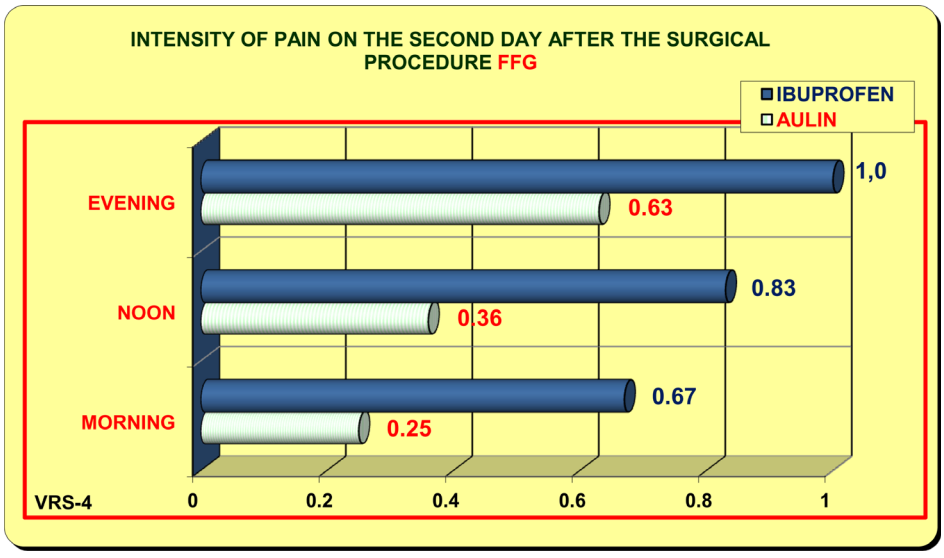
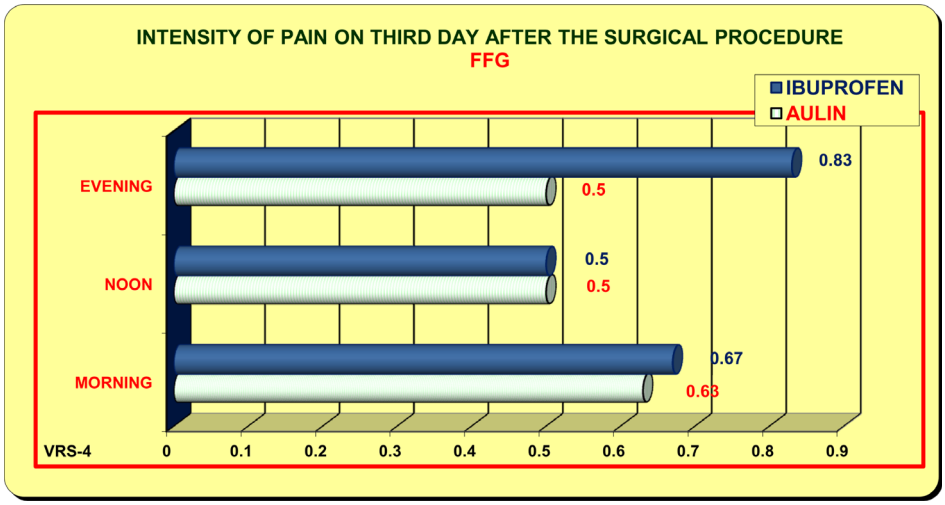


Fig. 5. Intensity of pain – third day.



CONCLUSION:

The results of this study are in agreement with the results from the literature on the effectiveness of NSAIDs in suppressing postoperative pain in various surgical procedures. The use of NSAIDs leads to a delay in the onset of pain symptoms after the surgical procedure and thus creates optimal conditions for postoperative repair. Based on their pharmacological characteristics, both drugs are justifiably examined in cases of periodontal surgery. NSAIDs inhibit peripheral mediators and show a significant analgesic effect. In the absence of a significant difference between the two drugs - Aulin® and Ibuprofen®, used to inhibit pain, we may confirm that according to our study they are both sufficiently effective in controlling postoperative pain in surgical periodontal procedures. They successfully suppress the pain and improve the comfort of the patients in the postoperative period, which increases the motivation of these patients for periodontal surgery in conjunction with the treatment of periodontal diseases and conditions.

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