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Efficiency and Safety of Cyclooxygenase-2 Inhibitors (Cox-2) as a Post-Surgical Pain Killer Related to Maxillofacial Surgery

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Abstract

Introduction: Powerful postoperative pain control requires a pain relieving with fast acting and long duration of activity. Non-steroidal anti-inflammatory drugs (NSAIDs) have an opioid impact when utilized postoperatively, however they tend to demonstrate a slower beginning of activity. A few studies showed that COX-2 inhibitors are t as powerful as NSAIDs. The aim of this review is to evaluate the efficacy and safety of Cyclooxygenase-2 inhibitors (Cox-2) for the relief of acute postoperative pain focusing on dental setting.

Methods: The electronic search of the literature in MEDLINE and EMBASE identified 132 articles which underwent full-text review and 10 met our inclusion criteria. The electronic search of the literature in MEDLINE and EMBASE identified 132 articles which underwent full-text review and 10 met our inclusion criteria. These articles examine the efficacy and safety of Cyclooxygenase-2 inhibitors (Cox-2) for the relief of acute postoperative pain in surgeries such as extraction of impacted third mandibular molar, open-flap debridement periodontal surgeries, mandibular fractures, cranial fractures.

Results: The effectiveness of Cox-2 inhibitors, found to be significantly different in Celecoxib in only one study, and with no significant difference in 3 studies, Etoricoxib with Celecoxib in one study also significantly reduce the postoperative pain, while in Parecoxib all the studies were significantly reduce the pain. Regarding the safety of Cox-2 inhibitors, the side effects were more in the Celecoxib than in placebo in some studies, and more in placebo than in Parecoxib in few studies. No significant differences found in some included studies.

Conclusion: The specific COX-2 inhibitor Celecoxib might be helpful for the treatment of severe pain. Its utilization might be especially attractive for elderly people and patients with a background marked by gastrointestinal issues.

Keywords: Pain killer, Surgery, Maxillofacial, Effectiveness

Introduction

A superior comprehension of pain mechanism has supported the advancement of new standards of pain control based on preemptive and multimodal methodologies. In spite of the fact that cyclooxygenase (COX)- 2-particular inhibitors (Coxibs) were initially created as constant torment prescriptions, and have exhibited adequacy like ordinary, nonselective non-steroidal calming drugs (NSAIDs) (1). They were extended to be incorporated in postsurgical and severe medicinal pain. The expansion of Coxibs to pain administration ideal models is a vital headway on the grounds that postsurgical and intense pain administration are regularly imperfect. It was noted about three decades back that roughly 73% of patients revealed direct to-serious pain following therapeutic and surgical systems [1].

Powerful postoperative pain control requires a pain relieving with fast acting and long duration of activity. Opioids, for example, Pethidine, are acceptable regimens yet their utilization is every now and again joined by antagonistic impacts, for example, respiratory depression, urinary incontinence, diminished circulatory strain and sedation, consequently prompting slower persistent recuperation [2]. Non-steroidal anti-inflammatory drugs (NSAIDs) have an opioid impact when utilized postoperatively, however they tend to demonstrate a slower beginning of activity (3). Diclofenac and Lornoxicam have been broadly utilized for this reason. The entry of particular COX-2 inhibitors, for example, Parecoxib, was extremely encouraging the extent that harming impacts were concerned, yet their use in correlation with non-selective inhibitors still can't seem to be resolved.

A few investigations have been done for this reason, the greater part of which guarantee that particular COX-2 inhibitors are in any event as powerful as non-selective ones. These COX-2–particular NSAIDs, don't prevent platelet aggregation like other ordinary NSAIDs, and can in this manner be directed before surgery to keep the start of the arachidonic course without the expanded dangers for perioperative and postoperative dying (3). Another favorable criterion of the Coxibs is their long duration of action, maintaining an extended dosing interval of the medication and encouraging the patient's adherence to treatment (4).

In the United States, Celecoxib is shown for the alleviation of the signs and side effects of osteoarthritis, rheumatoid arthritis and ankylosing spondylitis; for the administration of severe pain in adults and for the treatment of primary dysmenorrhea (3), and there is evidence that it might likewise be effective for severe pain following surgery, injury, and tooth extraction (4, 5). Clinical trials estimating the efficacy of analgesics in severe pain have been institutionalized over numerous years. Trials must be randomized and double blinded. Ordinarily, in the first couple of hours or days after an activity, patients create pain that is intense and will then be given the test pain relieving drug or placebo treatment.

Pain is estimated using standard visual scales prompt before the intervention, and after the intervention with the aid of scales over 4 to 6 hours for shorter acting medications and up to 12 or 24 hours for longer acting medications (6). The aim of this review is to evaluate the efficacy and safety of Cyclooxygenase-2 inhibitors (Cox-2) for the relief of acute postoperative pain focusing on dental setting.

Methods

The electronic search of the literature in MEDLINE and EMBASE identified 132 articles which underwent full-text review and 10 met our inclusion criteria. These articles examine the efficacy and safety of Cyclooxygenase-2 inhibitors (Cox-2) for the relief of acute postoperative pain in surgeries such as extraction of impacted third mandibular molar, open-flap debridement periodontal surgeries, mandibular fractures, cranial fractures.

Results

All included studies were randomized, double-blind placebo controlled, of ranging sizes of samples, from 17 in [3] to 513 [4] as demonstrated in table 1.

The mean age of the patients was 25.8 years in [3] to 49.6 years in [5]. The type of surgical procedures in this review were tonsillectomy in [3, 6] and, extraction of impacted third mandibular molar in [4] and [7], open-flap debridement periodontal surgeries in [8], and supratentorial craniotomy in [9] and [5].

The type of anesthesia reported only in [9] by Propofol/Remifentanil and in [5] Remifentanil alone. The three Cyclooxygenase-2 inhibitors (Cox-2) in this review were Celecoxib in 4 studies [3, 4, 6, 7], Parecoxib in 5 studies [5, 9-12] and etoricoxib combined with Celecoxib in one study [8]. The comparison in 8 studies was placebo and active in 2 studies, Loxoprofen 60 mg in [7] and Lornoxicam 16 mg or Diclofenac 150 mg in [12].

Concerning the effectiveness of Cox-2 inhibitors, found to be significantly different in Celecoxib in only one study [4], and with no significant difference in 3 studies [3, 6, 7], Etoricoxib with Celecoxib in one study also significantly reduce the postoperative pain [8] while in Parecoxib all the studies were significantly reduce the pain [9-12] except for [5].

Regarding the safety of Cox-2 inhibitors, the side effects were more in the Celecoxib than in placebo in [6], more in placebo than in Celecoxib in [3, 4], more in placebo than in Parecoxib in [9, 11], more in active control than in Parecoxib in [12]. No significant difference in [5, 7] and no side effects reported in [8, 10].

Discussion

A postoperative pain score should to be kept lower than 3 out of 10 at rest and with motion, stated by the Joint Commission on Accreditation of Healthcare [13]. Postoperative pain for the most on the next 24 hours, with the peak power at 6 to 8 hours (14). If no intervention regarding pain start after surgery to sedate patients, this may result in distress and may decrease the opportunity of complete treatment (15). Tension and anxiety appear to have a negative impact on postoperative pain (16).

The benefits of COX-2 selective medications versus NSAIDs are the less side effects identified with gastrointestinal issues; nonappearance of platelet aggregation, which may cause perioperative draining difficulties when a preemptive drug is utilized; long duration of action and half-life; and more prominent and enduring relief from discomfort. Likewise, negative impacts identified with the utilization of COX-2– selective medications, for example, kidney or cardiovascular issues, were just connected with their use [14].

A subjective survey reasoned that there are three factors that influence postoperative pain analgesics use: age, sort of surgery, and mental pressure (15). The kind of surgery may influence the efficacy of this combination of medications; for instance, in patients experiencing orthopedic surgery, the combination of Paracetamol and NSAIDs applies an opioid saving impact and lower pain scores, yet such an impact isn't found in patients experiencing soft tissue surgery (16), for example, tonsillectomy (6).

Powerful postoperative pain control, particularly in an intense period, is an issue of worry for obstetricians, on the grounds that insufficient pain control, particularly in the parturient, may not just influence physical stability and personal satisfaction, yet may likewise influence accomplishment in breastfeeding (15, 16).

Schwartz published an article on peri-intervention pain, said that post-intervention pain from dental, oral and maxillofacial surgical techniques is to a great extent affected by its pre-surgical medications (17). The intense stage of pain that is common with tooth extraction causes fast, extreme discomfort instantly after it begins, this is known to decrease over a nearly a short period of time (15, 16).

Iverson et al. confirmed that the utilization of a cyclooxygenase-2 inhibitor was related with less post-agent adverse reactions in light of the lower rate of gastrointestinal disturbance (17). Nonetheless, surgery-related elements that affect the rate of post-agent side effects include the site and type of surgery. Otolaryngological has been connected to a higher occurrence of post-agent side effects (17).

Celecoxib in a 200 mg dosing is less viable than conventional NSAIDs utilized as a part of a more typical dosage, subsequently its impact on controlling pain (15). White reasoned that 200 mg of Celecoxib was equal to 2 g of acetaminophen (Paracetamol) when regulated before otolaryngological surgeries (16). The pain-relieving efficacy of Celecoxib is dose related, with 400 mg being suggested as dosage for intense pain control. As the prescribed doses for Celecoxib is 400 mg for each day for severe pain, 200 mg of Celecoxib twice daily would appear to

give the required dose; be that as it may not be a sufficiently solid pain relieving agent when the accumulated day by day dosage of Celecoxib is isolated into two separate 200 mg measurements. Parecoxib has both quick beginning and long term of activity (16). Parecoxib lessens postsurgical pain from uterine damage, joined with a diminishment in physical injury pain from opioid impact (13). In 2009, a Cochrane review detailed that the doses of 20 or 40 mg Parecoxib, by either intramuscular or intravenous course, is a compelling prescription for intense postoperative pain and it can decrease pain over a 24-h period (17). Etoricoxib is a novel NSAID, exceptionally selective for COX-2. Its half-life is 25 hours (18).

Conclusion

The specific COX-2 inhibitor Celecoxib might be helpful for the treatment of severe pain. Its utilization might be especially attractive for elderly people and patients with a background marked by gastrointestinal issues. Pain is very subjective and may differ among patients. In this manner, multi methodological approach appear to be perfect for the assessment.

Table (1): Summary of the findings of the included studies

Study	Study design	Sample size	Mean age of patients	Type of anesthesia	Regime of Cox-2 inhibitors	Comparison group	Effectiveness of Cox-2 inhibitors	Side effects of Cox-2 inhibitors
(Ng et al., 2017)	A randomized, double-blind, placebo-controlled study	80	45.5 years old	General anesthesia	40 mg Celecoxib group	Placebo	No statistically significant difference in pain on any day between the groups	The number of vomiting episodes was higher in the Celecoxib group compared to the placebo group (p=0.001)
(Inthigood et al., 2017)	A double-blind randomized placebo-controlled trial	82	30 years old	Regional anesthesia	A single 40-mg intravenous (i.v.) dose of Parecoxib	Placebo	Parecoxib did not demonstrate effectiveness in . However, administration of a single 40-mg dose of Parecoxib after elective CD demonstrated effectiveness in reducing pain scores,	No patients in either group reported adverse effects from their assigned intervention.
(Van Daele et al., 2016)	A Prospective, Randomized, Double-Blind Placebo-Controlled Trial	17	25.8 years old	General	200 mg Celecoxib	Placebo	Pain and activity did not significantly differ between Celecoxib and control, but mean total acetaminophen equivalent and mean total morphine equivalent was found to be significantly lower in the Celecoxib group compared to the control group	Two subjects in the placebo cohort had vomiting in addition to nausea in the first 3 days, but only 1 subject in the active drug group hay vomiting that ultimately required Ondansetron as he had vomiting extending to the fifth day.

(Liu et al., 2016)	A multicenter, randomized, double-blinded, placebo-controlled trial	240	41 years old	Under combined spinal-epidural anesthesia received PCEA plus postoperative intravenous Parecoxib 40 mg or saline	Parecoxib	Placebo	The use of Parecoxib was associated with significant reductions in pain scores compared with the placebo ($P < 0.001$)	Postoperative vomiting was significantly reduced in the Parecoxib group. However, the groups were similar with respect to postoperative nausea, pruritus, and the time to the return of bowel function
(Yamashita et al., 2014)	RCT	107 Celecoxib 102 Loxoprofen	33.7	local anesthesia	Celecoxib 400 mg	Loxoprofen 60 mg	Celecoxib is of equal clinical v Loxoprofen alue to Loxoprofen for acute pain after third mandibular molar extraction.	Celecoxib group of whom two provided responses that might have constituted adverse events (three events,(comprising nosebleed, drowsiness, and malaise
(Saito et al., 2012)	A multicenter, randomized, double-blind, placebo-controlled, Phase II study	69	42 years old	local anesthesia	400-mg dose of Celecoxib Additional 200-mg dose of Celecoxib	Placebo	Significantly greater in the Celecoxib 200 mg group than in the placebo group ($P < 0.0001$)	20.3% (13/64) in the Celecoxib 200 mg group and 18.8% (25 (133among those receiving the initial 400-mg dose of Celecoxib only
(Williams et al., 2011)	RCT	100	41.5 years old	Propofol/remifentanil	Parecoxib, 40 mg i.v	Placebo	Pain intensity [excellent/very good pain relief in 78% of Parecoxib patients; 74% of control patients (P¼0.72)]	%51 Parecoxib patients
(Steffens et al., 2011)	A double-masked, parallel-group, placebo controlled, and randomized clinical trial	56	38 years old		200mg Celecoxib (and another 200 mg 12 hours after the first dose); 120 mg Etoricoxib	Placebo	Pain intensity levels in the Etoricoxib group were lower than in the placebo group There was no statistically significant difference between Celecoxib and Etoricoxib	No adverse side effects were reported for any medication
(Kyriakidis et al., 2011)	A prospective, randomized, double-blind study	513	48.5 years old		Parecoxib 80 mg daily i.v.	Lornoxicam 16 mg daily i.v. or Diclofenac 150 mg daily i.m	The level of analgesia was significantly better with Parecoxib than with Lornoxicam ($P < 0.01$) and Diclofenac ($P < 0.001$) s	Adverse events were significantly less common in the Parecoxib and Lornoxicam group, compared with Diclofenac group.
(Jones et al., 2009)	A prospective, double-blind, randomized, placebo-controlled study	82	49.6 years old	Remifentanil	single dose of Parecoxib 40 mg	Placebo	Parecoxib reduced pain scores at 6 h and morphine use at 6 and 12 h after operation. However, overall, it had only minimal impact on postoperative analgesia	There was a low overall incidence of nausea and vomiting (14%) and there were no differences in the incidence or severity of nausea and vomiting between the groups

Conflict of interests

The authors declared no conflicts of interests.

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