TREATMENT OF POSTOPERATIVE PAIN AFTER OPHTHALMIC SURGERY

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SUMMARY

For ophthalmic surgery we have to deal with a wide range of different patient characteristics. We treat young healthy children, in some cases even neonates, but on the other hand we have debilitated aging patients with multiple concomitant diseases. Treatment of postoperative pain is imperative for inpatients, but is even more important for patients who are treated on an outpatient basis. There also is a wide range of different types of ophthalmic surgical procedures.

The postoperative care after a cataract extraction is only seldom complicated by severe pain and is completely different of that after a vitrectomy with scleral buckling. More aggressive surgery as enucleation or evisceration of an eye often is a very stressful and painful procedure. We certainly have some excellent strategies to cope with postoperative pain. We can use topical anesthetics or non-steroidal anti-inflammatory medication. Regional anesthesia of the globe is extremely useful for anticipating on postoperative pain, especially when long-acting agents are used. We can administer analgesics by mouth or parenterally. Acetaminophen or paracetamol is widely used and can be supplemented with NSAIDs or opioids. Especially for children one has to use optimal doses of minor analgesics by an adequate route of administration in order to achieve a timely and efficient analgesia.

RÉSUMÉ

En chirurgie ophtalmique nous devons prendre en considération un large éventail de différentes caractéristiques du patient. D'une part nous traitons des jeunes enfants en bonne santé, le cas échéant des nouveau-nés, d'autre part nous avons des patients vieillissants et débilitants qui souffrent de plusieurs maladies concomitantes. Le traitement de la douleur postopératoire est impératif pour les patients hospitalisés, mais il est encore plus important pour les patients ambulatoires. Il y a aussi un large éventail de différents types de procédures chirurgicales ophtalmiques.

Le soin postopératoire après une extraction de la cataracte n'est que rarement compliqué par des douleurs aiguës et il est complètement différent du soin après une vitrectomie avec cerclage. La chirurgie plus agressive comme l'énucléation ou l'éviscération d'un œil est souvent une procédure très stressante et douloureuse. Nous disposons certainement de quelques stratégies excellentes pour combattre la douleur postopératoire. Nous pouvons utiliser des anesthésiants locaux ou des médicaments non-stéroïdiens anti-inflammatoires. L'anesthésie régionale du globe oculaire est très utile pour anticiper sur la douleur postopératoire, en particulier quand on utilise des agents à action prolongée. Nous pouvons administrer les analgésiques par voie orale ou parentérale. L'acétaminophen ou paracétamol est utilisé couramment et peut se compléter par l'utilisation des médicaments non-stéroïdiens anti-inflammatoires ou opioïdes. Spécialement pour les enfants il faut utiliser des doses optimales d'analgésiques moins forts moyennant un mode adéquat d'administration afin d'obtenir une analgésie opportune et efficace.

KEY-WORDS

Postoperative pain, non-steroidal anti-inflammatory agents, paracetamol, local anesthetics, postoperative nausea and vomiting

MOTS-CLÉS

Douleur postopératoire, médicaments non-stéroïdiens anti-inflammatoires, paracétamol, anesthésiants locaux, nausées et vomissements postopératoires

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PAIN AFTER OPHTHALMIC SURGERY

Cataract surgery is the operation most often performed worldwide. Koay et al. (10) studied the postoperative pain after this procedure and found that 55 % of patients had no pain or discomfort postoperatively, 32 % reported slight discomfort, 8 % of patients experienced mild pain and only 5 % suffered moderate to severe pain. Local anesthesia was shown to be more comfortable than general anesthesia in the immediate postoperative period. The level of pain scored on the day of surgery was significantly less in the local anesthesia group and analgesic consumption of paracetamol was lower compared with the general anesthesia group. We can measure postoperative pain on a visual analogue scale where the patient rates the amount of postoperative pain on a scale from 0 to 100. The left end of the scale (0) represents a completely pain free postoperative period and the right end (100) represents the most severe pain a patient could ever imagine. Mandelcorn et al. (13) performed a study to identify significant risk factors for the development of pain and nausea during the first 24 hours after outpatient vitrectomy or scleral buckling surgery. The procedures were performed under retrobulbar regional anesthesia given by the surgeon and conscious sedation administered by an anesthesiologist. The median pain scores were 1 for the patients who underwent vitrectomy, 47 for those who underwent scleral buckling and 35 for those who underwent combined vitrectomy-scleral buckling.The identification of the intraoperative use of narcotic analgesics for conscious sedation was identified as a predictor of postoperative nausea. Scleral buckling is most often accompanied by an appreciable amount of pain and nausea (3). This procedure necessitates more ocular muscle manipulation.

Loss of an eye is very distressing. Enucleation or evisceration is therefore often performed under general anesthesia. It is very useful to complement general anesthesia with a locoregional block for prevention of postoperative pain. Evisceration seems to be more painful than enucleation (1). When the procedure is combined with the primary insertion of a hydroxyapatite implant patients tend to experience more pain than those undergoing secondary implant surgery (22). The amount of postoperative pain has certainly been underestimated and is comparable with the amount of pain following general surgery. Calenda et al. (2) assessed peroperative and postoperative analgesia in eye enucleation or evisceration performed under peribulbar anesthesia. Analgesia was complete from the accomplishment of the peribulbar block to the 4th hour in all patients (efficacy 100%). From the 4th tot the 24th hour, pain remained absent in 35 % of patients. In 65 % of patients pain appeared between the 4th and the 10th hour and patients were relieved by paracetamol alone in 70 % of cases while 25 % of the patients required paracetamol and nalbuphine. In one patient who underwent evisceration the association of drugs was uneffective.

LOCOREGIONAL EYE BLOCK

Ophthalmic operations are frequently performed using locoregional block. A recent analysis of the literature on the effectiveness of regional anesthesia for cataract surgery indicated the superiority of retro- and peribulbar block for this procedure (6). The authors found good evidence that retrobulbar and peribulbar block provide better pain control during surgery than does topical anesthesia. There is fair evidence to assume that sub-Tenon's block even provides better pain control than retro- or peribulbar block. Sufficient akinesia is achieved with either of the three locoregional techniques. Sub-Tenon's block is less painful on administration than retro- or peribulbar block. Frequently a block of the facial nerve is performed to achieve an akinesia of the orbicularis oculi muscle. Most often this is experienced as being more painful than the retrobulbar block. In most of the cases the patient can be sedated during administration of the locoregional block. During monitored anesthesia care (MAC) the sedation is being administered by an anesthesiologist who monitors the vital signs of the ophthalmic surgical patient while the eyeblock is being performed and during the entire operation. Advantages for the patient are: reduced anxiety, less pain on the initial injection of local anesthetic,

amnesia for the surgical or procedural event, greater patient tolerance of long procedures and easier acceptance for subsequent surgery of the contralateral eye. This approach gives a modification of the stressresponse with minimal hemodynamic consequences because of a reduced sympathetic outflow, especially useful for patients with coronary heart disease. Ideally the patient remains cooperative or is easily arousable during surgery.
Regional anesthesia has seen the introduction of new local anesthetics: levobupivacaine (Chirocaine®) and ropivacaine (Naropin®). Bupivacaine is a mixture of two stereo isomers, compounds made up of the same atoms connected by the same sequence of bonds, but having different three-dimensional structures. Levobupivacaine rotates the plane of polarized light to the left (14). It has an overall safety-profile better than plain bupivacaine.
Ropivacaine is an amino-amide local anesthetic which is manufactured as a pure S enantiomer. It also has less central nervous system and cardiovascular adverse effects. Symptoms of central nervous system toxicity precede cardiotoxicity.
Gioia et al. (7) evaluated peribulbar anesthesia for vitreoretinal surgery with 0.75 % ropivacaine versus peribulbar anesthesia with a mixture of 2% lidocaine and 0.5 % bupivacaine. They found an onset time for ropivacaine similar to that of the lidocaine-bupivacaine mixture. Ropivacaine provides a better quality of postoperative analgesia, more patients were painfree at 1, 3,6 and 24 hours after surgery, more patients did not need analgesics.
Retrobulbar irrigation of local anesthetics is yet another modality of postoperative pain management (12). After conjunctival peritomy and dissection of Tenon's fascia a 21 gauge blunt irrigating cannula is used to irrigate local anesthetics in each of the four quadrants. Duker et al. (5) demonstrated that this is a safe and effective way to achieve postoperative pain relief after surgery for scleral buckling. It also can be used for secondary increase of a partial functioning retrobulbar block.

PARACETAMOL

Among analgesics administered orally or parenterally, paracetamol is most often used and very effective in the management of mild to moderate pain. Paracetamol (acetominophen) is water insoluble and for that reason can not be used parenterally. Propacetamol is a water-soluble precursor of paracetamol with the same properties (21, 23). Plasma esterases convert propacetamol to paracetamol in that way that 2 gr. of propacetamol is equivalent to 1 gr. of paracetamol. Paracetamol then diffuses to the cerebrospinal fluid. Only two hours after administration of paracetamol, concentration in the cerebrospinal fluid reaches its maximum (19). Analgesic activity of paracetamol depends on the speed and level of the peakplasma concentration. Only quick and repetitive administration of sufficient doses results in an effective pain relief. One gram of paracetamol seems to be the optimal dose and can be given four times a day. The speed with wich the peakplasma concentration is reached is another important determinant in analgesic efficacy. The bioavailability of a given preparation of the drug is very variable. The effervescent formulation of paracetamol reaches its peak plasma level 22 minutes after administration whereas dry tablets of paracetamol need 60 minutes. Paracetamol still remains the reference analgesic with good clinical efficacy without adverse reactions on the gastrointestinal tract and hematological system. True allergies for paracetamol are rare. It guarantees optimal safety for all ages, during pregnancy and breastfeeding and can be safely used in the presence of gastro-intestinal pathology and renal or hepatic insufficiency.
In children rectal paracetamol is widely used in the treatment or prevention of postoperative pain. The bioavailability however is much better after oral administration than after suppositories. Onset time of rectal paracetamol is 2 - 2.5 hours as compared to 0.6 hour for effervescent tablets. Furthermore the peak plasma concentrations are typically only one third of those reached by the oral route. Several studies have shown that indeed rectal paracetamol in doses recommended by the manufacturers is ineffective (9). Morton and Arana (15) recommend to start with an initial oral dose of 20 mg/kg or a rectal dose of 40 mg/kg and to continue with a maintenance dose of 15 mg/kg oral or rectal with an interval of 4 to 6 hours. Maximum daily dose is limited to 90 mg/kg. Dura-

Table 1: *Dosing regimen for oral and rectal paracetamol in infants and children*

Age group	Oral initial dose (mg/kg)	Rectal initial dose (mg/kg)	Maintenance dose (mg/kg)	Dosing interval (h)	Maximal daily dose (mg/kg/day)	Duration at max dose (h)
0-3 months	20	20	15	8	60	48
> 3 months	20	40	15	4 - 6	90	72

tion of the treatment at maximum dose is restricted to 72 hours. These are guidelines for healthy children over 3 months of age. In younger children one can give an initial oral or rectal dose of 20 mg/kg with subsequent doses of 15 mg/kg with a dosing interval of 8 to 12 hours and a maximum daily dose of 60 mg/kg. Duration of the treatment at maximum dose is limited to 48 hours. (Table 1.)

NSAIDS

Non-steroidal anti-inflammatory drugs can also be used for the treatment of postoperative pain. Stevenson et al. evaluated the efficacy of indomethacin for the management of pain after scleral buckling and cryotherapy (16). They found indomethacin to cause a significant reduction in pain scores both at 3 days and at 10 days postoperatively. The arachidonic acid cascade system plays an important role in the complex mechanism of pain perception. Oxidation of arachidonic acid via the cyclo-oxygenase pathway generates a series of prostaglandins and thromboxanes. Prostaglandines and thromboxanes are generated by tissue trauma and mediate nociception in synergy with other chemical mediators. NSAIDs block the synthesis of prostaglandines by inhibition of the enzyme cyclo-oxygenase (COX). The use of this class of drugs however is limited by contraindications and potentially severe side-effects. The synthesis of prostaglandines that are associated with tissue homeostasis in kidney, gastro-intestinal mucosa and platelets are also blocked by NSAIDs. Gastro-intestinal bleeding is indeed a known side-effect. Renal impairment is another problem especially in patients with arteriosclerosis, hypovolemia and patients with known kidney failure and congestive heart failure. These patients are dependent on high levels of renal prostaglandins for vasodilation of the afferent vessels of the glomeruli. Allergy to NSAIDs is another important issue. Especially patients who are allergic to acetylsalicylic acid are prone to cross-reactivity with NSAIDs. The cyclo-oxygenase enzyme exists as at least two different isoenzymes, the COX-1 and the COX-2 isoenzyme (17). The COX-1 isoenzyme mediates the synthesis of those prostaglandines responsible for normal homeostasis. The COX-2 isoenzyme is induced and upregulated during inflammation. NSAIDs with a high COX-2 specificity have a beneficial effect on inflammation and pain perception. They produce fewer side-effects. Celecoxib (Celebrex®) and rofecoxib (Vioxx ®) are NSAIDs with a high COX-2 to COX-1 ratio.

NSAIDs and paracetamol have different mechanisms of action. NSAIDs inhibit the cyclo-oxygenase in peripheral tissue and central nervous system while paracetamol inhibits the release of prostaglandin in the spinal cord and effects the serotonin mechanisms for spinal pain control. Coadministration of these two classes of drugs improves the quality of analgesia, ensures more rapid pain relief and pain free periods of longer duration (4).

RESCUE ANALGESICS

When pain is not adequately managed with minor analgesics, postoperative complications like bacterial endophthalmitis or rise in intraocular pressure must be excluded by the ophthalmologist.

Tramadol is a synthetically derived morphine analogue that can be used as a rescue analgesic. It has a low affinity for opioidreceptors and therefore it is devoid of any respiratory depressant effect. Maximum daily dose is 13 mg/kg. An intravenous loading dose can be given (3 mg/kg) followed by a maintenance dose of 10 mg/kg. Maintenance dose is reduced in patients over 70 years of age (6-8 mg/kg). For the treatment of more severe postoperative pain opioids are administered. Piritramide can be given intramuscularly in doses of 0.2 to 0.3 mg/kg, 4 to 6 times a day. Especially when remifen-

tanil is being used as analgesic drug during more painful operations one must anticipate on pain control. Remifentanil is an extreme powerful but very short acting opioid. For this purpose piritramide can be given in small incremental boluses intravenously under close supervision of an anesthesiologist.

POSTOPERATIVE NAUSEA AND VOMITING (PONV)

Nausea and vomiting can occur after any type of operative procedure under general anesthesia. Ocular surgery is reputed to be emetic in both children and adults. Van den Berg et al. (20) stated that intraocular surgery had no higher incidence of postoperative nausea and vomiting than other superficial operations. In contrast squint surgery is being complicated by a high incidence of postoperative vomiting. Many variables influence the incidence of PONV after strabismus surgery: age, sex, agents used for induction of anesthesia, postoperative use of opioids, intraocular pressure, use of nitrous oxide, ventilation strategies, operation on both eyes etc. In some studies very high incidences of 50 to 83 % are reported. Van den Berg et al. (20) found clinical evidence for the existence of an oculo-emetic reflex which is stimulated by intra- and postoperative manipulation of the extraocular muscles.
Odansetron is an agent from the class of 5-hydroxytryptamine receptor antagonists and has already shown to be very efficacious to prevent and treat PONV after different types of surgery (11). Sadhasivam et al. (18) demonstrated that the prophylactic use of 75 μg/kg odansetron was effective in the prevention of postoperative nausea and vomiting in children undergoing strabismus repair. This strategy reduced the incidence from 83 % to 30 %. By far the lowest incidence of PONV (7%) was found in the study evaluating clonidine premedication 4 μg/kg compared with diazepam 0.4 mg/kg before sevoflurane anesthesia. (8) Without clonidine intervention the incidence of PONV was 33%.

Table 2: *Multimodal pain management in adult patients.*

Multimodal analgesia
Locoregional analgesia
+
Optimal use of paracetamol
IV up to 4 x 2 gr
PO up to 4 x 1 gr (effervescent)
+
NSAIDs: Ibuprofen
PO up to 3 x 400 mgr
+
Opioid: piritramide
IM up to 4 x 0.25 mgr/kg

CONCLUSION

Postoperative course of most ophthalmic procedures is seldom complicated by severe postoperative pain. Locoregional eye block with long-acting local anesthetics is able to blunt postoperative pain for several hours. The effervescent formula of paracetamol is very effective when it is used in sufficient dosages and frequent intervals. Intravenous propacetamol can be used as an alternative to rectal administration of paracetamol, especially for children in the immediate postoperative period where oral intake is difficult and an IV infusion is still available. NSAIDs are effective agents but their use is still limited by side effects. In some case we need tramadol or an opioid like piritramide (Table 2). In treating postoperative pain close supervision of the ophthalmologist is necessary in order to detect and avoid postoperative complications of bacterial endophthalmitis or rise in intraocular pressure.

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