

# How Safe Is it to Use Nonsteroid Anti-inflammatory Drugs for Post-tonsillectomy Analgesia in Children? Implications for Clinical ENT Practice

Petros V. Vlastarakos<sup>1</sup> Efterpi Michailidou<sup>2</sup> Konstantinos Chondrogiannis<sup>3</sup>

<sup>1</sup>Department of ENT, MITERA Infirmary, Athens, Greece

<sup>2</sup>Department of ENT, Attikon University Hospital, Athens, Greece

<sup>3</sup>Department of Anaesthesiology, MITERA Infirmary, Athens, Greece

Address for correspondence Petros V. Vlastarakos, MD, MSc, PhD, IDO-HNS (Eng.), Department of ENT, MITERA Infirmary, 6 Erythrou Stavrou Str, Marousi, Athens 11523, Greece (e-mail: pevlast@hotmail.com; pevlast@yahoo.gr).

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Tonsillectomy is one of the most commonly performed operations in children, often associated with considerable postoperative pain, necessitating respective pharmacological management.<sup>1</sup> Nonsteroidal anti-inflammatory drugs (NSAIDs) are an attractive option for the control of post-tonsillectomy pain, as they demonstrate satisfying analgesic effect, without commonly encountered opioid-related adverse effects. However, NSAIDs inhibit platelet function, and this property may cause understandable concerns, as to the safety of their use in post-tonsillectomy analgesia.

Indeed, critical outcomes of tonsillectomy in children represent areas of major concern, and their monitoring is a determinant of quality for the surgical care provided. In this context, post-tonsillectomy hemorrhage may, on one hand, represent a common emergency encountered in ENT surgical practice, affecting 2.5 to 4.1% of patients with normal coagulation studies,<sup>2</sup> yet factors potentially implicated with its occurrence need to be identified, since it could prove fatal in 1:15000 to 1:40000 cases.<sup>3,4</sup>

Regarding the control of post-tonsillectomy pain, the major analgesic effect of NSAIDs is exercised through the inhibition of prostaglandin synthesis, thereby blocking the stimulation of nociceptors in the peripheral nervous system; this action is materialized through the reversible inhibition of the cyclo-oxygenase enzyme (COX). There are two separate COX isoenzymes, a constitutive one (COX-1), which is involved in platelet aggregation (thrombogenesis), and an inducible one (COX-2), primarily associated with inflammation.

As depicted in **Fig. 1**, a key determinant of thrombogenesis, apart from the platelets, is the presence of thromboxane A<sub>2</sub> (TxA<sub>2</sub>). However, nonselective COX inhibitor analgesic action results in undesirable TxA<sub>2</sub> inhibition, and reasonable concerns about the safety of NSAIDs in post-

tonsillectomy analgesia. Yet, given the clinical reality that most tonsillectomy patients do not bleed postoperatively, the debate remains.

Drawing closely on **Fig. 1**, we may observe another effect of nonselective COX inhibition; the synthesis of prostacyclin (PGI<sub>2</sub>) is also inhibited. PGI<sub>2</sub> is a known inhibitor of platelet aggregation. Hence, its blockage may theoretically facilitate the formation of the platelet plug.

Taking the aforementioned into account, we can surmise that with the exception of aspirin, which irreversibly acetylates COX for the entire lifespan of the platelets (10–14 days), and is anyway contraindicated in children under the age of 12, NSAIDs could be considered in the analgesic management of post-tonsillectomy patients, given that their effect on platelet function lasts approximately as long as they remain in sufficient concentrations in the blood<sup>5</sup> (i.e., 6–8 hours for ibuprofen<sup>6</sup>), and that they have not been associated with increased risk of post-tonsillectomy hemorrhage, readmission, or need of reoperation due to post-tonsillectomy hemorrhage, in a meta-analysis of 1,446 adult and 1,747 pediatric patients.<sup>7</sup> However, as the relative effect of a given NSAID on TxA<sub>2</sub> and PGI<sub>2</sub> formation cannot be determined so far, and given the fact that selective COX-2 inhibitors are not produced in liquid form for pediatric use, NSAID discontinuation after the fifth day of oral administration may be prudent, in order for the child to retain his/her full platelet aggregation potential between the sixth and tenth postoperative days, when most post-tonsillectomy hemorrhages are encountered. The aforementioned reservations seem to be further justified, by the increased odds ratio of postoperative bleeding (OR = 2.02) in patients only postoperatively receiving NSAIDs, in the meta-analysis mentioned above.<sup>7</sup> NSAID administration should also be avoided in patients prone to postoperative bleeding,

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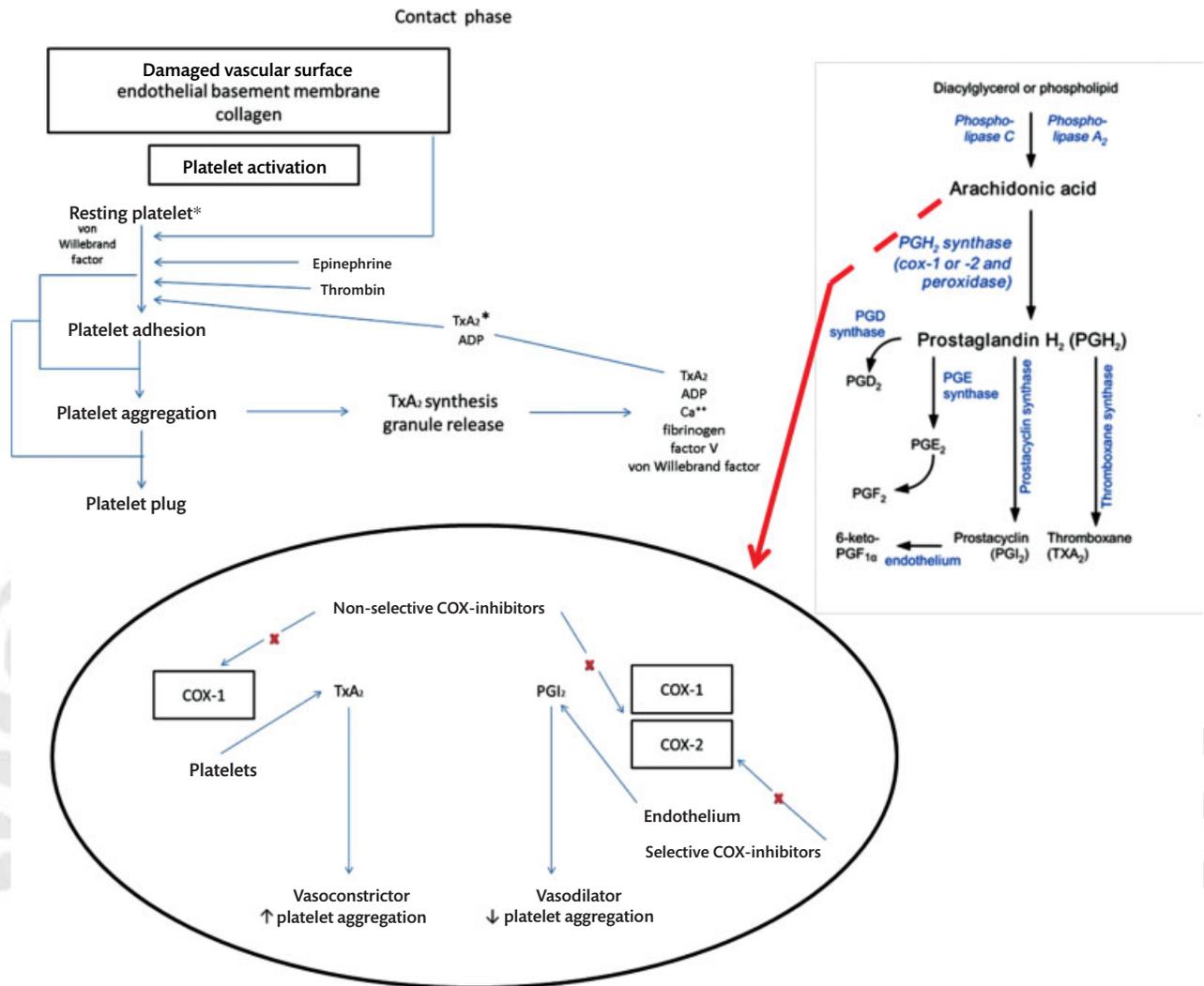
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**Fig. 1** Synthesis of the eicosanoid signaling molecules, formation of the platelet plug (upper-left quadrant, the central position of the platelets, and thromboxane  $A_2$  [ $TxA_2$ ] is marked with an asterisk), and effect of nonsteroidal anti-inflammatory drugs on  $TxA_2$  and prostacyclin ( $PGI_2$ ) synthesis (lower half). COX, cyclo-oxygenase enzyme.

whereas acetaminophen may safely be administered during the entire postoperative period.

#### Ethical Approval

This article does not contain any studies with human participants or animals performed by any of the authors.

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#### Conflict of Interest

None declared.

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