BJA

*British Journal of Anaesthesia*, 115 (5): 688–98 (2015)

**doi: 10.1093/bja/aev348**
Review Article

# Aspirin and spinal haematoma after neuraxial anaesthesia: Myth or reality?

R. S. Vela Vásquez* and R. Peláez Romero

Department of Anesthesiology, Reanimation and Pain Therapeutics, Son Llàtzer Hospital, Palma de Mallorca, Islas Baleares, Spain

*Corresponding author: E-mail: velarolando@hotmail.com, rsvela@hsll.es



## Abstract

The safety of aspirin therapy in neuraxial anaesthesia has been historically questioned, and the current recommendations are still heterogeneous. A comprehensive review of clinical evidence and a comparative analysis of European and American guidelines were performed. Low-dose aspirin produces a selective, complete and irreversible cyclooxygenase-1 blockade, and higher doses do not increase the antiplatelet effect. Additional cyclooxygenase-2 blockade by high-dose aspirin might decrease the antithrombotic efficacy by inhibiting endothelial prostacyclin synthesis. Different doses of aspirin have been shown to be safe in a broad population subjected to neuraxial anaesthesia or analgesia. In the few case reports of spinal haematoma involving aspirin therapy, additional complicating factors were present. Considering the available evidence, the majority of national scientific societies agree that the isolated use of aspirin does not increase the risk of spinal haematoma and does not represent a contraindication to neuraxial blocks. The precautions regarding higher doses do not seem to be justified. Although aspirin alone is considered to be safe in neuraxial anaesthesia, the concurrent administration of other antithrombotic drugs significantly increases the risk of spinal haematoma and the recommended safety times for each of these other drugs must be strictly followed. An individualized assessment of the risks and benefits should be performed, before performing a neuraxial technique or catheter removal in a patient receiving aspirin.

**Key words:** anesthesia, epidural; anesthesia, spinal; aspirin; spinal haematoma; platelet aggregation inhibitors

**Editor's key-points**

- In this review article, the authors explore the evidence base supporting our clinical practice in neuraxial anaesthetic techniques in patients taking aspirin.
- They explore the pharmacology of aspirin, and describe its impact on the risk of neuraxial bleeding.

Spinal haematoma is an infrequent but potentially catastrophic complication of neuraxial anaesthesia. The incidence was previously estimated at about 1/150000 in epidural anaesthesia and 1/220000 in spinal anaesthesia.[1–3] However, more recent data suggest that the frequency is increasing.[4–12]

Aspirin is the most recommended antiplatelet therapy in primary or secondary prevention of atherothrombotic vascular disease.[13–17] Likewise, it is the most widely used antiplatelet drug in perioperative period. In non-cardiac surgery, approximately 18% of patients receive antiplatelet drugs, of which, 82% have treatment with aspirin.[18] In a population with a greater risk of perioperative cardiovascular complications, the use of aspirin reaches 36–44%.[19–20]

Aspirin therapy has been associated with haemorrhagic complications into the spinal canal after neuraxial anaesthesia, resulting in the development of some precautions related to their use.[21–23] Although recently there has been a substantial change in the safety criteria regarding aspirin use, the recommendations of the national scientific societies are still heterogeneous.[24–32] Aspirin is an important component of many patients' treatment and their withdrawal can increase the risk of perioperative

vascular events.[33–37] On the other hand, neuraxial anaesthesia is a widely used technique, with some advantages related to general anaesthesia.[38 39] Proper knowledge can reduce the risk of unnecessary suspension of aspirin or avoid the rejection of a potentially beneficial anaesthetic technique.

For clarifying the safety of aspirin in neuraxial anaesthesia, we performed an exhaustive review of the published literature through PubMed and Medline, from 1995 until October 2014, with the key words: aspirin, antiplatelet, antithrombotic, regional anaesthesia, spinal anaesthesia, epidural anaesthesia, neuraxial blocks, spinal haematoma, and epidural haematoma. A comparative analysis of European and American scientific societies' guidelines was also performed. Additional literature was obtained from the references in the selected articles.

## Pharmacological considerations

Aspirin inhibits platelet aggregation by irreversible acetylation of platelet cyclooxygenase-1 (COX-1), thus blocking the formation of thromboxane A2, a potent platelet aggregation agonist. Because the platelets are enucleates and cannot synthesize cyclooxygenase-1 de novo, this effect persists until the affected platelets are replaced, a process that takes approximately seven to 10 days.[40–44] Although megakaryocytes are also affected by aspirin, these can regenerate cyclooxygenase-1 within 12 h.[45]

Aspirin is rapidly absorbed in the upper gastrointestinal tract, reaching peak plasma concentrations 30–40 min after ingestion, with a half-life of 15–30 min. However, three to four hours are necessary to reach peak plasma concentrations when using enteric-coated tablets.[40 42 44] A dose as low as 30 mg per day is sufficient to completely suppress thromboxane A2 production in five to seven days, and a dose of 100 mg achieved an almost complete suppression of cyclooxygenase-1 activity at 24 h. The increasing doses only reduce the time to maximum inhibition.[46–48]

Given that platelet replacement is relatively constant, 10–12% of circulating platelets are replaced every day.[40 43 44] However, the recovery of thromboxane A2 biosynthesis is faster than expected by the rate of platelet turnover, with a non-linear relationship between inhibition of platelet COX-1 activity and inhibition of thromboxane A2 biosynthesis.[49–51] *In vivo*, only 20–30% of platelets with normal COX-1 activity are necessary to retrieve the haemostatic function. Thus, 48–72 h after a last dose of aspirin, the clinical effect on the haemostasis practically disappears.[40 44 47 52 53]

Depending on the dose administered, aspirin can produce opposing effects on the haemostatic mechanisms. This phenomenon is related to dose-dependent selectivity of aspirin for inhibition of the two cyclooxygenase isoforms: cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2). Human platelets mainly produce thromboxane A2, a product derived from COX-1, and the vascular endothelium cells mainly produce prostacyclin (PGI2), derived mainly from COX-2. Thromboxane A2 induces platelet aggregation and vasoconstriction, whereas prostacyclin inhibits platelet aggregation and causes vasodilation. Low-dose aspirin preferentially inhibits platelet COX-1, preventing thromboxane A2 production. On the other hand, high-dose aspirin can also inhibit COX-2, decreasing the synthesis of prostacyclin of the vascular endothelium, possibly resulting in a paradoxical thrombogenic effect.[27 29 40 44 54] (Fig. 1)

When the thrombogenic stimulus is weak, platelet aggregation is dependent on thromboxane A2 production, and aspirin can interfere with primary haemostasis. However, when the thrombogenic stimulus is powerful, and is accompanied by thrombin generation and/or collagen exposure, it can produce activation and platelet aggregation without thromboxane A2 formation.[55–59]

Currently, there is no recommended test of platelet function for assessing the antiplatelet effect of aspirin in individual patients.[17 60]

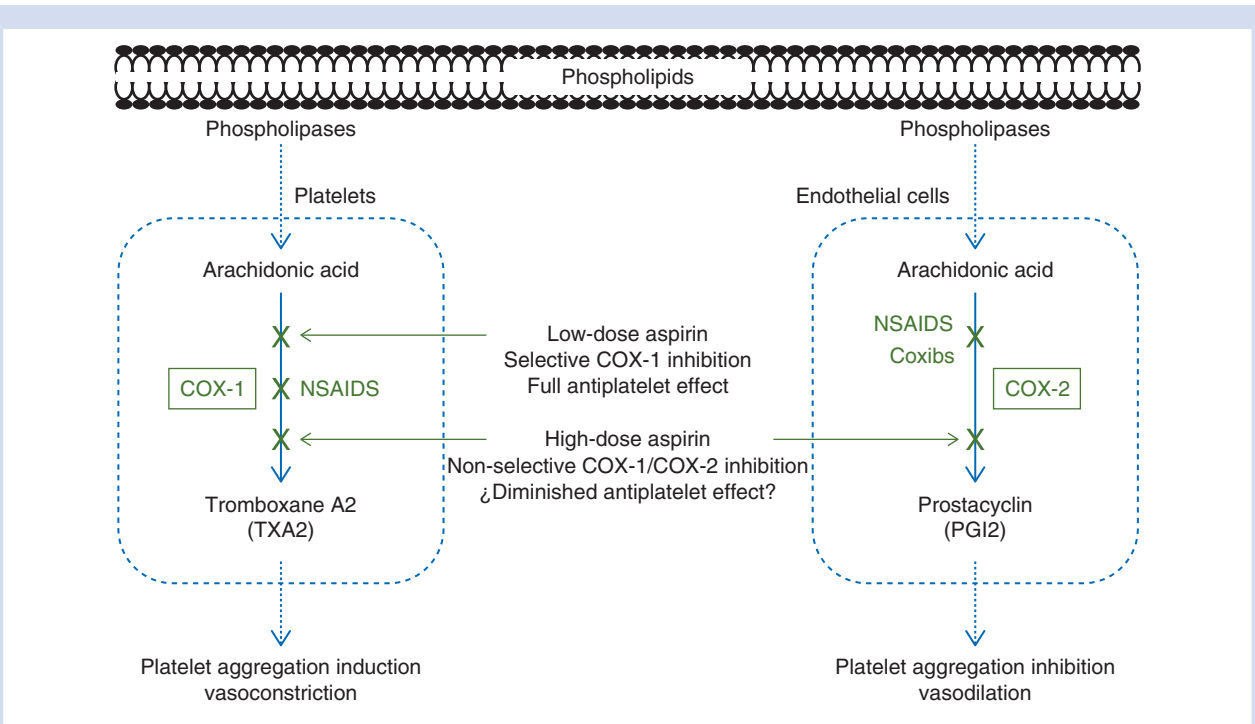


Fig 1 Dose-dependent effects of aspirin on haemostasis. NSAIDs, nonsteroidal anti-inflammatory drugs; Coxibs, selective COX-2 inhibitors.