Aspirin-like defect in platelet secretion on a patient undergoing cardiac valve and coronary graft surgery. Perioperative management

Roberto Julián*, Joaquín J. Valdunciel, José A. Sastre, Clemente Muriel
Servicio de Anestesiología y Reanimación, Hospital Universitario de Salamanca, Paseo de San Vicente 58-182, 37007 Salamanca, Spain

Received 3 August 2003; received in revised form 8 November 2003; accepted 11 November 2003

Abstract
We show the case of an adult male with a previous diagnosis of an ‘aspirin-like’ defect in platelet secretion responses scheduled for cardiac valve surgery. Perioperative management and bleeding prevention were made following experts’ recommendations.

© 2003 Elsevier B.V. All rights reserved.

Keywords: Aspirin-like defects; Perioperative bleeding; Cardiac surgery

1. Introduction
Anaesthesiologists know that haemostasis disorders in surgical inpatients increase bleeding risk due to both surgery and anaesthetic procedures. Despite all the articles published controversy still remains on what the correct attitude should be.

Dealing with primary haemostasis the most frequent disorders are those caused by the use of drugs. A series of disorders based on constitutional platelet diseases, in which we find several grades of severity and, consequently, different risks of bleeding [1] are less common.

The so-called aspirin-like defects receive their name from their similitude with the use of cyclooxygenase inhibitors and belong to this heterogeneous group.

2. Case report
A 69-year-old, 78 kg man, with aortic valvular and coronary disease (proximal stent in right coronary artery and medium portion stenosis) was scheduled for aortic valve replacement and revascularisation surgery. Up to that moment the patient was following treatment with acetylsalicylic acid (ASA) which was interrupted 10 days before the operation day. Two minor haemorrhagic events were reported (scrotal and inguinal haematoma after inguinal herniation surgery and heart catheterisation, respectively) in clinical history. Aspirin treatment had been interrupted 7 days before. Since there were no abnormalities in prothrombin time (PT), activated partial thromboplastin time (APTT) or fibrinogen levels, platelet aggregation tests were requested. Platelet count was normal but responses to weak agonists (adenosine diphosphate and epinephrine) were impaired. As a consequence these data led to a diagnosis of an Aspirin-like defect in platelet function [2] (Table 1).

Anaesthesia was induced with intravenous (i.v.) fentanyl $5 \mu g \text{kg}^{-1}$, etomidate 16 mg and cisatracurium besilate 16 mg. For maintenance fentanyl infusion $4 \mu g \text{kg}^{-1} \text{h}^{-1}$, propofol $4 \mu g \text{kg}^{-1} \text{h}^{-1}$, cisatracurium besilate boluses and $O_2/\text{air}$ were used. Electrocardiogram leads II and V5 with ST segment analysis, pulse oximetry, capnography, invasive blood pressure, central venous pressure, pulmonary artery pressure, pulmonary wedge capillary pressure, cardiac output, urine output, muscle relaxation and transoesophageal echocardiography were monitored.

In an attempt to make a normovolaemic acute haemodilution we proceeded to extract 200 ml of the patient’s blood before starting the intervention. In addition a cell saver was used during surgery. When surgery was finished 450 ml of recovered blood were infused together with the previous 200 ml. Before sternal incision $2 \times 10^6$ Kallikrein Inhibitor Units (KIU) aprotinin were administered followed by another $2 \times 10^6$ KIU aprotinin dose at the beginning of cardiopulmonary bypass (CBP) and a continuous i.v.
infusion at a rate of $5 \times 10^5$ KIU aprotinin till CBP was finished. Since abnormal bleeding was appreciated by the surgeons and because of the possibility of platelet dysfunction after CBP we proceeded to a transfusion of eight units of platelet concentrate as well as 20 $\mu$g of desmopressin (DDAVP) once CBP was finished. Total CBP time was 151 min. A total dose of 240 mg sodium heparin and 200 mg protamine sulphate was used. Baseline and final activated clotting time were 138 and 122 s, respectively.

The patient underwent aortic valve replacement and aorto-coronary bypass (1 proximal, 1 distal) using saphena vein to posterolateral coronary artery branch.

Finally the patient was transferred to the intensive care unit (ICU). Once there, total postoperative bleeding through chest drainage was 410 ml and no blood transfusions were needed. At our institution medium bleeding was 752.32 ml in patients not receiving transfusions and 1292.05 ml in those who were transfused (2.9 red blood cell concentrate units per patient) during that year.

Finally, 36 h after surgery the patient was discharged from ICU with subsequent favourable clinical course.

### 3. Discussion

Platelet constitutional pathology is much less common than the main cause of platelet dysfunction, i.e. the use of drugs. Actually, platelet aggregation and secretion tests are practised if haemorrhagic events are reported in clinical history. A recommended screening method is the use of questionnaires searching for haemostasis disorders in the pre-anaesthetic consulting.

From all plaquetary dysfunctions we can make a distinction between plaquetary membrane adherence defects, lack of intra-plaquetary granules and those characterised by impaired signal transduction when endothelial damage occurs. Two metabolic pathways for cellular membrane phospholipids initiate this signal’s transmission: the inositol and the arachidonic acid one. Aspirin-like defects seem to be caused by an impaired arachidonic acid metabolism [1]. No data are available regarding its incidence in the general population.

The first question to answer is the suitability of the clinical study our patient underwent to reach a correct diagnosis. Aspirin-like defects were first described in 1972 by Weiss [3]; a more precise description appeared in a later work [2]. They found a group of heterogeneous defects in plaquetary response to several agonists including two categories:

- On the one hand, impaired response to weak agonists (ADP, epinephrine and TXA2), i.e., those that produce an aggregation-dependent response. They were called weak agonists response defects (WARDs).
- On the other hand, they found a group of patients who showed a normal response to weak agonists and impaired function in the presence of strong agonists (arachidonate, collagen), i.e., those that produce an aggregation-independent response. Curiously, when collagen is present at low concentrations in the presence of weak agonists the secretory response induced is mainly due to these agonists. In fact, routine tests include aggregation tests in the presence of ADP-collagen and ADP-epinephrine.

In the diagnostic process for this entity aggregation-dependent and aggregation-independent responses are tested, as well as Thromboxane B2 (TXB2) serum levels as a signal of secretory response [4]. An impaired plaquetary aggregation in the presence of weak agonists and decreased TXB2 serum levels characterise WARDs [2]. Responses to weak agonists show a reliable relation to TXB2 serum levels [4], thus this is not a routine test. We can then assume that our patient was submitted to the correct clinical process in the characterisation of his disease.

A second matter to discuss is referred to the clinical attitude for a surgical patient with a Ward. Within the context of cardiac surgery, there are several factors that may lead to haemostasis disorders. It has been demonstrated that CBP causes plaquetary dysfunction and decreased platelet count [5]. These effects are enhanced by the use of heparin for CBP [6]. Thus prevention of perioperative bleeding is a priority in patient’s management.

Antifibrinolytic drugs have shown a decrease in perioperative bleeding [7]. In patients treated with cyclooxygenase inhibitors an improved plaquetary function and fewer blood transfusions can be achieved by the use of desmopressin (DDAVP) [8,9]. Low-dose protamine is used based on heparin–protamine dose titration since it reaches lower impairment of plaquetary dysfunction after CBP [10].

Based on the data expressed above and considering our patient’s context (plaquetary dysfunction, high haemorrhagic risk and subjective appreciation of excessive bleeding) besides the current anaesthetic protocol (use of antifibrinolytic drugs) extra measures were performed such as platelet transfusion and administration of DDAVP. This way we got a successful result with the absence of haemorrhagic events and favourable clinical course.
References


