Anesthesiology and Platelets

With clarification of the mechanisms by which platelets adhere to each other and release their constituents it has become possible to define the effects of a variety of compounds on platelet function. The role of platelets in hemostasis and thrombosis (these two processes are recognized as essentially the same) is now clearly understood, and the effects of a number of drugs on these two processes have been partially explored in animal and human studies. In general, these studies have shown that drugs or compounds that inhibit ADP-induced platelet aggregation also inhibit the extent of experimental thrombosis and can alter the hemostatic process. Drugs or compounds that inhibit the platelet release reaction have also been shown to inhibit experimental thrombosis in animals and to cause a hemostatic defect. Most drugs that inhibit ADP-induced platelet aggregation also block the platelet release reaction. However, some drugs inhibit only the platelet release reaction. It is against this background of information that the article by Ueda should be considered.

The author has found that a number of common volatile anesthetics added to platelet-rich plasma at pressures which correlate with those achieved clinically inhibit ADP-induced platelet aggregation. This observation, while perhaps not surprising, is potentially important. From the practical point of view, the most significant aspect would appear to be the possible effect of these anesthetics on the hemostatic process. Since anesthetics are primarily given in association with surgical procedures, any indication that anesthetics could inhibit hemostasis and thereby enhance blood loss from injured vessels has to be carefully considered. A few surgeons and anesthetists have believed that some anesthetics are more frequently associated with increased bleeding than are others. There has, until now, been no experimental basis for these opinions.

To establish the relative importance of the effects of these anesthetics on the hemostatic process, the studies of Ueda should be extended to include a careful definition of the effect of the volatile anesthetics on the platelet release reaction. This reaction, which is induced by a number of stimuli such as thrombin, collagen, antigen-antibody complexes, and other particulate material, involves release of the contents of the platelet storage granules. One of the most important compounds released is ADP, which causes the platelets nearby to adhere to each other. If it were found that the volatile anesthetics affected not only ADP-induced platelet aggregation but also the release reaction, then they would be altering two of the three primary mechanisms of hemostasis. The hemostatic process is believed to consist of: 1) the interaction of platelets with the injured vessel wall; 2) the release of ADP, followed by its effect in causing platelets in the circulation to stick to each other and to the platelets that are stuck to the vessel wall; 3) acceleration of blood coagulation by the platelet aggregate, leading to the production of thrombin and the formation of fibrin around the platelet mass. Experimentally it has been shown that interference with any one of these three reactions can lead to impaired hemostasis, and interference with two of them causes significant impairment.

Experiments should be carried out to determine whether these volatile anesthetics actually do affect platelet function in vivo. In such studies it should be determined whether ADP-induced platelet aggregation and the release reaction are altered, and concurrent studies should be carried out to determine whether the bleeding time from injured vessels is affected. Since many patients undergoing surgical procedures and receiving anesthetics also receive other medications, the effects of these
other agents on platelet function need to be taken into account. It is now recognized that the non-steroidal anti-inflammatory drugs alter platelet function and can impair hemostasis, particularly in patients with hemophilia or subjects receiving oral anticoagulants. 1-6 A number of other drugs, such as tranquilizers 7 and vasodilators, 8 have been shown to inhibit platelet function. 1 Administration of these compounds to individuals prior to anesthesia could contribute to a hemostatic defect in the presence of an added factor such as a volatile anesthetic which also inhibits platelet function. The list of compounds which affect platelets will probably grow as more and more attention is paid to the effect of drugs on platelets. For example, it is already known that local anesthetics 9 and antihistamines 10 alter platelet function.

Studies with platelets may provide clues to understanding some of the general aspects of cell function that are very difficult to explore in other systems. Similarities have been recognized between the platelet release reaction and the release reactions of other cells, such as those of the adrenal medulla and the posterior hypophysis of the pituitary, leukocytes, and probably neurons. 11, 12 As pointed out by Michal and Firkin in a recent review, 13 “platelets are readily isolated and have great potential usefulness in the study of some of the parameters of drug action.” The elucidation of the mechanisms by which anesthetics affect platelet function might help in explaining their effects on other cells and organ systems.

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References

Drugs

GLUCAGON Administration of glucagon to patients with severe coronary artery disease improved the myocardial extraction ratio of lactate. The left ventricular work index increased 39 per cent above control values obtained prior to the administration of glucagon, with no change in the coronary arteriovenous oxygen difference. Left ventricular dp/dt increased 20 per cent. (Bourassa, M. G., and others: Effects of Glucagon on Myocardial Metabolism in Patients with and without Coronary Artery Disease, Circulation 42: 53 (July) 1970.)