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Pre-operative management of patients on drugs affecting blood coagulation

In contemporary medicine when cardiology and cardiosurgery develop rapidly, the number of patients on drugs affecting blood coagulation is on the increase. Anti-coagulants are applied in the primary prevention of thrombophlebitis before surgery, when other risk factors for thrombophlebitis occur e. g., in cases of long-lasting immobilization, in primary and secondary prophylaxis of ischemic stroke in the treatment of thrombosis of deep venous thrombosis and pulmonary embolism, in the treatment of unstable stenocardia and cardiac infarct, in patients with atrial fibrillation, with artificial cardiac valves, and following cardiovascular by-pass transplants.

The number of patients treated with anti-coagulants increases both in in-patient hospital care and in family practice. Proper monitoring of blood coagulation in patients on anti-coagulants is a doctor«s responsibility, because both excessive hemorrhage and thrombophlebitis may threaten health and life of the patients. This is extremely important when the patient is prepared for the surgery. It should be mentioned that management required for urgent surgery is different from the one for required surgery.

DRUGS AFFECTING BLOOD COAGULATION

Drugs commonly used in medical practice that affect blood coagulation are as follows:

1. Acetylosalicylic acid (Aspirin, Bestprin, Polopiryna S, Polopiryna, Upsarin, combination products: Alka-Prim, Ascodan, Aspirin C, Aspirin Forte, Calcipirina) (7) – prevents platelet formation, inhibits irreversibly the production of thromboxane by inhibition of cyclooxygenase, and this effect lasts till the end of blood platelet life (7–10 days); the effect of other nonsteroidal antiinflammatory drugs (NSAIDs) that inhibit cyclooxygenase may be reversed.
2. Ticlopidine (Aclotin, Ticlid, Ticlo) (7) – one of anticoagulants –inhibits the aggregation of thrombocytes and the release of platelet coagulation factors, extends bleeding time by the inhibition of binding of fibrinogen to thrombocyte membrane; anti-coagulant effect occurs after two days following drug administration, and subsides a week after the drug is withdrawn, its half-life is 30-50 h.
3. Acenocumarol (Acenocumarol, Sintrom) (7) – anticoagulant, antivitamin K, inhibits the synthesis of coagulation factors II, VII, IX, X; its half-life is 8,7 h.
4. Unfractionated heparin, UFH (Calciparine, Heparin, Heparinum) (7) – one of anticoagulants, inhibits blood coagulation by activation of antithrombine III; antithrombine III and the complex antithrombine III combined with heparin are inhibitors of thrombine and Xa factor; its half-life in blood serum is 60–120 min and depends on the dose.
5. Dalteparin (Fragmin) (7) – low molecular weight heparin (LMWH).
6. Enoksaparin (Clexane) (7) – LMWH.
7. Nadroparin (Fraxiparin) (7) – LMWH, strongly inhibits Xa factor, and slightly inhibits IIa

factor; after subcutaneous administration the anticoagulant effect lasts 24 h.

8. Altepase (Actilise, Activase) (7) – tissue activator of plasminogen, fibrinolytic drug, activates the conversion of plasminogen into plasmine that produces fibrine breakdown; its half-life is about 5 min (80% is eliminated within 10 min).

9. Streptokinase (Streptase) (7) – a thrombolitic drug, stimulating fibrinolysis by activating conversion of plasminogen into plasmine; its initial half-life is 10 min, that extends to 80 min; after the withdrawal the process of fibrinolysis is inhibited within several hours.

PRACTICAL GUIDELINES FOR THE PREPARATION OF PATIENTS ON DRUGS AFFECTING COAGULATION FOR THE SURGERY

The patient undergoing surgery, who is on drugs affecting coagulation, should have the following parameters determined: blood platelet count, prothrombin time, kaolin-kephalin time, thrombin time, bleeding time if he is on non-steroid anti-inflammatory drugs and fibrinogen concentration in blood plasma.

ACETOSALICYLIC ACID AND TICLOPIDIN

Acetosalicylic acid and Ticlopidin cause the extension of bleeding time (normal bleeding time is less than 6 min (8)). Before planned required surgery it is recommended to withdraw the administration of acetylosalicylic acid for 5–7 days before the surgery, and Ticlopidin for 10–14 days (6) to avoid the risk of excessive bleeding. In cases requiring emergency or urgent surgery patients taking acetylosalicylic acid or Ticlopidin should be administered the concentrate of red blood platelets to obtain thrombocyte level 75–100,000mm^3, if the excessive bleeding occurs. Following administration of 1 unit of the concentrate of red blood platelets the level of thrombocytes increases by 5–10,000mm^3 (6).

UNFRACTIONATED HEPARIN (UFH) AND LOW MOLECULAR WEIGHT HEPARINS (LMWH)

Monitoring the treatment with UFH is based on determining kaolin-kephalin time (normal value at 37° C is 30–50 sec (8)). There is no need to determine kaolin-kephalin time when LMWH is administered. A possible, but rare complication is thrombocytopenia following the treatment with heparin (1, 10). LMWH should be withdrawn 24 h before planned surgery, and UFH should be withdrawn 4–6 h before the surgery. If the risk of thrombophlebitis is very high and the risk of bleeding is low, heparin is administered in preventive doses (5). If it is necessary to reverse the effect of heparin quickly, it may be obtained by administering 1 mg of protamine (2, 3) per every 100 units of heparin. Taking into account adverse side effects (decrease in blood pressure, sensitivity to the drug) protamine should be administered slowly. In operated patients where antithrombotic prophylaxis is required, the following drugs are administered alternatively: UFH – 5,000 U subcutaneously 1–2 h prior to surgery, dalteparin – 2,500 U subcutaneously 1–2 h prior to surgery, enoxaparin – 20 mg subcutaneously 1–2 h prior to surgery, or 40 mg 12 h prior to surgery, nadroparin 2,850 U subcutaneously 2–4 h prior to surgery (9). Antithrombotic prophylaxis in the post-operative period depends on the risk of complications resulting from thrombus and embolus in particular patients (usually from 3–5 days up to 1 month, and sometimes longer).

ACENOCUMAROL

Checking the effectiveness of treatment with Acenocumarol is based on determining the prothrombine time (normal value 13–18 sec) or International Normalized Ratio (INR) recommended

by WHO (in healthy individuals 0.7–1.5 (8)). Acenocumarol is withdrawn 3–5 days prior to the surgery. Antithrombotic treatment is continued by subcutaneous administration of LMWH or UFH in intravenous infusion. On the day preceding the surgery INR should be determined (it should be 1.3–1.5). If INR is elevated, small doses of vitamin K_1 (from 1 to 4 mg orally) should be administered. The effect of vitamin K on coagulation following oral administration is observed after 6 h (2). After several hours – more than 10 – normalization of INR may be obtained. If emergency surgery is required, transfusion of fresh frozen plasma or the concentrate of coagulation factors of prothrombine complex is performed. Preventive administration of 1,200–2,400 U of the concentrate of coagulation factors of prothrombine complex is recommended (6). In patients with artificial mitral valve acenocumarol is withdrawn 1–2 days before the surgery and vitamin K is administered orally (4). Simultaneously, taking into account a high risk of thrombophlebitis, heparin is administered 12 h prior to the surgery. In patients with mitral valves of old type it is recommended to withdraw oral coagulants several days before the surgery and antithrombotic prophylaxis is continued by administering heparin (4).

ALTEPLASE AND STREPTOKINASE

Fibrinolytic drugs extend the thrombine time (normal value 17–24 sec (8)) and decrease the fibrinogen level (normal value 2–4.5 g/l (8)). After the administration of fibrinolytic drugs the surgery should be delayed over 24 h (10). If urgent surgery is required, the surgery should be delayed about 20 min after administering Altepase. Low fibrinogen level that may be observed for 24–36 h is supplemented by administering fresh frozen plasma or cryoprecipitate (3), compatible with ABO antigenes without considering Rh factor. Fresh frozen plasma contains all coagulation factors. The average dosage of fresh frozen plasma is 8–10 ml/kg of the body weight (6). Obtaining fibrinogen level over 1 g/l is recommended. The indication for the transfusion of fresh frozen plasma prior to the surgery is the level of prothrombine time exceeding 1.5 -fold standard time or kaolin-kephalin time (6).

The cryoprecipitate transfusion is performed depending on the fibrinogen content. The amount of cryoprecipitate for transfusion depends on the fibrinogen content 1–4 packages per 10 kg body weight (1 package of kryoprecipitate may contain from 100 to 200 mg of fibrinogen). If, after administering Streptokinase it is necessary to perform the surgery, fresh frozen plasma or cryoprecipitate is administered to compensate the level of fibrinogen. Apart from that, if urgent surgery is necessary, after administering fibrinolytic drugs the administration of a dose of 6.0 g of EACA may be considered, and then 1 g every hour (2, 10).

In hospital practice an internist is responsible for the evaluation of patient's condition before the patient undergoes surgery. A full medical consultation in a surgical ward includes the evaluation of the efficiency of the circulatory system, respiratory system, biochemical parameters including blood electrolite level and coagulation ability. The responsibility of the consultant is to prepare the patient for the surgery so that his life is not in danger during the surgery e. g., as a result of massive hemorrhage.

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SUMMARY

The aim of the study is to present practical guidelines for the pre-operative management of patients taking commonly applied drugs that affect blood coagulation. In hospital practice it is the responsibility of an internist to evaluate the patient's condition before the patient undergoes surgery. Among the patients consulted by the internist prior to the surgery the number of patients taking the drugs affecting coagulation is on the increase. The surgery performed on these patients carries the increased risk of bleeding that may threaten health or even life of the patient.

Przygotowanie do zabiegu operacyjnego chorych przyjmujących leki wpływające na układ krzepnięcia krwi

Celem pracy jest przedstawienie praktycznych wskazówek, które dotyczą przygotowania do zabiegu operacyjnego chorych przyjmujących najczęściej stosowane leki wpływające na układ krzepnięcia krwi. W praktyce szpitalnej lekarz internista staje przed codzienną koniecznością oceny stanu zdrowia pacjenta w celu przygotowania do zabiegu operacyjnego. Wśród pacjentów konsultowanych internistycznie przed zabiegiem operacyjnym jest coraz większa grupa chorych przyjmujących leki wpływające na układ krzepnięcia krwi. Operacje u tych chorych łączą się ze zwiększonym ryzykiem krwawienia, które może stanowić zagrożenie dla zdrowia, a nawet życia pacjenta.