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To decrease the risk of iatrogenic thromboembolic complications during interventional procedures with coaxial catheter systems, aspirin and systemic heparinization were used in 57 consecutive cases. No thromboembolic complications occurred. This group was compared with a second group of 25 patients who also had interventional procedures with coaxial systems but who had only a continuous heparinized drip infusion flushing the inside of the coaxial system. Two patients had an embolic complication and two others had thrombus formation inside or outside the catheters without neurologic symptoms. The use of systemic heparinization has been extended to all prolonged angiographic procedures except in cases of acute or recent subarachnoid hemorrhage.

Iatrogenic thromboembolism has become a major complication of vascular catheterization, cardiopulmonary oxygenators, dialysis membranes, vascular grafts, etc. It is the most catastrophic event occurring in diagnostic and interventional angiography. During interventional angiography, the combination of prolonged catheterization time and the manipulation of catheters of a large caliber (7–8 French) containing inner small catheters in a coaxial system considerably increases the risk of thrombus formation inside and outside the catheter lumens.

Even with the use of heparin-coated guide wires and catheters and the concomitant flushing with heparinized solution [1–14], we have had embolic complications in patients undergoing extra- and intracranial therapeutic embolizations. Many authors are using heparin and acetyl salicylic acid (ASA) to prevent thrombus formation [15–25]. We describe our technique of systemic heparinization and ASA premedication, and its use in prolonged diagnostic and therapeutic angiographic procedures when a coaxial system and manipulation of large catheters are mandatory.

Clinical Materials and Methods

Two groups of patients undergoing prolonged interventional procedures with coaxial systems were studied. In group A, for 25 interventional procedures, a catheter infusion containing heparinized saline and aspirin solution was used. In group B, for 57 consecutive interventional procedures, systemic heparinization was added.

In the 82 patients, traumatic carotid-cavernous fistulas, vertebral fistulas, or unclippable aneurysms were treated by embolization with detachable balloons. A system of three coaxial catheters was required in all cases. The catheter introducer (7 or 8 French) was positioned in the internal carotid or vertebral artery and through it a coaxial system consisting of a 0.8 × 1.1 mm polyethylene catheter containing a Teflon catheter of 0.4 × 0.6 mm with the balloon attached at the tip was passed. The procedures lasted 3–4 hr.

Technique and Results

Group A

In 25 consecutive interventional cases during a 3 year period, only catheter infusion (1,000 U of herapin diluted in 500 ml of normal saline at an approximate rate of 250 ml hr) was used. When using a Cordis sheath with a second drip infusion, this amount was doubled. To each 500 ml bag of saline, 1 g of acetyl salicylate of lysine (Aspegic) was also added. When Aspegic was not available, the patient was given 1 g of aspirin 1 hr before the procedure.

The partial thromboplastin time (PTT) was measured [26, 27]: intraarterial samples of blood were taken at zero time immediately before flushing the introducer or the Cordis sheath with heparinized infusion at every half hour until the end of the procedure and then 30 min after removal of the introducer from the groin or neck.

In most cases, PTT levels were about 60 sec (fig. 1), and the range was considered to be therapeutic (40–70 sec). Nevertheless, we had two embolic complications in this group, and demonstrated clot formation within the catheter in two other cases. The two embolic complications both occurred after detachment of the balloons (two balloons in one case) in patients with giant cavernous carotid aneurysms. Both cases were difficult, requiring long procedures. In the first case, after detachment of the second balloon and removal of the coaxial system from the introducer, angiography demonstrated an embolus in the right middle cerebral artery. The patient had a left hemiparesis but total recovery occurred in a few hours. In the second case, a left-sided giant cavernous aneurysm was occluded with a silicone-filled balloon. The carotid blood flow was preserved but the balloon stenosed the carotid siphon. After detachment of the balloon, the patient became dysphasic with right arm weakness and the angiogram showed an embolus in the left middle cerebral artery. The patient had a partial recovery but exhibited a permanent minor motor deficit and dysphasia. Computed tomography (CT) showed an infarct in the left middle cerebral artery distribution.

Thrombi were seen in two other patients. In one patient, after detachment of the balloon but before obtaining the angiogram, a long thrombus was aspirated from the introducer (fig. 2). In the second case, the angiogram demonstrated the existence of thrombi around the introducer (fig. 3). No complications occurred in either of these two cases.

Group B

In group B, the PTT levels were purposely maintained above 110 sec (fig. 4). As soon as the Cordis sheath was positioned in the femoral artery, a bolus injection of 2,000 U of heparin was given intravenously. The Cordis sheath, as well as the introducer, were then perfused with an infusion of 3,000 U of heparin diluted in 500 ml of saline, and every hour a new bolus of 1,000 U of heparin was injected intravenously. PTT samples were taken immediately before the injection of the first bolus of heparin, every half hour to the end of the procedure, and 30 min after having reversed
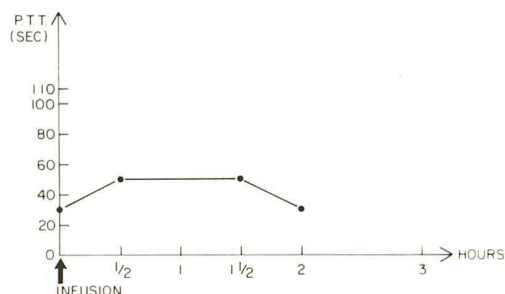

Fig. 1.—PTT levels (normally 27–29 sec) below 60 sec with heparinized drip infusion only (1,000 U of heparin in 500 ml of saline).
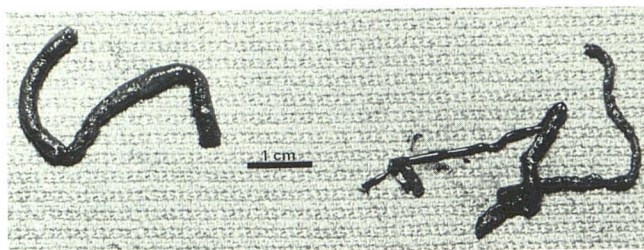

Fig. 2.—Thrombus removed from introducer during treatment of cavernous carotid aneurysm with coaxial system. Systemic heparinization was not carried out.

the systemic heparinization with protamine sulphate. Ten mg (1 ml) of protamine sulphate immediately neutralizes 1,000 U of circulating heparin. We injected an amount of protamine sulphate approximately equal to two-thirds the number of a thousand units of heparin that had been injected. For example, if 15,000 U of heparin had been injected, we intravenously injected 10 ml of protamine sulphate and waited 5 min before removing the Cordis sheath. A local compression time at the puncture site of 10–30 min was necessary to control bleeding, but this time was not different from the group A patients who had had only partial heparinization.

All of these patients were also given 1 g of aspirin at bed time the night before and 1 g of aspirin 1 hr before the procedure if there was no contraindication to aspirin. No embolic complication occurred in this group of patients and we never encountered a thrombus in the introducer on aspiration before angiography.

Discussion

It has been repeatedly stressed in the literature that there is a strong and direct relationship between the size of catheters and introducers, the duration of the procedures, and the appearance of iatrogenic thromboembolic complications [10, 13, 18, 20].

It has also been demonstrated that the introduction of artificial surfaces into the blood stream (catheters and wires

Fig. 3.—Treatment of ioatrogenic vertebral fistula. Thrombus outside introducer positioned in vertebral artery. Systemic heparinization was not carried out.
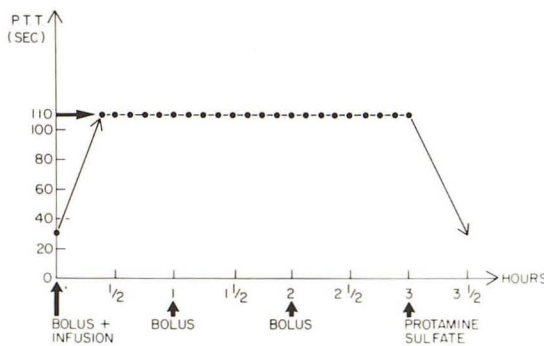

Fig. 4.—PTT levels above 100 sec with heparinized drip infusion and bolus of heparin every hour.

in our case) promotes formation of thrombi [8, 11–13]. The pathogenesis of such thrombogenic response has not been defined, and no synthetic material has been produced that is totally free from the activation of some clotting processes leading to concomitant platelet adhesion and aggregation.

The adsorption of fibrinogen to artificial surfaces occurs very rapidly and it is probable that this protein, factor VIII, and "the contact factor" are of major importance in the development of a fibrin thrombus [7, 17]. This fibrin throm-

bus apparently mediates platelet adhesion and from this a small fibrin-platelet thrombus may develop.

All these early mechanisms of thrombus formation are readily amplified by the so-called "platelet-release reaction" [8]. After adhesion and aggregation upon the foreign surface, platelets release agents such as prostaglandins and thromboxane that increase the effect of the stimulatory agents which are released originally [7, 17].

To prevent clot formation, different authors have advocated: (1) a "local approach" (the use of heparin-coated catheters and wires) [1, 3, 6, 11, 14], (2) a systemic approach (use of heparinization [2, 13, 18, 24, 28] and/or aspirin [16, 18, 21] as premedication), or (3) a combination of both techniques.

Heparin, the most widely used agent for immediate anticoagulation, decreases blood coagulation by potentiating the inhibitory effect of antithrombin 3 on thrombin and other proteins involved in the clotting mechanism. It also decreases platelet aggregation and release, which is induced by thrombin [19, 22, 29–31). These two effects of heparin are now believed to be the primary mechanism of its action.

Platelet aggregation and release reactions are inhibited after the injection of aspirin, probably through inhibition of the synthesis of prostaglandins and thromboxane. This inhibition can be detected for 4–7 days after administration of 0.3–1.5 g of the drug, which has an irreversible effect on all platelets circulating at the time of administration [30, 32, 33].

All the factors, previously described, that increase the risk of thrombus formation in or on catheters are acting during interventional procedures. We now always use aspirin and systemic heparinization, heparin-coated catheters and guide wires, vigorous aspiration of the introducer (with a 20 ml syringe) and aspiration of 10 ml of blood before each injection, and permanent perfusion of the introducer with a heparin solution, either with a pressure bag or a pump.

We initially used systemic heparinization in all our cases of cerebral arteriovenous malformations embolized with bucrylate using a Silastic calibrated-leak balloon. There were five instances of dissection in single feeding vessels of the arteriovenous malformations with consequent subarachnoid bleeding. Two of these occurred in patients under systemic heparinization. We immediately reversed the heparinization with protamine sulphate and the patients recovered. We have since been using a new Latex "calibrated-leak" balloon, which, when inflated, does not overdistend the vessel. There have been no dissections and we have resumed using systemic heparinization during our embolizations with bucrylate.

Contraindications to the use of systemic heparinization are recent subarachnoid hemorrhage or any hemorrhage diathesis. In our experience, systemic heparinization has not produced a hemorrhagic diathesis or the need for prolonged local compression at the puncture site.

Convinced that systemic heparinization was advantageous in our interventional cases, we extended its use to all routine cases in atherosclerotic patients who needed a

complete study of both carotid arteries, both vertebral arteries, and the aortic arch. Since we replaced the double flush technique by continuous infusion of heparinized saline (1,000 U of heparin in 500 ml of saline), the number of neurologic complications that could be related to emboli decreased from 3.4% to 0.75%, and it is our feeling that systemic heparinization is one of the main factors explaining this difference.

The use of local and systemic anticoagulation plus proper catheter manipulation and flushing is important in the prevention of iatrogenic thromboembolism. We also feel that the combination of premedication with aspirin and systemic heparinization has an important role in the prevention of these complications when prolonged intravascular procedures using coaxial systems and large catheters are performed. If systemic heparinization is not contraindicated, we use it for all angiographic procedures.

We believe that the risks of systemic heparinization are far outweighed by the benefits of decreased thrombus formation associated with introducers, catheters, and guide wires except in cases of recent subarachnoid hemorrhage. Therefore, we recommend this regime for diagnostic neuroangiography and for interventional neuroradiologic procedures.

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