Article
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Bridge-therapy with enoxaparin in the preoperative period of endarterectomy

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ABSTRACT
Cervical clot is one of the complications of endarterectomy. This risk may be higher in patients using aspirin or clopidogrel. On the other hand, stroke may occur if the medication is interrupted before surgery. We carried out a prospective study of 124 endarterectomies in 119 patients in which aspirin or clopidogrel was stopped and a bridge-therapy with enoxaparin was administered preoperatively. There was no case of stroke during the period of the bridge-therapy. One patient developed cervical clot (0.8%) in the fifth postoperative day. Mortality rate in this series was 0.8%. There was no complication directly related to the use of enoxaparin. Bridge-therapy with low molecular weight heparin is a safe strategy for patients elected for endarterectomy.
Key words: antiplatelet drugs, cervical clot, endarterectomy, enoxaparin, stroke.

Terapia-ponte com enoxaparina no período pré-operatório da endarterectomia

RESUMO
Hematoma cervical é uma das complicações graves de endarterectomia. O risco dessa complicação pode ser maior em pacientes em uso de antiagregante plaquetário. Por outro lado, a suspensão de antiagregante plaquetário no período pré-operatório de endarterectomia eleva o risco de acidente vascular cerebral (AVC). Realizamos estudo prospectivo de 119 pacientes submetidos a endarterectomia (124 procedimentos), nos quais foi suspenso antiagregante plaquetário (aspirina ou clopidogrel) e foi administrada terapia-ponte com enoxaparina subcutânea no período pré-operatório. Nessa série, não houve ocorrência de AVC no período pré-operatório. Um paciente (0,8%) desenvolveu hematoma cervical no quinto dia pós-operatório. A mortalidade nessa série foi de 0,8%. Não houve nenhuma complicação atribuída diretamente ao uso de enoxaparina. A terapia-ponte com heparina de baixo peso molecular demonstrou ser estratégia segura no preparo de pacientes para endarterectomia
Palavras-chave: antiagregante plaquetário, AVC, endarterectomia, enoxaparina, hematoma cervical.

One of the most dangerous complications of endarterectomy is cervical clot that may obstruct the airways with high risk of death, if the clot in not promptly diagnosed and surgically evacuated.

The interruption of treatment with antiplatelet drugs in the preoperative period of endarterctomy is one of the strategies used to avoid this complication. However, this strategy means to interrupt the best medical treatment for severe carotid stenosis with potential risk of stroke in this period.

The objective of this paper is to evaluate the efficacy of bridge-therapy with low molecular weight heparin, enoxaparin, in the preoperative period of endarterectomy. The rate of stroke in this period and the development of cervical clot in the postoperative period were evaluated in this series.

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METHOD

The charts with prospectively collected data of 128 patients submitted to endarterectomy between January 2002 and May 2008 at Biocor Institute were evaluated. All patients signed the informed consent upon admission and the study was approved by the Hospital Ethics Committee. All patients had 70% or more degree of carotid stenosis disclosed by duplex scan and confirmed by angioMRI or angio TC of the carotid and vertebral systems. 124 procedures in 119 patients were included in this search. All patients received bridge-therapy with subcutaneous injection of 40 mg/day enoxaparin, five days before the procedure. Patients without adequate follow-up and those that did not receive bridge-therapy were excluded. After local anesthesia (111 patients) or general anesthesia (8 patients) 50 Ul/kg of heparin was administered intravenously. Reversion of heparin was not used after the procedure. In the first postoperative day, after withdrawal of the drainage system (BioVac, PE, Brasil) Aspirin (325 mg/day) or clopidogrel (75 mg/day) were orally administered. All complications were evaluated, with special enfasis in the development of cervical clot and the rate of stroke in the peroperative period. Data were collect in excel (Microsoft) and exported to EPI INFO 2000 for statistical analysis.

RESULTS

124 endarterectomies were performed in 119 patients, 82 male and 42 female. Bilateral surgery was performed in five cases. The interval between bilateral procedures was always superior to 30 days. The mean age was 71.5 years (standard deviation 9.0). The mean time of cross-clamping of the carotid artery ranged from 12 to 60 minutes, mean time of 23.85 minutes (standard deviation of 8.73). Six patients (4.8%) developed transient neurological deficit. Shunt was used in 3 of these patients (2.4%).

There were no strokes in the period of the bridge-therapy with enoxaparin. Cervical clot surgically evacuated occurred in one case (0.8%), without neurological or clinical repercussion. In the postoperative period four cases of stroke ipsilateral to the endarterectomy were diagnosed (3.2%). One patient died due to clinical complications after a stroke (0.8%). There was one case of asymptomatic myocardial infarction (0.8%) diagnosed 30 days after the procedure, during regular cardiological consultation.

DISCUSSION

One of the problems regarding the indication of endarterectomy is whether or not interrupt antiplatelet therapy in the preoperative period. Since antiplatelet therapy interferes definitively in the function of a pool of platelets without possibility to reverse its effects, the use of aspirin and/or clopidogrel raises the risk of hemorrhagic complications of surgical procedures. Cervical clot is one of the most dangerous complications of endarterectomy, since it obstructs the airway with risk of death. Surgical drainage in emergency basis is mandatory.

Chiesa et al.[1], in a large series of 5425 endarterectomies report 20 deaths (0.37%), one of them due to respirator failures caused by cervical clot.

Welling et al.[2] reported a 1.9% rate of cervical clot in a series of 1222 patients submitted to endarterectomy. The medical charts of 23 patients that required surgical drainage for cervical clot were compared with 122 patients without this complication, chosen randomly, with the objective to identify factor that could facilitate the development of cervical clots. Hypertension in the postoperative period was significantly higher in the group with hematoma, compared with the control group. More patients received antiplatelet drugs in the preoperative period in the group with cervical clot (43% versus 25%)

De Sousa et al.[3], in a series of 175 consecutive cases of endarterectomy reported a 5.7% rate of cervical clot. In three of these cases (1.7%) the clot were considered significant.

The results of New York Carotid Artery Surgery Study (NYCAS) were reported by Greenstein et al.[4] They evaluated the results of 9308 endarterectomies, performed by 482 surgeons in 167 hospital, in New York State, USA, in the period between January 1998 to June 1999. The general rate of cervical clot was 5% and were associated to 3 to 4 fold chance of stroke or combined death and nonfatal stroke.

Bourke e Crimmins[5] reported one case of cervical clot in a series of 148 consecutive cases of endarterectomy.

Assadian et al.[6] compared the use of non-fractionated heparin with enoxaparin for anticoagulation during endarterectomy. 120 patients received 0.5 mg/kg of enoxaparin and 40 patients received 5000 UI of non-fractionated heparin in the preoperative period. The rate of thromboembolism was 0.8% in the enoxaparin group, compared to 2.5% in the group of regular heparin. The rate of hemorrhagic complications was 1.7% in the enoxaparin group compared to 5% in the group of regular heparin. There was no case of thrombocytopenia related to heparin in this series. The difference between the two groups, however, did not show statistic significance.

It is a common practice to interrupt antiplatelet drugs five to 10 days before surgical procedures, in order to avoid hemorrhagic complications. However, if a patient has a severe carotid stenosis with indication for endarterectomy it is not wise to interrupt the best medical treatment to avoid stroke.

Surgeons must choice either to interrupt or not the antiplatelet treatment before endarterectomy. With the first approach, the risk of stroke during the period of interrup-

tion may be high. With the second, there is a increased risk of development of cervical clot after the procedure.

Since 1998 our protocol for endarterectomy includes the use bridge-therapy with enoxaparin, in the dose of 40 mg/day subcutaneously.

Enoxaparin is a low molecular weight heparin that binds to antithrombin, potencializing its effects. Moreover, enoxaparin inhibits the factors of coagulation XIa, IXa, Xa e IIa (thrombin), preventing the development of clots[7].

In spite of fact that the effects of enoxaparin are due to its antithrombin effect, Pleym et al.[8] demonstrated elevation of platelet activation by enoxaparin in their study of coronary surgeries.

Brophy et al.[9] also demonstrated that enoxaparin has an antiplatelet effect due to its antithrombin activity. They studied the activity of antifactor Xa, gold-standard to monitor low molecular weight heparin, and three new parameters: thrombin generation time (TGT), platelet contractile force (PCF) and clot elastic modulus (CEM). PCF is the force produced by platelets during the clot retraction, measuring the platelet activity. PCF is dependent of the production of thrombin as well as the number a viability of the platelets. The authors studied the effects of enoxaparin in patients with renal dysfunction, comparing with normal individuals as a control group. In both groups there was correlation between PCF and the antifactor Xa activity of enoxaparin.

In their series of patients operated on laparoscopic gastric surgery and used 40 mg/day of enoxaparin with hemorrhagic complications, Kligman et al.[10] identified significant decrease of platelet-dense granule. These authors suspected that this decrease was the responsible for the hemorrhagic complications in their series.

It seems that enoxaparin has not only the antithrombin effect that prevents the formation of red clots, but an antiplatelet effect as well. These effects limit its use as an universal antithrombotic therapy. However, its use as bridge-therapy in the preoperative period of surgeries like endarterectomy is justified.

Bridge-therapy with enoxaparin has been recommended for cardiac surgery[8,11].

The present series is a prospective study of 124 procedures in 119 patients in which bridge-therapy with enoxaparin has been used in the preoperative period of endarterectomy. There was no stroke during the bridge-therapy period. Cervical clot as a complication of the procedure occurred in one patient (0.8%). This patient had an uneventful initial course after the procedure and was discharged home in the second day after surgery, with prescription of 325 mg/day of aspirin. Five days later she developed cervical clot requiring surgical evacuation. The only risk factor detected was hypertension. The suture line was intact and after surgical drainage she had a good outcome.

The rate of cervical clot in this series was smaller than our previous report[12]. In that series there were 3 cases of cervical clot in 110 procedures (2.72%). Two of those patients were using aspirin in the preoperative period.

Despite the fact that we do not have a control group in the present study we concluded that bridge-therapy with enoxaparin is safe, preventing stroke during the preoperative period and with low rate of hemorrhagic complications in the postoperative period.

New prospective studies with control groups are necessary to confirm our impression of the possible antiplatelet effects of low molecular weight heparin.

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