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Application of GlycoProtein IIb/IIIa antagonist (Integrilin) in peri-percutaneous transluminal catheter angioplasty and stent implantation in Chinese

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Abstract: Objective: to report the application of GPIIb/IIIa antagonist (Integrilin) in peri-percutaneous transluminal catheter angioplasty and stent implantation in Chinese. Method: Twenty-one patients who underwent percutaneous transluminal catheter angioplasty (PTCA) and stent implantation were included. After arterial puncture, integrilin was injected at dose of 180ug/kg, and then maintained at 2μg/kg•min for 18 hours. Asprine, plavix (clopidogrel) and heparin were used at the same time. ACT, PT, KPTT and blood routine were routinely monitored. Results: All sheaths were drawn out 2 to 4 hours after the procedure.. There was no severe complication such as hematoma, acute and subacute thrombosis in coronary artery, or thrombocytopenia. ACT returned to less than 150 seconds in 2 hours in 15 patients; in 4 hours in 6 patients. There was no significant difference between the pre- and post-procedure value of PT and platelet count. KPTT was significantly higher than pre-procedure value at 2 hours after the procedure . No recurrence of angina pectoris was observed in the first nine patients within one year follow-up, and no restenosis occurred in stents in the five patients who had coronary angiography one year later. Conclusion: Application of GPIIb/IIIa receptor antagonist (Integrilin) in peri-percutaneous transluminal catheter angioplasty and stent implantation in combination with aspirin and plavix could significantly reduce the dosage and duration of heparin with benefit of shortening the indwelling time of sheaths, but did not increase risk of bleeding or lead to thrombosis in stent.

Key words: GPIIb/IIIa receptor antagonist, Integrilin, Percutaneous translumind catheter angioplasty (PTCA), Stent

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INTRODUCTION

A acute and subacute thrombosis is an early serious postoperative complication of PTCA. The conventional preventive measure for this complication is using large dose of heparin in the course of surgery and maintaining the drug for a time postoperatively. But this may increase the incidence of serious hemorrhagic complication subsequently. Platelet GPIIb/IIIa is a platelet receptor of fibrinogen, which cause later platelet aggregation in combination with fibrinogen, comprising an important link in the pathogenesis of coronary thrombosis. The blocking of this common pathway by platelet GPIIb/IIIa receptor antagonist resulted in a strong antiplatelet action. The notable effect of GPIIb/IIIa receptor antagonist in reducing the complication of PTCA and stent implantation in high risk patients had been reported in foreign literatures; the method reduces the dosage of heparin, therefore, decreasing the hemorrhagic complication evidently (Firshman et al., 1995; Kereiakes et al., 1998) To our knowledge, there is no report on this subject in China. What we report here is our experience in the preliminary use of GPIIb/IIIa antagonist, Integrilin in PTCA perioperative patients.

MATERIALS AND METHODS

Selection of patients

Among twenty-one patients with coronary

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heart disease admitted to our hospital in April 2000 (nine patients) and April 2001 (twelve patients), one patient had acute myocardiac infarction, three had subacute myocardiac infarction, six had stable angina pectoris, and eleven had unstable angina pectoris. Nineteen patients were males and two were females. Their ages ranged from 35 to 75 years with the average being 61.

The administration of Integrilin

Integrilin (eptifibatide) injection was provide by the medicine center of Ohio State University, and manufactured by COR Therapeutics, Inc. South San Francisco. LOT RO197A1 was used in nine cases, LOT RO216A2 was used in twelve cases.

The Integrilin was administered at a dose of 180(g/kg after arterial puncture, and then maintained at a dose of 2(g/kg·min for 18 hours.

The administration of other anticoagulants and antiplatelet drugs

Aspirin 300 mg plus Plavix 75 mg /per day for 3 days before the operation and /per day for 1 month postoperatively. Plavix (clopidogrel) was discontinued 1 month after the operation, and aspirin was maintained at a dose of 100 mg /per day; heparin 50μ/kg was administered immediately after arterial puncture to keep ACT at a range from 200 to 250 seconds during operation, if ACT < 200 seconds, an additional dose of heparin should be administered; heparin were not used for maintenance after procedure.

Observation on indices

After testing the ACT、PT and KPTT once prior to operation and every two hours after operation, the sheaths could be removed until ACT < 150, KPTT < 35s. Blood cells are measured once before operation and re-examination of blood cells is carried out at the time of discharge and 1 − 2 month after leaving hospital.

Statistics

Use paired t-test.

RESULTS

1. All patients had their sheaths removed 2 − 4 hours after operation, no hematoma at the site of puncture was found; no acute and subacute thrombosis of coronary artery were noted. The first nine patients were followed-up one year postoperatively and no relapse of angina pectoris happened. Of them, five patients received coronary angiography again, and in-stent restenosis did not occur.

2. The common clinical materials and results of PTCA and stent implantation: Thirty-five stents (including two Nir stents, four Occam stents, eight JOMED stents and twenty-one AVE stents, ranged from 2.5 to 4.0 mm in width and from 8 to 26 mm in length and three Cutting Balloons were used in the procedure on of twenty-one patients with thirty lesions, which included fifteen cases of single-vessel disease, three cases of two-vessel disease and three cases of triple-vessel disease.

3. The changes of PT, KPTT, ACT、white blood cell and platelet count (pre- and post-PTCA and stent implantation) are presented in Table 1.

Table 1 Changes of PT, KPTT, ACT, white blood cell and platelet counts

	PT(s)	KPTT(s)	ACT(s)	WBC($10^3/\mu$L)	Platelet (10^3/L)
Pre-operation	12.9±1.2	31.3±4.1		5.8±1.4	189±63
Post-operation(2 hours)	13.2±1.6	45.5±9.4*	152±9		
(4 hours)	13.1±1.5	32.1±2.9	143±4		
Discharge				6.1±1.8	192±58
Post-operation(1 month)	12.8±1.7	30.2±3.8		5.6±1.6	201±67

* Compared with pre-operation $P<0.05$

DISCUSSION

GPIIb/IIIa is the platelet receptor of fibrinogen, which cause later platelet aggregation in combination with fibrinogen. It is an important link in the pathogenesis of coronary thrombosis. The blocking of this common pathway by GPIIb/IIIa receptor (Frishman et al., 1995) antagonist resulted in a strong antiplatelet action. Multiple center large scale clinical trials showed that (Kereiakes et al., 1998, Pitts et al., 1999) GPIIb/IIIa receptor antagonist can not only reduce the incidence of coronary thrombosis and the mortality of myocardiac infarction, but also help to prevent the complications, coronary artery restenosis , and also reduce the mortality in the patients with PTCA and stent implantation. Thirty-five stents which ranged from 2.5 to 4.0 mm in width and from 8 to 26 mm in length had been implantated in twenty-one patients. The first nine patients had no reccurrence of angina in the one year follow-up, of them; five patients (with seven stents) who had received coronary angiography angian showed no in-stent restenosis. Past clinical study (Kereiakes et al., 1998) indicated that patients treated with GPIIb/IIIa receptor antagonist (Abciximab) and routine dosage heparin, had a hemorrhagic rate as high as 14%; which could be reduced to 3.8% by decreasing the heparin dosage ; and even to 2% (approximately, the same as placebo) when heparin dosage was decreased furthermore. The incidence of complication, coronary artery restenosis and mortality were notably reduced. The heparin used in these patients was at a half routine dosage; all patients had their sheaths removed 2 – 4 hours after operation, no postoperative hemorrhage or thrombosis in stent happened. It is worth mentioning that the Plavix used in combination with Integrilin was the same antiplatelet drug as Ticlid (ticlopidine HCl) which acted mainly through inhibition of ADP, but with inhibiting action on white blood cells being far lower than Ticlid. The multicenter clinical trial showed that Integrilin has the same action as other GPIIb/IIIa receptor antagonist. The blood examination (including PT, KPTT, ACT, white blood cells and platelet count), prior to and after the operation, revealed that Integrilin has no side effects on white blood cells and platelet count. And used in combination with small dosage of heparin, Plavix and aspirin, it is not likely to increase the risk of hemorrhage.

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