

CONCOMITANT THERAPY OF A HEMOPHILIA-A PATIENT WITH INHIBITOR BY USING LOW DOSE BY-PASS AGENTS

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Background:

Factor VIII or factor IX inhibitors may develop in patients with hemophilia-A and -B due to several different reasons. Patients with hemophilia A and B who develop inhibitors and become refractory to replacement therapy with factor VIII or IX, respectively can be treated effectively by activated prothrombin complex concentrates (APCC, e.g. FEIBA) or by recombinant factor VIIa (rFVIIa).

Aim

We present here a 14 year-old boy with hemophilia-A, who had 24 BU inhibitor of F VIII, and were given only a total of 8000 u doses of F VIII product before the circumcision.

Case report

The patient was admitted to our hospital because of recurrent epistaxis when he was at 3 years of age. His factor VIII level was < 1%. Due to low social and cultural level of his family, he could not come for follow-up regularly. He was hospitalized with severe bleeding after strabismus operation at 10 years of age and was treated with factor VIII products for a week. F VIII products had not been used even though he had a few epistaxis and hematuria. Later, he had been administered only once a dose of 500 u F VIII product for hemarthrosis. F VIII inhibitor was negative during this period.

He was hospitalized for circumcision at the pediatric surgery clinic when he was 14 years old. Before circumcision, he was injected a dose of 1000 u F VIII concentrate after taking the blood sample for inhibitor assay. Although he had no severe bleeding during operation and 2 days after the circumcision, severe bleeding started on the third day.

It was surprisingly learned that he had developed an F VIII inhibitor of 24 BU. Priority, he was given recombinant factor VIIa (rFVIIa) at standard doses of 90 mc/kg to yield hemostasis, but effective hemostasis could not be yielded.

Concomitant infusion of low doses of rFVIIa and FEIBA was started after four days and effective hemostasis could be yielded within one week. After circumcision, he was given a total dose of 5500 u of FVIII product, 63 mg of rFVIIa, and 18000 u of FEIBA, respectively, for hemostasis. The total cost of circumcision was 66000 USD.

Discussion

Some hemophilia patients with inhibitors may become refractory to therapy with either rFVIIa or APCC. Management of such patients is difficult, being associated with higher morbidity and potential mortality, as well as very high costs. Combination therapy with both drugs was suggested as a 'last resort' treatment for bleeding episodes in such patients. Combination therapy with sequential administration of standard doses of APCC and rFVIIa, has been recently reported to be safe and effective in 35 refractory bleeding episodes in four young hemophilia patients. In a retrospective review of surgical interventions in a cohort of hemophilia A patients with inhibitors, combined therapy with both agents, given at standard therapeutic doses either sequentially or concomitantly (e.g. bolus doses of FEIBA applied during continuous infusion of rFVIIa) was also described. The use of sequential therapy in patients suffering refractory bleeding episodes was recently recommended within the guidelines for optimal care of high-titre inhibitor patients, published by an international panel of physicians.

Therapy cost is an important consideration using bypassing agents for inhibitor patients and the cost of treating individual patients may greatly magnify the cost of treating the inhibitor population in general. The use of lower than standard drug doses and the single administration required, may lead to significant cost reduction. Our patients were treated by combination of rFVIIa and FEIBA, saving the consequences of prolonged bleeding as well as the cost of repeated doses. The main concern of haemophilia treaters who use bypassing agents is their fear of potential thrombotic complications. Thrombotic events, although rare, may occur with either of both products. Thrombosis occurs mainly in patients with preexisting risk factors

Conclusion

In developing countries, the coordination among patient, family, and the doctors may lead to the problem-free conduct of operations such as circumcision in patients with hemophilia who had inhibitor and reduce the costs.

Literature

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