

Gastrointestinal Bleed with Clopidogrel and Aspirin

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ABSTRACT

Anti-platelet drugs have been used to prevent thrombosis of systemic to pulmonary artery shunts. Aspirin has traditionally been used. Clopidogrel is being studied as an alternative and in combination with aspirin for shunt patients. We report a near fatal gastro-intestinal bleed in a patient with shunt and on aspirin and clopidogrel. This combination has been known to produce similar bleeds. The authors recommend caution in combining them. Prospective studies currently underway should evaluate this aspect of the antiplatelet drugs. [Indian J Pediatr 2010; 77 (1) : 101-102]

Key words: Clopidogrel; GI bleed; Cyanotic CHD

Modified Blalock Taussig shunt is performed as a palliation to augment pulmonary blood flow. Acute thrombosis and blockage of the shunt may be fatal or result in severe deterioration in patients' clinical condition. Prevention of shunt thrombosis has traditionally been achieved by using aspirin in patients with Blalock-Taussig shunts. Clopidogrel has been considered as an alternative to or has been used in combination with aspirin for its antiplatelet aggregating effect as evidenced by CLARINET (Clopidogrel in neonates /infants with systemic to pulmonary artery shunt palliation) and PICOLO (Platelet Aggregation Inhibition on Children on Clopidogrel) trials.^{1,2}

Among the side-effects of aspirin, gastro-intestinal (GI) bleeding remains to be a major concern. We report one such case where a patient had been on clopidogrel and aspirin for a Blalock-Taussig shunt. He presented with an acute upper GI hemorrhage which was near fatal and resulted in the shunt getting blocked.

The child was diagnosed at birth to have a tracheo-esophageal fistula for which he underwent a repair in the early newborn period. He was also noted to have pulmonary atresia with ventricular septal defect with a patent ductus arteriosus. He underwent an emergency BT shunt at the age of 3 mth for severe desaturation at the time of first presentation to our institution; the patent ductus arteriosus was not ligated. The child received

oral aspirin supplement as is routine in our unit for all patients following the BT shunt. A few weeks after surgery, the child was started on clopidogrel in addition to the aspirin in view of transient low saturations. At the age of 3 yr, almost 2.5 yr after the shunt was implanted, the child reported to the emergency room with massive upper GI bleed. The child was in shock, with a heart rate of 180 bpm, blood pressure 50/30 mmHg, and saturations of 30-40%. The admitting hemoglobin was 6.8 g%. Fluid resuscitation and blood replacement were done in addition to intubation and ventilation. An upper GI endoscopy was performed which showed a mid-esophageal 1 cm ulcer with suggestion of this being the source of bleeding. Antral ulcers suggestive of gastritis were also present. Pantoprazole was initiated and further GI bleed was prevented. A bleeding time and a clotting time were also performed which were normal. The platelet count, prothrombin time, thromboplastin time and INR were normal too.

The child also underwent an angiogram in view of the desaturation which revealed a blocked BT shunt. To augment the pulmonary blood flow, stenting of the patent ductus arteriosus (PDA) was performed during the same procedure with significant improvement in saturations. Post procedure, clopidogrel was re-initiated in view of the presence of stent.

The risk of gastrointestinal bleeding generally increases by a factor of two to three with the use of even low-dose aspirin by substantially inhibiting gastric cyclooxygenase and causing gastric ulceration.³

It is for this reason that clopidogrel as an alternative to aspirin has been sought. It is anticipated from the

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mechanism of action of the two drugs that aspirin is more likely to cause GI bleeding than clopidogrel. Aspirin prevents thrombosis and blocks platelet aggregation through inhibition of the cyclooxygenase enzyme. It induces GI ulceration also through the same mechanism. The antithrombotic effect of clopidogrel is by blocking the platelet activation of adenosine diphosphate (ADP) which prevents the activation of the glycoprotein IIb/IIIa complex.⁴

Various studies have commented on the safety of clopidogrel use in the pediatric age group. In a retrospective study of 15 children, the authors reported one patient with an episode of GI bleeding while on 3 antiplatelet drugs.⁵ In another prospective consecutive cohort study of 17 children with arterial ischemic stroke who received clopidogrel, 2 patients developed subdural hematomas.⁶ It has been suggested by these authors that the combination of clopidogrel and aspirin is more likely to cause complications especially in the presence of risk factors.

Contrary to current literature, Chan *et al* showed that patients receiving clopidogrel had an astonishing increase in the rate of recurrent upper gastrointestinal bleeding from ulcers, as compared with those in the group taking aspirin plus esomeprazole (8.6 percent *vs.* 0.7 percent, $P=0.001$).⁴ Impairment of healing induced by clopidogrel may be the primary mechanism which may explain the increased bleeding by this antiplatelet agent. Apart from the aspirin and clopidogrel issue, possibility of previous esophageal surgery as a cause of the bleeding was also evaluated. It did not seem to the authors that that was the cause of the bleeding 3 years later.

We have changed our practice after the present,

patients experience and the review of literature. Our preference is to use a single drug *i.e.* aspirin alongwith lanzoprazol even in infants. The results of the trials using clopidogrel may provide the necessary evidence to prefer clopidogrel over aspirin.

In conclusion, the combination of aspirin and clopidogrel can possibly result in massive near fatal bleeds as in the present case and single drug use may be preferred.

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