CLOPIDOGREL FOR THE TREATMENT OF CHILDREN WITH A SYSTEMIC-TO-PULMONARY ARTERIAL SHUNT

Background

Clopidogrel is a thienopyridine drug, it is a prodrug metabolized by CYP450 in the liver, yielding an active form that selectively and irreversibly binds to the adenosine diphosphate (ADP) receptor on platelets. This prevents ADP from binding, and GP IIb/IIIa complex from activation, so platelet aggregation is consequently inhibited (see picture 1). Clopidogrel is used to prevent ischemic events in adult patients with myocardial infarction, ischemic stroke or vascular disease and in patients with acute coronary syndrome who also underwent percutaneous intervention in combination with ASA. Prolonged use is not authorized because of limited information about efficacy and safety. The few studies have given good results but have been carried out on a restricted population of patients.

Purpose

To illustrate our experience in the three-month-long use of clopidogrel in children with a systemic-to-pulmonary arterial shunt, prior to definitive surgical intervention.

Materials and Methods

On February 2012 “Cardiornotrofia e Cardiologia Pediatrica e Congenita” division of “Azienda Ospedaliero Universitaria di Ancona” placed a temporary systemic-to-pulmonary arterial shunt in a four months old patient, affected by Tetralogy of Fallot with hypoplasia of the infundibulum and pulmonary valve. Because of the high risk of hemodynamic closure of the shunt and on the basis of previous negative experiences we administered two antiplatelet drugs, ASA 16 mg and Clopidogrel 1 mg/kg once a day as reported in scientific literature [1,2,3,4,5]. The pharmacy was involved to support the request to Ethics Committee (1-2) for urgent off-label use and for the galenic preparation of Clopidogrel 0,75 mg (see picture 2). A liquid form was evaluated but rejected because of doubts about long-term stability incongruent with home therapy. We chose an enteral preparation of capsules type 5 with lactose as a disintegrant. After that, four other children (from 2 months to 4 years old) were treated with Clopidogrel, mostly associated with ASA alone or together with enoxaparin (see table 1).

Results

We prepared capsules from 0.75 to 3.5 mg, we acquired the authorization by the Ethics Committee and the parent’s informed consent for all patient. After surgery, children were observed for 3-4 days depending on clinical follow up and complications. We controlled blood count and shunt patency with clinical observations, analyses and echocardiograms. After discharge, patients were first recalled 10-15 days later, than after 1-2 months for medical skill, ECG blood exams and echocardiograms. It was necessary, no serious side effects have been observed.

Treatment should continue until definitive intervention for cardiac disease and removal of the shunt.

Conclusion

Clopidogrel therapy on children is rapidly increasing. A wider number of cases, a comparison with other professional experiences, and, most of all, controlled clinical trials would be desirable.

Table 1

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References
2. Nationwide Children’s Hospital and Lorain Hospital for Six Children Department of Pharmacy Experience since September 2009.