Aspirin resistance in a paediatric population with congenital heart diseases

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Introduction: Aspirin resistance in adults has an incidence of 5% to 50% depending on the laboratory test used. Data in paediatric setting are lacking. Our aim was to evaluate the incidence of ASA resistance in a paediatric population with congenital heart diseases.

Methods: Included were children (6 months to 18 years old) on maintenance aspirin therapy (3-5mg/kg/die). Venous blood samples were collected 4, 5 and 6 hours after drug administration and plasma concentrations of ASA and salicylic acid were assayed by HPLC. The effect of aspirin on platelet aggregation was assessed using the ASPItest.

Results: Since July 2016 20 patients were enrolled. There were 11 ASD, 5 univentricular hearts, 1 interrupted aortic arch, 1 TOF, 1 AV canal, and 1 post-actinic cardiomyopathy. The results of ASPItest are available for 17 patients. There were 2 patients (12%) with high on-treatment platelet reactivity (HPR) (cut off >39U). No clinical thrombosis occurred.

Demographics | Mean | SD | Pharmacokinetics & pharmacodynamics | Mean | SD |
---|---|---|---|---|---|
Sex (M/F) | 10/10 | - |
Age (years) | 8.2 | 4.3 |
Weight (Kg) | 28.1 | 15.7 |
Height (cm) | 126.8 | 27.0 |
Dose (mg) | 79.7 | 28.2 |
Dose/Kg (mg) | 3.12 | 0.67 |
Aspirin | AUC (ng/mLxh) | 80 | 83 |
| Cmax (ng/mL) | 53.7 | 55.3 |
| Tpeak (h) | 4.80 | 0.77 |
Salicylic acid | AUC (ng/mLxh) | 4,528 | 5,004 |
| Cmax (ng/mL) | 3,127 | 3,286 |
| Tpeak (h) | 4.35 | 0.74 |
Aspi Test | AUC (U) | 24.9 | 11.4 |

The time courses of mean ASA and salicylate concentrations were similar to those outlined in adults (Figure 1 and 2). The ASPI test values were linearly correlated with ASA concentrations ($r^2 = 0.36; p = 0.0113$). The other variables analysed (CBC values, age, weight) were not related to aspirin response. High blood cellularity might play a role in HPR (neutrophil count and MCV reached borderline significance, respectively $p=0.062$ and $p=0.075$). When dichotomous variables were analysed, significance was reached using a lower cut off for the ASPItest suggestive of effective COX-1 inhibition (ASPItest cut off> 30, ASA concentration cut off >100ng/mLxh, $p=0.005$).

Conclusions: Aspirin resistance had a non-trivial incidence in our small population. High plasmatic ASA concentration correlates with HPR. Limitations are a low population number and the use of only one platelet reactivity test.