

## Aspirin resistance in a paediatric population with congenital heart diseases

Padrini M. (1), Padrini R. (2), Spiezia L. (2), Castaldi B. (1), Milanese O. (1)

(1)Pediatric cardiology unit, department of woman and child health, university of Padua, Italy (2) Department of Medicine, university of Padua, Italy

**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.

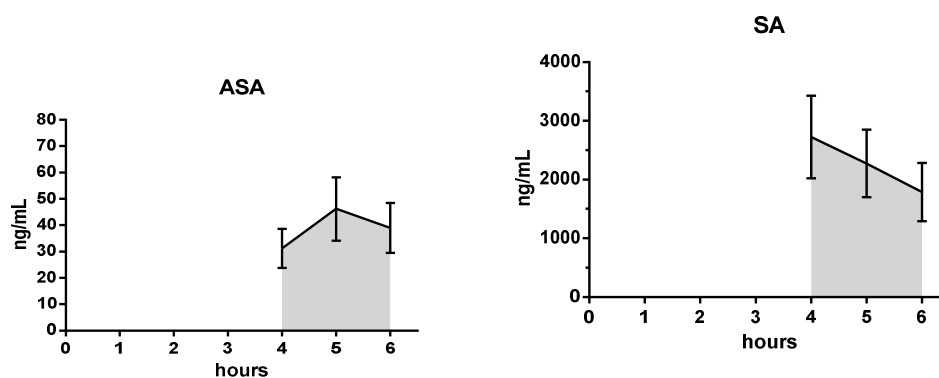
**Methods:** Included were children (6 months to 18 years old) on maintenance aspirin therapy (3-5mg/kg/die). Venous blood samples were collected 4, 5 and 6 hours after drug administration and plasma concentrations of ASA and salicylic acid were assayed by HPLC. The effect of aspirin on platelet aggregation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

Pharmacokinetics & pharmacodynamics		Mean	SD
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.