OP4 - Validation of Serum 17-Hydroxyprogesterone Concentration Reference Ranges by ELISA Method in Infants During the First Year of Life

Cestino ML [1], *Breyer FA* [1]

[1]Hospital Pediátrico Dr. Humberto Notti

Introduction: The 17α-hydroxyprogesterone (17OHP) measurement is useful to confirm the diagnosis of congenital adrenal hyperplasia (CAH) in neonates and nonclassical forms of CAH in symptomatic children. During the first year of life, methods may be affected by interfering steroids produced by the fetal zone of the adrenal gland. This zone produces high concentrations of 17-hydroxypregnenolone sulphate carrying immunoreactive epitopes similar to the 17OHP molecule. Numerous authors agree that these interferences could be removed efficiently via a solvent organic extraction before measuring the 17OHP. Since the degree of interference may vary among different commercially available assays, reference intervals (RI) for 17OHP should be method specific, especially during the first year of life.

The aim of our study was to verify the specified RI for the ELISA method, and correlate this with values obtained after organic solvent extraction in infants during the first year of life.

Materials and methods: Serum 17OHP was measure via ELISA method (DRG) in 217 infants aged <1 year classified in 4 groups: I (0-30 days), II (31-60 days), III (61-180 days) and IV (181-360 days), who attended the hospital between Dec 2014 and Jul 2019, before (17OHP NE) and after (17OHP E) modified extraction procedure (Makela et al.)

Results: A significant difference between NE and E results was observed for all groups (p<0,001), especially during the first two month of life. 93.0, 60.5, 90.9 and 90.4% of patients were inside RI proposed by the manufacturer for groups I, II, III and IV respectively. Regression values in each groups E and NE were low (r2<0.36), demonstrating high interference variability in the same group. The serum concentration was log-transformed to reach normal distribution. We used one-way ANOVA showing significant differences between groups. Tukey post hoc could differentiate all groups, except I and II.

Conclusions: According to the CLSI Evaluator Protocol (EP) C28-A3, a result is satisfactory for validation of RI when more than 90% of the results are inside the range proposed by the manufacturer. In our study group II couldn´t be validated, but it is similar to group I, so we should establish our own RI for this population. As was previously showed for RIA methods, solvent extraction procedure is also required in the ELISA DRG method to minimize cross-reaction with interfering steroids during the first year of life.

Keywords: *Congenital adrenal hyperplasia; Interfering steroids; 17α-hydroxyprogesterone*

OP5 - Inhibition Of IGF1R by IGF-1R/IR Inhibitor OSI906 as a Targeted Therapy for Glioblastoma: In Vitro & in Vivo Studies

Fernández MC [1], *Martin A* [2], *Clément F* [2], *Venara MC* [2], *García Lombardi M* [3], *Bergadá I* [2], *Gutiérrez M* [4], *Pennisi PA* [2]

[1]Centro de Investigaciones Endocrinológicas Dr. César Bergadá, CEDIE, CONICET-FEI-División de Endocrinología, Hospital de Niños Dr. R. Gutiérrez; [2]1- Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE) CONICET – FEI – División de Endocrinología, Hospital de Niños Dr. R. Gutiérrez; [3]Servicio de Oncología. Hospital de Niños Dr. R. Gutiérrez; [4]Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE) CONICET – FEI – División de Endocrinología, Hospital de Niños Dr. R. Gutiérrez

Background: CNS tumors are the most frequent solid tumors in children. In paediatric gliomas, IGF-1R nuclear localization was associated with high grade tumours and increased risk of death, contributing to the aggressive phenotype of glioblastoma. For children chemotherapy after surgical resection is the mainstay of therapy. However, the best regimen needs to be determined.

Aim: To characterize the response of glioblastoma cells to treatment with OSI906 (IGF1R/IR dual inhibitor) alone or in combination with Temozolomide used as a current adjuvant chemotherapy for paediatric patients.

Methods: stably transfected U87Mg glioblastoma cells with 5 times basal expression of wild type mature GFP-IGF1R fusion protein (wt-IGF1R, WtU87) or GFP-IGF1R fusion protein mutated in Lys1025-1100-1120 to avoid IGF-1R nuclear translocation (m-IGF1R, MutU87) were used for in vitro and in vivo assays. Proliferation assays were carried out for 3 days using complete media (10%FBS) alone or with the addition of IGF-1R/IR inhibitor OSI906 (0.5uM), Temozolomide (TMZ, 40 or 100uM) or the combination of both. Male nude mice were injected with 1,5e6cells/flank/mice. OSI906 (50mg/kg) and TMZ (400mg/kg) were given by gavage once daily or as a single dose respectively. Treatments were started when tumors reached 150 mm3.

Results: After 24 h of culture, MutU87 cells showed decreased proliferation when treated with TMZ40 and OSI906; OSI906 had an additive effect when combined with TMZ40 compared to control condition. However, cells resumed proliferation after 3 days in culture. On the contrary, treatment with TMZ100 had a strong inhibitory effect, that was not increased by the combination with OSI906. WtU87 treated with TMZ40 or 100 also resumed proliferation after 24 h treatment, although the total number of cells was decreased compared to control. OSI906 was able to abolish proliferation of WtU87 cells when used alone or in combination with TMZ 40 or 100, having the latter the strongest effect. In vivo studies showed similar trends.

Conclusion: The capacity of the IGF1R to translocate to the nucleus, renders glioblastoma cells sensitive to the IGF-1R targeted therapy alone or in combination with TMZ, in vitro and in vivo. These results suggest that the use of IGF1R inhibitors in pediatric patients showing nuclear localization for this receptor, could be useful to reduce TMZ doses and or avoid radiotherapy in children.

Keywords: *IGF1R; Pediatric glioma; OSI906*