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Oral Communication Abstract
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P-gp and/or HDAC2 regulates steroid responsiveness in childhood nephrotic syndrome

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Objectives: P-glycoprotein (P-gp) over expression in peripheral blood mononuclear cells (PBMCs) has been reported in patients with steroid resistant nephrotic syndrome (NS). Glucocorticoids suppress NFκB-associated co-activator activity by deacetylation of histones by enzyme histone deacetylase (HDAC)-2. Interaction between HDAC2 activity and P-gp expression in childhood NS patients is not clear.

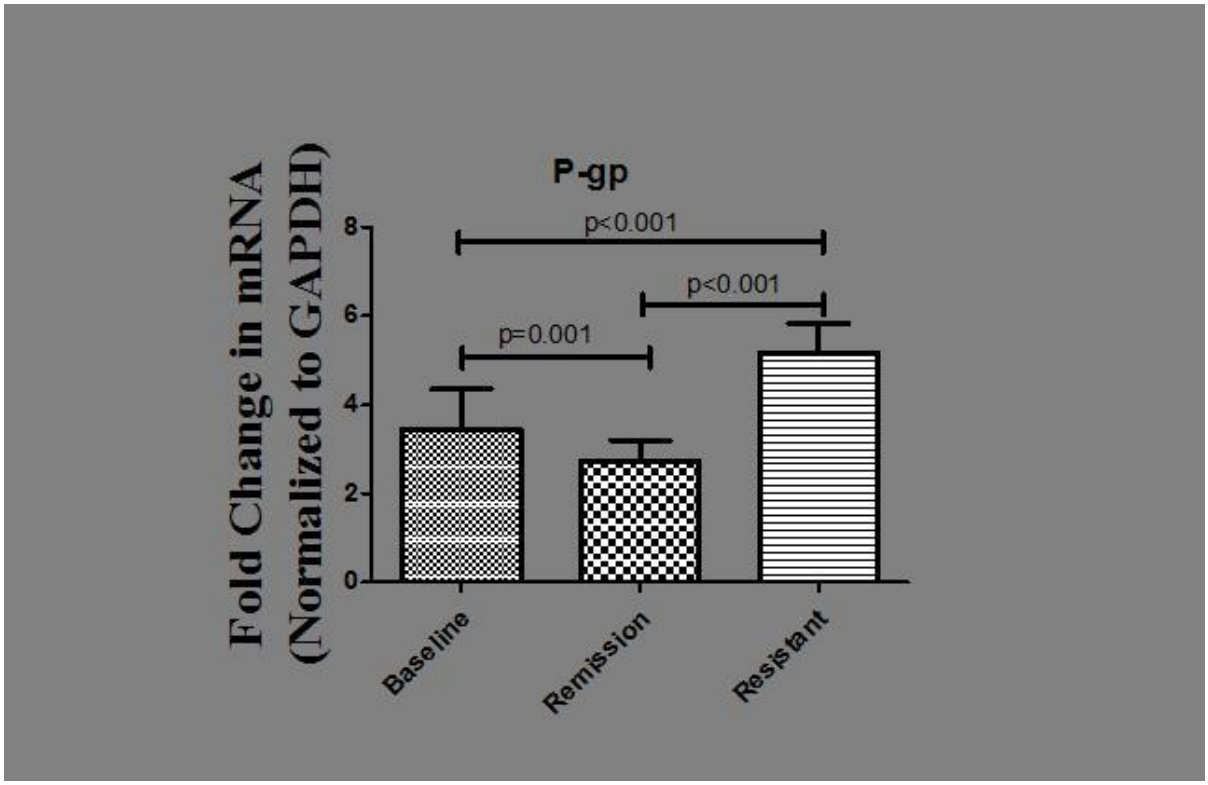
To evaluate the role of HDAC2 and P-gp expression on PBMCs and steroid responsiveness in patients with childhood NS.

Methods: 131 patients were recruited at baseline (n = 131) (before initiating steroid therapy); After six weeks of steroid therapy, 91 patients achieved remission (n=91 mean age, 8.96±3.90), whereas 40 were resistant to steroids (n=40, mean age 9.00±3.55). mRNA expression of HDAC2/P-gp and functional analysis of P-gp and enzymatic activity of HDAC2 were analyzed at baseline, at 6 weeks of steroid treatment and at the time of relapse, respectively.

Results: The expression of P-gp on PBMCs were significantly higher in SRNS (11.56±4.56 v/s 4.36±2.15, $p<0.001$). The mRNA expression of P-gp was significantly lower in SSNS and who achieved remission at 6-weeks of steroid therapy compared to baseline and those who were steroid resistant (n=40,$P<0.005$). mRNA Expression of HDAC2 was significantly lower in SRNS ($P<0.005$) as compared to baseline and those who achieved remission following 6-weeks of steroid therapy. The function of P-gp was significantly lower in NS patients who achieved remission after 6-weeks of steroid therapy as compared to baseline ($p<0.005$) and SRNS patients ($p<0.005$). The enzymatic activity of HDAC2 was significantly higher in patients who achieved remission as compared to those who were resistant at 6-weeks of steroid therapy ($p<0.005$).

Conclusions: Expression and function of P-gp and HDAC2 may affect steroid response in NS patients. Combined therapy of steroids with P-gp inhibitor and/or HDAC2 inducers may have rationale in the management of steroid resistant NS patients.

mRNA expression of P-gp



mRNA expression of HDAC2