

ORAL PRESENTATION

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Pediatric scoliosis predictive blood tests: progress and challenges for clinicians

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Purpose

There are great needs for innovative pharmacotherapies in combination with clinical tests to identify asymptomatic children at risk of developing scoliosis and symptomatic ones to predict who may be at risk of scoliotic curve progression. Early detection of scoliosis is critical to broaden the range of treatment options and increases effectiveness. Currently, there are no FDA cleared “pre-symptomatic” diagnostic tests available for assessing scoliosis in paediatric patients. We have developed a cell-based screening assay for the early diagnosing of presymptomatic subjects and a biochemical blood test for asymptomatic individuals and patients at different disease stage.

Methods

Peripheral blood samples for AIS patients, asymptomatic children and control subjects were collected in blood collection tubes containing EDTA and then centrifuged on a Ficoll-Plaque solution to obtain peripheral blood mononuclear cells (PBMCs) and plasma. Gi-coupled receptor signal transduction was measured by cellular dielectric spectroscopy (CDS) in presence of varying concentration of melatonin or other ligands. Plasma concentrations of OPN and sCD44 were measured by ELISA methods adapted to be performed on a robotic platform.

Results

In a cross-sectional clinical study, we have shown that mean plasma OPN levels were significantly increased in AIS patients (n=320) and correlated with disease severity

with average values of 743 ± 326 and 975 ± 389 ng/ml for moderate and severe spinal deformities, respectively, when compared to the healthy control group (568 ± 216 ng/ml; n=120). Elevated plasma OPN levels were also found in the asymptomatic at-risk group (871 ± 387 ng/ml; n=87), suggesting that these changes precede scoliosis onset. Data obtained using PBMCs revealed a melatonin signaling impairment only in IS patients at different disease stages when compared to healthy controls showing a high specificity (100%) and sensitivity (100%). Risk of developing a scoliosis in asymptomatic children was determined by CDS in 33% of asymptomatic children at risk.

Conclusion

Both tests have a unique advantage since they can be performed without any prior knowledge of mutations in any defective genes causing AIS. The standard of care for scoliosis has not changed in any significant manner in decades. Patients today are treated in a substantially similar manner to those twenty or thirty years ago – observation, bracing, and fusion as a last resort. Our diagnostic blood-assay may have the potential to change the way scoliosis patients are diagnosed and treated.

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