Combination of Steroid and Flavonoid for the Treatment of Regressive Autism

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Autism spectrum disorder (ASD) is a neurodevelopmental disorder of early childhood with symptoms of impairments in social interaction and communication with accompanying repetitive behaviors or restricted interests. Treatment options available for the core symptoms are limited despite increasing prevalence. But in recent years, our knowledge was expanded about immunological dysfunctions in patients, particularly having marked regression after a period of normal development[1]

Previous studies reported that patients with regressive autism could benefit from immune-based therapies such as steroids, flavonoids, and intravenous immunoglobulin.[2-4] Here, I want to share my clinical experience about a novel treatment protocol combined steroids with flavonoids.

Seventeen children (3 girls and14 boys) diagnosed with ASD were enrolled in steroid treatment. Social development of children before autistic regression was evaluated from previous video recordings and parent reports. All had adequate eye contact and reciprocal social interaction before regression. Regression was defined as loss of acquired social skills and words used communicatively. The treatment protocol was designed as 1 mg/kg deflazacort for 3 months, followed by slow tapering for 6 months. One month before cessation of steroid therapy, 250 mg/day quercetin supplementation was initiated and planned for at least 16 months. Two patients dropped out treatment, one from gastrointestinal side effects and the other due to emerging masturbation behavior. Fifteen patients aged between 4 and 8 years and 8 months completed steroid treatment and still on quercetin treatment (10–25 months; mean, 18 months). All patients had electroencephalography (EEG) recording before treatment. Six patients had bilateral central spikes. None of them reported seizures. One patient had corpus callosum agenesis and one had mild periventricular leukomalacia at magnetic resonance imaging. One patient was diagnosed as cerebral palsy before the diagnosis of autism. During treatment, parent reports of progression and analysis of daily activity videos were recorded in every 3 months. Global improvement score (CGIC) was very much improved in seven patients, much improved in five patients, and minimally improved in three patients. Improvement at social interaction (increased eye contact, reciprocal interaction, and playing with peers) was marked in eight patients, moderate in four patients, and minimal in three patients. Receptive language skills improved marked in six patients, moderately in six patients, and minimal in three patients. Expressive language improved minimal to moderate only in 11 patients. After steroid treatment, epileptic discharges markedly diminished (<%50) in one patient with much global improvement. Two patients were very much improved, three patients were much improved, and one patient was minimally improved with EEG findings. Ten patients reported restlessness during first month of protocol but these complaints subsided. None of the patients re-regressed after the completion of steroid treatment and weight gain of patients were mild.

Steroids are among the oldest anti-inflammatory agents, which can inhibit the production of proinflammatory cytokines, modify T-cell activity, and may also downregulate the microglial activity.[1] Duffy et al[2] retrospectively analyzed 4-Hz frequency modulated evoked response originating from language area of the superior temporal gyrus from 24 patients aged between 3 and 5 years, treated with 2 mg/kg oral prednisolone for 9 to 12 months. After steroid treatment, they observed a significantly increased evoked response magnitude and improvement in receptive and expressive language and behavior scores. All of their patients experienced significant weight gain and two patients manifested slight language re-regression after completion of the steroid taper. None of our patients showed re-regression in language or social skills after steroid taper because of quercetin maintenance treatment. Furthermore, lower dose of steroid and weight neutral properties of deflazacort could be protective for weight gain. Unlike the study of Duffy et al, improvement in language was more prominent at receptive area. This could be an effect of lower steroid dose.

Microglia activation and increased plasma levels of tumor necrosis factor α and interleukin-6 in patients with autism had repeatedly proven.[4] Two major flavonoids, quercetin and luteolin, inhibit the release of leukotrienes, histamine, interleukin-6, and tumor necrosis factor-α from culture of human

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mast cells. At the study of Tsilioni et al,[5] 40 patients diagnosed as autism was treated with a luteolin-containing dietary supplement for 26 weeks and showed improvement autism symptoms and reduction in serum levels of interleukin-6 and tumor necrosis factor α. Quercetin was added to our treatment protocol for prolongation of immunotherapy as a steroid sparing agent.

In conclusion, a subset of patients with autism could benefit from immune-based treatment. Marked regression in the patient's history is a valuable tip for patient selection. Finally, protocols combining agents could save patients from side effects and may prevent deterioration after the therapy.

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Conflict of Interest
None declared.

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