Methotrexate improves Quality of Life in JIA

BY KATE JOHNSON

Methotrexate significantly improved health-related quality of life in children with juvenile idiopathic arthritis. Although the information on the efficacy and safety of second-line agents is "abundant," little is known about the effect of current treatments on the health-related quality of life (HRQOL) of patients with JIA, reported Dr. A. Céspedes-Cruz from the Rheumatology International Adult Trials Organization in Genoa (Italy) and associates.

In their study of 321 children with the disorder, methotrexate (MTX) treatment produced a significant improvement across a range of HRQOL domains, especially in the physical domain, they reported. "Although similar studies in adults with rheumatoid arthritis have been reported, to the best of our knowledge this is the first time that HRQOL has been examined in JIA, demonstrating that effective therapies such as MTX can reverse the impairments of HRQOL and substantially improve a patient’s life." The 521 children (mean age, 8 years) were selected from a larger randomized trial aimed at evaluating the safety and efficacy of various doses of MTX (2.5 mg/m² per week to 20 mg/m² per week) in young patients who had polycyclic-course JIA (systemic, polyarteritis, or extended oligoarthritis categories), and were newly treated with a standard dosage of MTX (10 mg/m² per week) for 6 months. After this period, non-responders were randomized to receive either intermediate (15 mg/m² per week) or high dosages (30 mg/m² per week) for a further 6 months. No other drug was allowed for the duration of the trial, except low-dose steroids and one nonsteroidal anti-inflammatory drug. A total of 3,313 healthy children were used as controls. Patients were included in the analysis if they had completed at least 6 months of treatment with MTX and had an HRQOL assessment at baseline and/or at 6 months. The Child Health Questionnaire (CHQ), designed to capture the physical, emotional, and social components of health status, was used to assess HRQOL in patients and controls.

In general, patients in the study had relatively short disease duration (mean, 2.8 years) and high disease severity and disability at baseline. Their HRQOL was poor at baseline, particularly in the physical domain, with many health concepts being 2 standard deviations (SD) below the mean for healthy children, noted the authors. "Body pain/discomfort was the most impaired CHQ health concept, with values that were 60% below the threshold of absence of pain," they wrote. "Also at baseline, patients showed other health concepts related to physical well-being that were below 2 SD of the mean of healthy controls, such as perceiving themselves having less opportunity and energy to participate in social and physical activities because of their impaired global health." Patients' psychosocial domain were also significantly lower than those of healthy controls, and not as impaired as the physical domains.

After 6 months of treatment with standard-dose MTX, a total of 403 (77%) of the 521 participants were considered responders. A further 39 and 16 patients, respectively, were eligible for randomization to 6 subsequent months of intermediate- or high-dose treatment, noted the authors. Significant improvement in HRQOL was noted after 6 months in all CHQ health concept scores for the initial responders, "indicating that the physical and psychosocial consequences of the disease are partly reversible as a result of medical intervention," they wrote. This improvement in HRQOL was also seen after the non-responders were randomized to intermediate- or high-dose MTX, they added. "It is notable that almost all the health concepts that at baseline were < 2 SD of the mean of healthy control reached median mean values above this level except physical health, which, despite improvements, remained close to the cut-off of 2 SD of healthy children," they wrote.

"This finding suggests that a major functional impairment remains in these patients despite the observed improvement in disease activity measures," they concluded. The study also sought to identify the determinants of change in HRQOL between baseline and psychosocial well-being after MTX treatment. It found that a greater baseline disability was the strongest determinant of persistently poor psychosocial well-being (odds ratio, 5.2), with weaker determinants being erythrocyte sedimentation rate, parents' assessment of child's pain, and antimicrobial antibody-negative status. These findings "may allow doctors to identify children at greater risk of retaining poor physical health despite treatment with MTX," they wrote. "These children would require additional medical and/or psychological interventions to decrease this risk."

The strongest determinant for persistently poor psychosocial well-being was the number of limited joints (OR 6.5), followed by the parents' assessment of child's well-being, and to a lesser extent, the doctor's global assessment of disease activity and an antimicrobial antibody-negative status. The authors noted the unexpected findings in controlling and conflicting finding that, while the parents' assessment of increased baseline disability and child well-being was associated with persistence of poor psychosocial well-being, the doctors' assessments of fewer joints with limited range and a lower level of disease activity were also associated with persistently poor psychosocial scores. "This highlights the discrepancy in the evaluation of the child between the parent and the doctor, with the former being more concerned about psychosocial well-being and the latter being influenced by physical features of the child's disease," they wrote (Ann. Rheum. Dis. 2008;67:309-14).

Future studies will need to evaluate the effect of other medication, particularly biological agents, on HRQOL, the researchers concluded.