One JIA Type Involves Injury to Salivary Glands

BY DIANA MAHONEY
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The salivary glands of children with oligoarticular-type juvenile idiopathic arthritis may be targets of inflammatory, oxidative stress–mediated injury, a study has shown.

In an investigation of the salivary gland involvement and saliva and serum antioxidant profiles in patients with juvenile idiopathic arthritis (JIA), Dr. Riva Brik of Meyer Children's Hospital in Haifa, Israel, and colleagues observed a major increase in antioxidant enzyme activity in the serum and saliva of children with systemic, polyarticular, and oligoarticular-type disease, as well as significant and specific damage to the salivary glands in those children with oligoarticular JIA.

Although there is a scarcity of data on salivary gland involvement or alterations in JIA, previous studies in adults with rheumatoid arthritis have shown direct relationships between disease severity and increased levels of antioxidant enzymes in secreted saliva and serum, suggesting that saliva—which is easier and less invasive to collect—might be suitable as a window into serum composition in children. Because adult studies also have identified oxidative stress as a major contributing factor to the chronic inflammatory process within the inflamed joint, the ability to measure such changes in saliva could have therapeutic implications in JIA (J. Rheumatol. 2006;33:2532-7).

Toward this end, the investigators studied the salivary composition and the saliva and serum antioxidant profiles of 22 children with JIA according to the American College of Rheumatology criteria and 15 healthy controls. Of the children with JIA, 10 had oligoarticular, 7 had polyarticular, and 5 had systemic-type disease. The mean age of the 15 girls and 7 boys with JIA was 12.2 years and the mean durations of follow-up and disease activity were 5.8 years and 5.1 years, respectively.

Only patients with oligoarticular-type disease showed evidence of specific injury to the salivary glands, reflected by low flow rate and other changes.

Saliva and serum samples were obtained concomitantly from each study participant. Saliva was analyzed for flow rate (volume of saliva secreted per minute), chemistry (pH, calcium, phosphate, magnesium, total protein, albumin, lactate dehydrogenase, and amylase), total antioxidant status, peroxidase activity, and uric acid. Serum was analyzed for total antioxidant status, peroxidase activity, uric acid, total protein, and albumin.

The analyses showed that the median salivary flow rates of the JIA patients as a whole were within normal range and were similar to those of the healthy controls. The median flow rate of children with oligoarticular arthritis was 33% lower than that of the control group. The difference did not reach statistical significance, however, due to the large standard error values, according to the authors.

Sialochemistry analysis findings indicated the saliva composition in children with oligoarticular JIA contained significantly lower levels of magnesium, total protein, amylase, and lactate dehydrogenase compared with the other JIA subtypes. Additionally, levels of salivary calcium and phosphate were low, bordering on a statistically significant difference. Compared with controls, there were no significant differences between the total JIA group and the healthy controls in measures of salivary calcium and albumin; however, patients with systemic disease showed increased levels of salivary total protein and polyarticular patients had significantly increased levels of amylase. Salivary pH was higher in all of the JIA patients compared with controls, and was highest in the oligoarticular group.

The salivary antioxidant analyses showed that salivary peroxidase activity was significantly higher (8.5%) in the JIA group as a whole compared with controls, and most notably among the polyarticular group, whose levels were 17% higher than controls. The antioxidant enzyme superoxide dismutase was significantly increased in the JIA patients, particularly in those with systemic-type disease in whom a 74% increase was noted, the authors wrote. Measures of salivary uric acid and total antioxidant status in the JIA patients were not statistically different from those of the controls. The results of the serum analyses showed significantly higher levels of serum peroxidase activity in the JIA group, with the maximal increase of 17% observed in the polyarticular subgroup. All of the JIA subgroups showed nonsignificant reductions in uric acid concentrations compared with controls and nonsignificant differences in total antioxidant status. A significant increase in serum albumin concentrations was seen in all three JIA subgroups, with a mean 9.3% increase in the total group compared with the control group.

"Our main finding was significant alterations in the saliva of patients with oligoarticular JIA compared to controls and also to other patients with JIA," the authors wrote. "Whereas the total group of patients showed increased levels of antioxidant enzyme activity both in serum and in saliva, presumably as a result of the ongoing inflammatory process, only the patients with oligoarticular-type disease showed evidence of specific injury to the salivary glands, as reflected by a reduced salivary flow rate, low levels of amylase and LDH activity, and lower concentrations of total proteins." The changes observed in the saliva of the children with oligoarticular-type disease "may designate the salivary glands [in similarity to joints] as target organs of inflammatory, oxidative stress–mediated injury," they stated.

"We also showed that saliva is a reliable representative of serum composition and can be used for pertinent testing in children," they noted. ■

Specific Changes Distinguish Atypical, Incomplete Kawasaki's

BY JEFF EVANS
Senior Writer

WASHINGTON — Atypical and incomplete Kawasaki disease may be distinguished from other common childhood febrile illnesses by characteristic changes to the extremities, mucosa, conjunctiva, and blood laboratory values, Dr. Fernanda Falcini reported at a poster session of the annual meeting of the American College of Rheumatology.

In a chart review of 1,499 children discharged from the hospital with a diagnosis of Kawasaki disease (KD), 225 (15%) did not fulfill the Centers for Disease Control and Prevention's case definition criteria of KD. The CDC identifies KD patients as those having four of the following five clinical signs: rash, cervical lymphadenopathy of at least 1.5 cm in diameter, bilateral conjunctival injection, oral mucosal changes, and peripheral extremity changes.

Of those 225 patients, 172 had incomplete KD (median age 21 months) and 53 had atypical disease (median age 50 months), according to Dr. Falcini of the rheumatology unit in the department of pediatrics at the University of Florence (Italy).

Patients with incomplete KD did not meet all of the CDC case definition criteria, whereas atypical disease referred to patients who also had a problem that generally is not seen in KD.

Lip and oral redness, skin extremity changes, and nonexudative conjunctivitis occurred significantly more often among children with incomplete or atypical KD than in 55 children who had other febrile illnesses that mimic KD. These other illnesses were cytomegalovirus (in 21 children), adenovirus (16), systemic juvenile idiopathic arthritis (12), Epstein-Barr virus (5), and staphylococcal scalded skin syndrome (1).

The erythrocyte sedimentation rate and total platelet count of children with incomplete and atypical KD also were significantly higher than in children with other KD-mimicking illnesses. But children with febrile diseases other than KD were significantly more likely to have lymphadenopathy than were those with incomplete or atypical KD.

Coronary artery diseases, including dilatation and aneurysms, were detected only in patients with incomplete (47) or atypical KD (15), reported Dr. Falcini. ■

Researchers Identify a Recessive Form of Osteogenesis Imperfecta

BY SARAH PRESSMAN LOVINGER
Contributing Writer

A mutation of the gene for cartilage-associated protein may lead to a recessive and lethal form of osteogenesis imperfecta, according to Dr. Joan C. Marini of the National Institute of Child Health and Human Development in Bethesda, Md.

"We identified a recessive form of lethal osteogenesis imperfecta, caused by null mutations in [cartilage-associated protein] CRTAP, a gene that encodes a protein that is essential for one of the posttranslational modifications of types I and II collagen," Dr. Marini and her colleagues reported.

While mutations in type I collagen lead to most cases of osteogenesis imperfecta (OI), researchers in the field had sought a recessive form of the disease. The authors screened dermal fibroblasts from 10 children with lethal (type II), or very severe (type III) OI who had type I collagen with excess posttranslational modification of the alpha chain helical region but a normal primary structure, using a fibroblast cell line from newborn foreskin as a control. They also evaluated 11 patients who had severe OI without the excess modification described above and without a collagen defect, 6 normal control subjects, and 1 control patient with classic (type III) OI. The authors used polymerase-chain-reaction (PCR) assays to amplify DNA sequences in the subjects' genomes. They used reverse-transcriptase PCR assays to determine CRTAP mRNA levels.

After sampling mRNA from the fibroblasts of 10 children with type II or III OI who had excess posttranslational modification but lacked a collagen mutation, they determined that 3 infants had CRTAP mRNA levels that were 0%-25% of the normal range. In addition to low levels of CRTAP mRNA, the infants had defects in both CRTAP alleles, they lacked CRTAP protein, and they had minimal hydroxylation of type I collagen. All of these infants died within the first year of life. Fibroblasts from the parents of two of these three infants (one set of parents did not participate in the analysis) had normal CRTAP mRNA levels, a finding that suggests that the infants had more than one defective allele. As in all children with lethal OI, those with the recessive form of the disease have severely undermineralized bones that result in multiple prenatal fractures. Those children with the recessive mutation also have a small head circumference, proptosis, and white or light blue sclerae (N. Engl. J. Med. 2006;355:2757-64).

Defects in the CRTAP gene are likely to cause 2%-3% of all cases of lethal OI. ■