

Study Tracks Endothelial Function in Kawasaki

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SAN DIEGO — Systemic arterial endothelial dysfunction was significantly related to higher levels of triglycerides and fasting blood glucose, but not to other cardiovascular risk factors in a long-term follow-up study of patients with Kawasaki disease, Brian W. McCrindle, M.D., reported at an international Kawasaki disease symposium.

Those particular factors “may be indicators of ongoing inflammation, which may be addressed by long-term aspirin use, antioxidant vitamins, or, in extreme cases, use of a statin,” Dr. McCrindle, a pediatric cardiologist at the Hospital for Sick Children, Toronto, told FAMILY PRACTICE NEWS.

The findings suggest systemic arterial endothelial dysfunction is not present in the long term after Kawasaki disease and that brachial artery activity is not related to the degree of past or current coronary artery involvement.

Dr. McCrindle said that he was surprised by the findings, which conflict with similar reports from Japanese investigators.

“The difference may be in the control population used for comparison, with North American children being more sedentary, having poorer nutrition, and being more overweight [compared with Japanese children], meaning that even normal is abnormal.”

Dr. McCrindle and his associates enrolled 52 patients, aged 10-20 years, who had their initial episode of Kawasaki disease between 1982 and 1998 and who had been followed for a mean of 11 years. A group of 60 normal controls matched for age and gender.

The investigators performed a cardiovascular risk assessment of all participants, including questions about smoking and smoke exposure, family history of cardiovascular disease, and attitudes and practices regarding physical activity. Patients completed a food frequency questionnaire and were asked to recall food they’d consumed in the last 3 days; they also underwent detailed height and weight measurements, fasting blood work, a fasting lipid profile, and urinalysis. Systemic arterial endothelial function was obtained assessing brachial artery reactivity (BAR).

The mean BAR dilatation in Kawasaki disease patients was 8.9%, which was not significantly different from the controls (9.4%), and was not related to any disease characteristic or measure of current or past coronary artery lesions.

In addition, the investigators observed no differences between the BAR of Kawasaki disease patients and that of controls in terms of age, gender, Tanner stage, skinfold thickness percentile, body mass index z score, physical activity levels of the patient or family members, or responses to the dietary assessment.

The lab results showed no differences between the two groups in terms of total cholesterol; HDL; LDL; apolipoproteins A1, B, or E; lipoprotein (a); homocysteine or fibrinogen levels; or 24-hour microalbumin excretion.

However, decreased BAR in Kawasaki disease patients was significantly and independently related to higher triglyceride levels and higher fasting blood glucose levels.

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Cardiac Abnormalities May Appear Late in KD Patients

SAN DIEGO — Cardiac abnormalities in patients with Kawasaki disease may appear well after their short-term treatment phase, even in those with no previous evidence of cardiac involvement, results from a follow-up study show.

The results “further support a need for long-term follow-up of all patients with Kawasaki disease,” Rosie Scuccimarri, M.D., reported at an international Kawasaki disease symposium. “Patients who have had normal echoes at 8 weeks should also have echocardiograms at least every 5 years.”

For the study, she and her associates contacted 221 patients who had been admitted to Montreal Children’s Hospital with a diagnosis of Kawasaki disease during January 1985 to December 1999 and who were treated in the acute phase of their disease with intravenous immunoglobulin and low-dose aspirin. The aim was to conduct late follow-up echocardiographic evaluations, and of the 221 patients contacted, 159 participated in the study.

Patients identified as having echocardiographic abnormalities within 8 weeks of Kawasaki disease diagnosis or during later follow-up visits (38) were matched to those in which no prior abnormalities were detected (121). The mean age of disease diagnosis was 3 years, and the mean age at study visit was 11 years.

Of the 38 patients in whom abnormalities had been detected previously, 12 had coronary artery lesions, which translated into an incidence of 7.5% in the entire study group.

A coronary vessel was defined as abnormal if its diameter was greater than 3 mm in a child younger than 3

years, greater than 3.5 mm in a child aged 3-5 years, greater than 4 mm in a child aged 5-11 years, and greater than 5 mm in a child older than 11 years.

All 38 patients with abnormalities had complete resolution of their original abnormalities, but 8 (21%) had developed new pathology on long-term follow-up.

The investigators also observed that 7 of the 121 patients (6%) with normal echocardiograms on early follow-up had abnormal results on late follow-up, including one with a new coronary artery lesion.

“There was a significant interest by patients to participate [in the study],” noted Dr. Scuccimarri, a pediatric rheumatologist at McGill University Health Center, Montreal. “We were lucky enough to have patients who came [from] as far as Hong Kong, Western Canada, and the United States at their own expense.”

In another part of the study, a subgroup of 35 patients underwent a stress test using technetium-99m sestamibi (stress MIBI) with continuous ECG monitoring: 18 who had echocardiographic abnormalities at early or late follow-up and 17 who had no such abnormalities.

Among the 18 patients with abnormalities at early or late follow-up, 1 had an abnormal stress ECG, Dr. Scuccimarri said at the meeting, which was sponsored by the American Heart Association. Among those without evidence of abnormalities, one had an abnormal ECG, and one had an abnormal stress MIBI.

She concluded that the role of stress-MIBI testing and long-term follow-up “needs to be evaluated further.” ■

Long-Term Study of Kawasaki Targets Risk of Atherosclerosis

SAN DIEGO — Long-term survivors of Kawasaki disease with or without a history of coronary aneurysms had no evidence of accelerated carotid atherosclerosis, results from a controlled, multicenter study have shown.

“Discussion of these findings with patients and their families may be helpful in preventing unwarranted psychological effects,” Dorota Gruber said at an international Kawasaki disease symposium. “The need for unusual or frequent serum screenings has not been established.”

Investigators, led by Rubin S. Cooper, M.D., director of pediatric cardiology at New York-Presbyterian Hospital, New York, assessed 28 Kawasaki disease patients at least 5 years after the acute phase of their disease and compared them with 27 age- and gender-matched controls.

There were no differences between

the groups in terms of age, gender, race, BMI, blood pressure, cigarette smoking, family history, and diet, reported Ms. Gruber, a clinical research coordinator at the hospital.

Traditional serum atherosclerotic risk markers such as LDL and HDL levels were also similar between the two groups, she said at the symposium, sponsored by the American Heart Association.

Males in the Kawasaki disease group had significantly higher levels of cystatin C and apolipoprotein B, compared with males in the control group, but these levels were still within the normal range. Males in the Kawasaki disease group also had a higher median body mass index than males in the control group (24 kg/m² vs. 21 kg/m², respectively).

Investigators observed no differences in carotid intima-medial thickness or ventricular size and function. ■

Study Assesses Interaction Between Warfarin, Antibiotics in Children

SAN DIEGO — Children on warfarin should get an international normalized ratio measurement within 2-3 days of starting antibiotic therapy, since they may experience significant changes in INR value, Kathy Hinoki, R.N., reported in a poster session at an international Kawasaki disease symposium.

“I have proactively cut back on a warfarin or Coumadin dose when the parent has told me the child is sick and has been started on an antibiotic,” Ms. Hinoki, a cardiology nurse with Children’s Hospital Los Angeles, said in an interview. “This prevents the lab values from getting out of whack and [lessens the] risk for bleeding.”

She noted that while physicians typically order antibiotics for warfarin-treated children, “they usually don’t have the background about the seriousness of the warfarin-antibiotic interaction, so they probably should consult with someone who [has the expertise].”

In a 5-year study of 3,582 lab encounters in the anticoagulation clinic at Children’s Hos-

pital Los Angeles, Ms. Hinoki and her associates selected 28 children who had a stable INR on the same dose of warfarin for greater than three consecutive lab encounters prior to the initiation of antibiotic therapy. The three most common reasons for anticoagulation were prosthetic valves, Fontan procedure, and Kawasaki disease.

The investigators measured the INR 1-7 days after the antibiotics were started, and they calculated the percent change in INR.

Of the 28 cases, eight females and four males demonstrated INR increases of more than 20%. Of the 16 children who demonstrated either no change or a decrease in INR, 12 were males and 4 were females.

Ms. Hinoki noted that erythromycin, cefuroxime, clindamycin, levofloxacin, and doxycycline were associated with significant increases in INR, while ampicillin, cephalexin, and amoxicillin-clavulanic acid were associated with no changes in INR. Griseofulvin and azithromycin appeared to cause mild to moderate decreases in INR. ■