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CASE REPORT

Treatment of Acute Rheumatic Carditis with Choline Magnesium Trisalicylate in a Patient Needing Surgery

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Acute rheumatic fever is a post-infectious illness characterized by diffuse inflammation. Typically, high-dose anti-inflammatory agents are used as primary therapy for this disorder. In addition to their anti-inflammatory properties, these agents, most frequently aspirin, also have anti-platelet properties. We describe the case of an 11-year-old patient with rheumatic fever who needed to undergo surgery. The use of traditional anti-inflammatory agents would have posed a potential problem with post-surgical bleeding, so a lesser-used anti-inflammatory agent (i.e., choline magnesium trisalicylate) was selected.

KEYWORDS: acute rheumatic carditis, anti-inflammatory, choline magnesium trisalicylate, pediatric, Trilisate

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An 11-year-old male with a history of Trisomy 21 and obesity presented to our hospital with complaints of shortness of breath and tachypnea. He had no known history of congenital heart disease. On review of systems, he had a 1-month history of arthralgias but did not have any history of fever or sore throat. In addition, he had a prolonged history of loud breathing during sleep and occasional apnea. His vital signs were notable for mild desaturation with a room air oxygen saturation of 88%.

His physical examination was remarkable for facies consistent with Trisomy 21, obesity, tonsillar hypertrophy, diminished breath sounds at his lung bases bilaterally, and quiet heart sounds with an intermittent III/VI holosystolic murmur heard best at the apex. There were no diastolic murmurs. His liver edge was palpable approximately 3–4 cm below the right costal margin. His chest radiograph showed an enlarged cardiac silhouette, bilateral pleural effusions, and increased pulmonary vascular markings. His laboratory studies were remarkable for an elevated erythrocyte sedimentation rate (ESR) of 106 mm/hour (nl=0–20 mm/hour), an elevated C-reactive protein of 8.4 mg/dL (nl=0– 1 mg/dL), and an elevated antistreptolysin (ASO) of 400 IU/mL (nl <250 IU/mL). An echocardiogram performed showed normal intracardiac anatomy with severe aortic regurgitation, moderate mitral regurgitation, no evidence of vegetations, a dilated left atrium and left ventricle, and good left ventricular function. His left ventricular shortening fraction was 41%, and he had qualitatively good right ventricular function.

He met the criteria for acute rheumatic fever (major criteria = carditis, 2 minor criteria = elevated ESR and history of arthralgias, and evidence of recent streptococcal infection = elevated ASO).[1] In addition, he was believed to have clinical features consistent with obstructive sleep apnea, and it was recommended that he undergo tonsillectomy & adenoidectomy.

The patient was started on choline magnesium trisalicylate (Trilisate, Purdue Frederick Co, Stamford, CT) 1000 mg by mouth every 6 hours (66.7 mg/kg/day). After 24 hours of therapy, the serum salicylate concentration was 14.1 mg/dL (nl=20–30 mg/dL).

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He was continued on this dose for 4 days, until the serum salicylate trough concentration reached a high of 30.9 mg/dL. The dose was then decreased to 750 mg by mouth every 6 hours (50 mg/kg/day). The concentration stayed between 18.2 and 28.4 mg/dL for the remainder of inpatient therapy.

He underwent tonsillectomy and adenoidectomy without any complications or bleeding. At recent follow-up, approximately 4 months after initial admission, he was asymptomatic from a cardiovascular standpoint with no orthopnea or shortness of breath. His most recent echocardiogram shows severe aortic regurgitation, moderate mitral regurgitation, and normal left ventricular function.

DISCUSSION

Therapy with an anti-inflammatory agent was indicated for the patient's rheumatic fever. Typically, large doses of salicylates are used and serum salicylate concentrations are followed. Aspirin is typically the primary agent. However, due to its anti-platelet activity and the patient's risk of bleeding from the surgery, aspirin was not a viable option. Other considerations included cyclooxygenase-2 (COX-2) inhibitors such as rofecoxib (Vioxx, Merck & Co, Inc., West point, PA) or celecoxib (Celebrex, GD Searle LLC, Chicago, IL). One limitation of the use of these agents is the inability to individualize therapy using serum concentration monitoring. Given the above consideration, we chose to use choline magnesium trisalicylate as our anti-inflammatory agent.

Salicylates are effective in reducing pain and inflammation in diseases such as juvenile rheumatoid arthritis, osteoarthritis, rheumatic fever, and other painful conditions.[2] The benefits of salicylates are produced via cyclooxygenase inhibition and reduction of prostaglandins, which reduces inflammation and pain.[2] However antiplatelet aggregation can induce bleeding, a detrimental side effect of some salicylates, particularly aspirin.[2] The acetyl moiety in aspirin has been identified as the primary cause of decreased platelet aggregation; hence, those agents without the acetyl moiety have a reduced risk of bleeding.[3] Choline magnesium trisalicylate is an anti-inflammatory agent in which the acetyl moiety of aspirin is replaced by magnesium or a choline moiety.[2] Theoretically, this reduces the antiplatelet effects and thereby decreases the incidence of bleeding that is typically seen with large doses of aspirin. Clinically, adverse bleeding events with choline magnesium trisalicylate are markedly decreased when compared to aspirin.

A study in adults with known increased risks of bleeding demonstrated that platelet aggregation due to choline magnesium trisalicylate is minimal.[4] Importantly, therapeutic benefit is not compromised by using choline magnesium trisalicylate in lieu of aspirin. Studies in adult patients have shown that serum salicylate concentrations and salicylates elimination rates are equivalent to those reported for aspirin.[5,6] It has also been demonstrated that serum salicylate concentrations are comparable in febrile children given aspirin given choline salicylate and aspirin.[7] All of the available medical and pharmacology literature supports the successful use of choline magnesium trisalicylate in pediatric patients. However, there are no current data regarding its use in pediatric patients for treatment of rheumatic carditis.

The current recommended initial dose of aspirin for treatment of rheumatic carditis in pediatric patients is 60 mg/kg/day in divided doses every 6 hours for 4 to 8 weeks.[8] The goal salicylate serum concentration required for treatment of rheumatic carditis ranges between 20–30 mg/L.[8] In order to achieve these concentrations, the dose of aspirin can be escalated to 100 mg/kg/day, divided every 6 hours if needed. Individualization of dosing should be guided by serum trough salicylate concentrations.[8]

A COX-2 inhibitor may have been a viable option in the patient we describe, due to the decreased bleeding risk associated with the class of agents. However, serum salicylate concentrations cannot be followed with COX-2 inhibitors, and therapeutic efficacy would be difficult to measure. A choline magnesium trisalicylate dose was determined by using a milligram-to-milligram aspirin dose equivalent, and serum salicylate trough concentrations were drawn daily to ensure that therapy was appropriate. Based upon the adult literature, the small amount of pediatric pharmacokinetic data, and the patient presented in this case, we conclude that choline

magnesium trisalicylate will produce therapeutic serum salicylate concentrations in patients with rheumatic carditis who have an increased risk for bleeding.

CONFLICTS OF INTEREST: The authors declare no conflicts of interest or financial interest in any product or service mentioned in the manuscript, including grants, equipment, medications, employment, gifts, and honoraria.

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