Effects of dietary n-3 fatty acid supplementation versus thromboxane synthetase inhibition on gentamicin-induced nephrotoxicosis in healthy male dogs.

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OBJECTIVE: To evaluate the protective effects of dietary n-3 fatty acid supplementation versus treatment with a thromboxane synthetase inhibitor (TXSI) in dogs given high-dose gentamicin. DESIGN: Clinicopathologic and renal histopathologic changes induced by gentamicin (10 mg/kg of body weight, IM, q 8 h, for 8 days) were compared in dogs fed an n-3 fatty acid-supplemented diet containing a fatty acid ratio of 5.7:1 (n-6:n-3), dogs treated with CGS 12970 (a specific TXSI given at 30 mg/kg, PO, q 8 h, beginning 2 days prior to gentamicin administration), and control dogs. The TXSI-treated and control dogs were fed a diet with a fatty acid ratio of 51.5:1 (n-6:n-3). Both diets were fed beginning 42 days prior to and during the 8-day course of gentamicin administration. ANIMALS: Eighteen 6-month-old male Beagles, 6 in each group. RESULTS: After 8 days of gentamicin administration, differences existed among groups. Compared with n-3-supplemented and control dogs. TXSI-treated dogs had higher creatinine clearance. Both TXSI-treated and n-3-supplemented dogs had higher urinary prostaglandin E2 and E3 (PGE2/3) and 6-keto prostaglandin F1a (PGF1a) excretion, compared with control dogs. Urinary thromboxane B2 (TXB2) excretion was higher in n-3-supplemented and control dogs, compared with TXSI-treated dogs. Urine PGE2/3-to-TXB2 and PGF(in)-to-TXB2, ratios were increased in TXSI-treated dogs, compared with n-3-supplemented and control dogs, and these ratios were increased in n-3-supplemented dogs, compared with control dogs. In addition, TXSI-treated and n-3-supplemented dogs had lower urinary protein excretion, compared with control dogs. Proximal tubular necrosis was less severe in TXSI-treated dogs, compared with control dogs. CONCLUSION: Treatment with CGS 12970 prior to and during gentamicin administration prevented increases in urinary TXB2 excretion and reduced nephrotoxicosis. CLINICAL RELEVANCE: Increased renal production/excretion of thromboxane is important in the pathogenesis of gentamicin-induced nephrotoxicosis.

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