Antibiotics Yield Modest Decrease in Recurrent UTIs in Children

For children with risk factors for recurrent urinary tract infections (UTIs), long-term antibiotic prophylaxis has a small but significant preventive benefit, concludes a randomized trial in The New England Journal of Medicine.

The Australian multicenter trial included 576 children with at least one symptomatic UTI. The median age was 14 months; about two-thirds of patients were girls. Vesicoureteral reflux was present in 42 percent, grade III or higher in more than half of cases. Rates of microbiologically confirmed UTIs were compared for children assigned to prophylactic antibiotics (trimethoprim 2 mg/dL plus sulfamethoxazole 10 mg/kg) versus placebo.

Over 12 months, 13 percent of children in the antibiotic group had recurrent UTIs, compared to 19 percent of the placebo group. The number needed to treat to prevent one UTI was 14. The reduction in absolute risk was about the same—six to eight percentage points—across subgroups defined by age, sex, reflux status, or number of previous UTIs. Large numbers of children receive long-term antibiotics with the goal of preventing recurrent UTIs and resultant kidney damage. However, in the absence of randomized trial data, this practice has been questioned.


Erythropoietins Linked to Increased Mortality in Kidney Transplant Patients

Especially when high hemoglobin levels are achieved, the use of erythropoietins in kidney transplant recipients may lead to an increased risk of death, reports a study in the British Medical Journal.

The retrospective analysis included Austrian registry data on 1794 patients who survived at least three months after kidney transplantation between 1992 and 2004. The use of erythropoietins increased from 12 percent in 1992 to 28 percent in 2001. Unadjusted Kaplan-Meier analysis suggested lower 10-year survival in patients treated with erythropoietin: 57 versus 78 percent. With adjustment for confounding factors, hemoglobin levels of greater than 125 g/L tended to be associated with increased mortality—but only in patients receiving erythropoietins. This difference became significant at hemoglobin levels of 147 g/L or higher: hazard ratio 3.0 for erythropoietin-treated patients.

There is continued uncertainty over just how high hemoglobin levels can be safely increased with erythropoietin. Previous studies have suggested increased mortality among erythropoietin-treated patients with chronic kidney disease and end stage renal disease. This registry study suggests a possible increase in mortality among kidney transplant patients receiving erythropoietins to raise hemoglobin levels, especially above 140 g/L. Although no causal association can be proved, the authors advise against giving erythropoietins to kidney transplant recipients with hemoglobin levels over 125 g/L [Heinze G, Kainz A, Hirsch A, Oberhauser R. Mortality in renal transplant recipients given erythropoietins to increase haemoglobin concentration: cohort study. Brit Med J 2009; 339:4018].

Serum Amyloid P: A New Inhibitor of Renal Fibrosis?

Serum amyloid P (SAP)—a known inhibitor of pulmonary and cardiac fibrosis—may also have antifibrotic effects in the kidneys, according to a study published in Science Translational Medicine.

In experiments in two models of renal fibrosis in mice, administration of human SAP (hSAP) was associated with dose-dependent reductions in fibrosis. Although fibroblasts were still present in similar numbers, hSAP treatment was associated with down-regulation of fibrotic collagen gene transcription and collagen protein deposition. Further experiments suggested that hSAP selectively localized to the injured kidneys, mainly associated with apoptotic and necrotic cells. In humans, more severe kidney disease was associated with lower plasma concentrations of hSAP.

In the kidneys, fibrosis depends on inflammatory monocytes and macrophages, rather than fibroblasts. The antifibrotic effect of hSAP appeared to occur via monocyte/macrophage binding and suppression, dependent on interleukin-19 and regulated binding to Fcy receptors.

There is an urgent need for new treatments directed against chronic inflammation with fibrosis. A natural soluble pattern recognition receptor, SAP has been shown to recognize danger-associated molecular patterns (DAMPs) on the membranes of apoptotic cells and promote Fcy receptor-dependent phagocytosis.


ASN Grants

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