Reviewer's report

**Title:** Angiotensin converting enzyme inhibitor therapy in children with Alport syndrome: Effect in urinary albumin, TGF-beta, and nitrite excretion

**Authors:**

- Liora Adler (weinste@aecom.yu.edu)
- Roy Mathew (rom_75@yahoo.com)
- Stephen Futterweit (trachtma@lij.edu)
- Rachel Frank (frank@lij.edu)
- Bernard G Gauthier (gauthier@lij.edu)
- Kashtan E Clifford (kasht001@maroon.tc.umn.edu)
- Howard Trachtman (trachtma@lij.edu)

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**Reviewer:** Dr Markus Ketteler

**Level of interest:** A paper of limited interest

**Advice on publication:** Other (see below)

Adler et al. report on a clinical study performed in 11 children with biopsy-proven early-stage Alport-syndrome. These children were treated with the ACE inhibitor enalapril for 14 days, and the effects of enalapril on urinary albumin, TGF-beta and nitrite excretion were measured. At baseline, these parameters appeared not to be stimulated, and ACE inhibitor treatment did not influence these three parameters significantly. The authors conclude that in early Alport-syndrome routine administration of ACE inhibitors is not warranted. The major difficulty in the evaluation of this study relates to the question at which time point in Alport-syndrome ACE inhibitor therapy may become important and by which means this time point may be identified.

Further comments:
1. Urinary nitrite excretion does not necessarily reflect renal NO synthesis, and measuring nitrite is less interpretable than nitrate/nitrite excretion, since a proportion of 50 - 90 % of NO related end-products may be present as nitrate in biological fluids. If nitrate is measured, however, study subjects should receive a low nitrate diet.

2. ACE inhibitor treatment led to small decreases in urinary nitrite excretion, although ACE inhibitors have the potential to increase endothelial NO production. This finding may be associated with changes in glomerular filtration/hemodynamics, however, data on GFR at the end of the 14-day-treatment period are unfortunately missing. The authors should comment on this finding.

3. This reviewer suggests long-term follow-up of these children and a repeat experiment using an ACE inhibitor when a larger proportion develops significant albuminuria. The observation that ACE inhibition indeed blunted albuminuria in two children with increased baseline albuminuria may indicate a role for preemptive intervention.

**Competing interests:**

None declared.