Author’s response to reviews

Title: The Impact of IgM Deposits on the Outcome of Nephrotic Syndrome in Children

Authors:

Sandra Juozapaite (sandra.melnik10@gmail.com)
Rimante Cerkauskiene (rimante.cerkauskiene@vuvl.lt)
Arvydas Laurinavicius (Arvydas.Laurinavicius@vpc.lt)
Augustina Jankauskiene (augustinajankauskiene@yahoo.com)

Version: 2 Date: 31 Mar 2017

Author’s response to reviews:

Editor Comments:

Thank you giving us an opportunity to review the revised manuscript. Unfortunately the requested comments/information have not been clearly addressed. I am happy to invite you to submit one further revision which carefully addresses the concerns raised by Reviewer 1. I look forward to your revised manuscript.

Reviewer 1 comments:

Guido Filler, Ph.D., M.D. (Reviewer 1): The editor and this reviewer asked for the inclusion of those patients who were diagnosed with nephrotic syndrome in the same setting during the same study period, and this request was not considered.

The exact criteriae for performing a renal biopsy still remain elusive.

The criteria to perform a renal biopsy are set in the internal guidelines of our institution for the management of patients with NS and include: patient’s age < 1 year or > 10 years at the time of first manifestation of NS or additional clinical features (hematuria, arterial hypertension, decreased kidney function or extrarenal symptoms), and a frequently relapsing, steroid-dependent or steroid-resistant form of NS. These criteria were in place and not changed throughout all the study period.

These criteria are listed in Methods section, part Patient selection.

The fact that renal biopsies in NS patients were performed strictly following a standardized procedure allows to clearly define the study group in whom the effect of IgM positivity was
assessed. The only patients that were excluded from the study were those with systemic diseases causing IgM deposition (as outlined in Methods section, part Patient selection).

As stated in the table 2, we have selected and matched the IgM-negative patients as the control group. IgM-positive and IgM-negative patient groups were homogenous and eligible for the comparison. Using general population as a control (patients without a kidney biopsy) group would be misleading, because the status of IgM presence would be unknown.

It is highly unusual that an institution like yours continued to use the Jaffe method during the long study period of 2000 to 2015. Please provide documentation that your creatinine measurement is still not IDMS-traceable.

Although ID/MS-traceable enzymatic method was introduced in our institution since 2016, indeed serum creatinine was measured by Jaffe method during the study period. We have added to the Methods section, Diagnostic definitions part:

Serum creatinine was measured by Jaffe method and GFR was calculated using the respective Schwartz formula described elsewhere (ref. 15).

Your conclusions must stop after the first sentence, everything after "however" is not justified by your results. There was no difference between patients with IgM positivity and those without. The cumulative steroid dose was identical. There were no significant differences with regards to cyclosporine and MPA levels. The null hypothesis was rejected.

We agree to this comment and we have changed the conclusion as suggested.

It would be good to include the MPA levels. That information has never been published in the literature on childhood nephrotic syndrome.

MPA levels are not routinely measured in our institution for patients with childhood NS. The statement from our previous response “MPA levels were not significantly different between the groups” was an involuntary mistake. The standardized dosing of MPA was indeed the same, but the levels were not measured.

Reviewer 2 and reviewer 3 have no further comments.