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Renal function and renal histopathology in assessment of course and prognosis in Henoch Schönlein Nephritis and IgA nephropathy

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ABSTRACT

Background: Henoch Schönlein Nephritis (HSN) is a common childhood vasculitis disease that generally has a self-limiting course but the long-term outcome varies with the clinical picture at onset. Morbidity is high among the most severe cases, and therefore there is a need for intervention. Immunoglobulin A nephropathy (IgAN) is the most frequent glomerulonephritis in the world, and the risk of disease progression to chronic renal disease (CKD) is as high in paediatric population as among adults. There is no consensus regarding treatment strategies in the two diseases. **Aim:** To identify patients at risk and to identify predictors of a poor outcome in HSN and IgAN patients and to study the results of treated patients with severe forms of HSN and IgAN. **Results:** In study I 73 patients with HSN, investigated within 5 years from onset, we observed that GFR at the first investigation was lowest among patients with nephrotic syndrome or with a nephritic-nephrotic picture at onset. The clinical picture at onset was related to the histology findings. Advanced biopsy findings were found in 60% of patients with nephrotic syndrome and in 70% of patients with a nephritic-nephrotic picture at onset. Among patients with non- nephrotic proteinuria, generally considered to be a benign group, 69% showed advanced biopsy findings, despite the fact that their GFR showed only a moderate reduction at onset. In **study II** the results of treatment of the most severe cases of HSN (n=24) and IgAN (n=19) were presented. All patients were treated with ACEi/ARB. In group A (n=18) Methylprednisolone/oral prednisolone was combined with Cyclophosphamide given as 3-6 monthly pulses. In group B (n=25) 15 patients received corticosteroids and 10 only ACEi/ARB. In group A proteinuria was reduced after Methylprednisolone and further declined after Cyclophophamide treatment. GFR improved during follow-up in group A. In group B the proteinuria decreased during follow up and the GFR remained unchanged. There was a greater fall in the protein reduction in the group treated with corticosteroids and ACEi/ARB than in the group treated without corticosteroids. The results presented in **study III** identify the predictors of a poor outcome in 78 HSN patients followed mean 5 years. 26% progressed to a poor outcome (active renal disease or CKD stage 4-5/ESRD). Both severe clinical features at onset and advanced biopsy findings were related to a poor outcome. Proteinuria at one year follow-up was assessed as a strong individual predictor. The combination of proteinuria at one year and the histology grading showed highest discriminative ability. The results in **study IV** validate the new Oxford classification and assessed the predictability of the of the histology findings identified in the Oxford MEST score: mesangial (M) and endocapillary (E) hypercellularity, segmental glomerulosclerosis (S) and tubular atrophy/interstitial fibrosis (T). 99 children were followed > 5 years. 18% progressed to a poor outcome. 90 biopsies were reviewed according to the MEST score: M, E and T were each associated with a poor outcome but S did not reach significance. Instead, presence of crescents and of global sclerosis was predictive of poor outcome in our cohort.
Conclusion: Morbidity is high among severe cases of HSN and IgAN. Identification of predictors of a poor prognosis will improve medical intervention and reduce the risk of deterioration of the diseases.