

## **Specific management of IgA nephropathy: role of tonsillectomy**

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### **GUIDELINES**

**No recommendation possible based on Level I or II evidence**

### **SUGGESTIONS FOR CLINICAL CARE**

(Suggestions are based on Level III and IV evidence)

Numerous retrospective cohort studies and case reports have suggested that tonsillectomy may reduce proteinuria and serum total IgA concentration, decrease episodes of macroscopic haematuria and slow progression to end-stage kidney disease (ESKD) in patients with tonsillitis. In retrospective series, tonsillectomy has been associated with improved renal outcome in patients with IgA nephropathy, over and above standard therapy. However, these results have not been consistent in all studies. Moreover, these results are confounded by indication making the true role of tonsillectomy difficult to interpret.

- Komatsu et al (2005) examined renal outcomes in 237 patients with IgA nephropathy (aged  $31 \pm 14$  years, mean  $\pm$  SD) who had been followed-up for at least 6 months (follow-up periods,  $62.3 \pm 45.5$  months). On univariate analysis, tonsillectomy was the only significant treatment that contributes to the maintenance of normal renal function. In addition, urinary abnormalities disappeared at a significantly higher frequency when patients were treated by tonsillectomy. However, the severity of baseline renal disease was not equivalent in all groups and the protective effect of tonsillectomy was eliminated after adjusting for other baseline variables.
- Rasche et al (1999) retrospectively reviewed data on renal outcome in 55 patients with IgA nephropathy. In this study, there was no significant correlation between tonsillectomy and ESKD after  $3.4 \pm 4$  years of follow-up, when adjusting for baseline risk factors.
- Xie et al (2003) retrospectively reviewed data from over 15 years in 118 patients with idiopathic IgA nephropathy, including 48 patients who had undergone tonsillectomy and 70 who had not. After adjusting for baseline risk factors, only five (10.4%) of patients ( $n = 48$ ) who had undergone tonsillectomy entered dialysis, whereas 18 (25.7%) of 70 patients who had not undergone tonsillectomy required dialysis ( $P =$

0.04). Cox regression analysis showed that the relative risk for terminal renal failure in patients following tonsillectomy was lower compared to control patients (hazard ratio 0.22, 95%CI: 0.06–0.76, P = 0.0164).

- lino et al (1993) reviewed 50 patients with IgA nephropathy and chronic tonsillitis, including 35 patients with and 15 without tonsillectomy. In patients with a serum creatinine level of < 1.4 mg/dL, renal function remained normal in all subjects with tonsillectomy but worsened in 3 of 13 patients without tonsillectomy. There was no effect seen in patients with a serum creatinine level of > 1.4 mg/dL at the time of renal biopsy. They proposed that tonsillectomy might have a role for patients with IgA nephropathy complicated by tonsillitis when the operation was performed before deterioration of renal function.
- Barta et al (1996) followed 75 patients with biopsy-proven IgA nephropathy for an average of 12.2 years, including 35 patients who had undergone tonsillectomy. Although the level of microhaematuria 6 months after tonsillectomy was similar to before the procedure, tonsillectomy stopped gross haematuria appearing in the acute exacerbation of the disease in more than two-thirds of patients. ESKD was detected only in 4 of 35 patients 10 years after tonsillectomy, compared to 8 of 40 patients from a non-tonsillectomised control group with IgA nephropathy.
- Hotta et al (2002) conducted a retrospective review of the renal outcome in 329 patients with IgA nephropathy, with an observation period longer than 36 months (82.3 ± 38.2 months). Their results showed that there were no significant differences between the tonsillectomy and non-tonsillectomy groups regarding the incidence of progressive renal functional loss (defined as a 50% increase in baseline serum creatinine). However, tonsillectomy had a significant impact on clinical remission by multivariate Cox regression analysis.
- Sato et al (2003) retrospectively reviewed 70 patients with IgA nephropathy and renal impairment (serum creatinine > 1.5 mg/dL). Steroid pulse with tonsillectomy, and conventional steroid and supportive therapy were performed in 30, 25 and 15 patients, respectively. The incidence of ESKD in the patients treated by steroid pulse with tonsillectomy was significantly lower than the incidences in the patients treated by conventional steroid and supportive therapy at a baseline creatinine level of 1.5–2 mg/dL, but no statistical difference was observed at a level of > 2 mg/dL. Like the findings of lino et al (1993), the authors concluded that steroid pulse therapy combined with tonsillectomy may be more effective than conventional steroid therapy in patients without moderate to severe renal impairment.
- Akagi et al (2004) performed a 10-year retrospective case-control study of 71 patients with IgA nephropathy to evaluate the long-term effects and prognostic factors associated with tonsillectomy. A total of 41 patients who had undergone tonsillectomy were compared with 30 patients who had not. After over 12 years of follow-up, the clinical remission rate was 24% in the tonsillectomy group and 13.3% in those not receiving

tonsillectomy. Similarly, renal survival was higher in patients who had undergone tonsillectomy.

- Nishi and colleagues (2004) reviewed long-term renal survival in 46 patients who had undergone tonsillectomy, and 74 patients with IgA nephropathy who had not. Five (10.9%) of the tonsillectomy group reached ESKD whereas 19 (25.8%) of the non-tonsillectomy group did.

In summary, tonsillectomy could reduce proteinuria and haematuria in those patients without moderate to severe renal impairment. These studies are retrospective and potentially confounded by indication, making the clinical significance of this intervention difficult to interpret.

## **Background**

IgA nephropathy is the most common glomerular disease in Australia and New Zealand. Although the natural history of IgA nephropathy is variable, many patients develop progressive loss of renal function over many years. ESKD is said to develop in 20% of cases after 10 years and in 30% after 20 years, whereas another 30% show some decline in renal function (Rekola et al 1991). In addition to non-specific renal interventions (control of hypertension, ACE inhibition, etc.) there is evidence that interventions that specifically treat IgA nephropathy may also slow the progression to ESKD.

The macroscopic haematuria seen in IgA nephropathy is commonly precipitated by a mucosal stimulation (e.g. pharyngitis) suggesting the possibility of an aberrant mucosal immunity in the pathogenesis of IgA nephropathy. The tonsils are also a significant source of under-glycosylated IgA1, implicated in the pathogenesis of IgA deposition (Horie et al 2003). Tonsillectomy also decreases the levels of serum IgA levels. The objective of this guideline is to evaluate the available clinical evidence pertaining to the impact of tonsillectomy on renal functional decline in IgA nephropathy. This guideline does not address the role of tonsillectomy in those patients with appropriate ENT indications.

## **Search strategy**

**Databases searched:** MeSH terms and text words for IgA nephropathy were combined with MeSH terms and text words for tonsillectomy. This search was carried out in Medline (1966 to September Week 2, 2004). The Cochrane Renal Group Trials Register was also searched for trials of IgA nephropathy not indexed in Medline.

**Date of searches:** 17 September 2004.

## **What is the evidence?**

There have been no randomised controlled studies.

## **Summary of the evidence**

No recommendations can be made regarding tonsillectomy for disease progression in patients with IgA nephropathy on the basis of currently available retrospective studies and case reports. Tonsillectomy should be performed in those patients with appropriate ENT indications. Controlled trials are needed before tonsillectomy should be considered for any other group.

## **What do the other guidelines say?**

**Kidney Disease Outcomes Quality Initiative:** No recommendation.

**UK Renal Association:** No recommendation.

**Canadian Society of Nephrology:** A tonsillectomy could reduce proteinuria and hematuria in those patients with recurrent tonsillitis (Iino et al 1993).

**European Best Practice Guidelines:** No recommendation.

**International Guidelines:** No recommendation.

## **Implementation and audit**

No recommendation.

## **Suggestions for future research**

Patients with IgA detailed in the ANZDATA database should be questioned as to whether they have undergone tonsillectomy in the past.

## **References**

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