

# The Influence of Tonsillectomy on Total Serum Antibody Levels

To the Editor

Tonsillectomy, the surgical removal of the palatine tonsils, is recommended for patients with recurrent tonsillitis or tonsillar hypertrophy, as these medical conditions can cause chronic pain, repeated antibiotic use and airway obstruction such as obstructive sleep apnoea syndrome (OSAS) and secondary otitis media or speech impairment [1–3]. The palatine tonsils are glands of lymphoid tissue located in the upper aerodigestive tract, forming part of the Waldeyer's lymphatic ring and therefore playing an important role in mucosal immunity.

Although tonsillectomy has been performed for many years, some believe that the procedure increases the patient's risk of infection as it involves removal of major parts of lymphoid tissue where B and T cells can be stimulated and differentiated, consequently impairing both humoral and cellular immunity [4, 5]. Conversely, recurrent tonsillitis leads to fibrosis and atrophy in the tonsils, hence decreasing the amount of lymphoid tissue [6, 7]. As a result, the palatine tonsils lose their local immune function even if they are not removed. This is not thought to compromise the general immune system, and it has been postulated that other tonsils in the Waldeyer's ring may take up the function of the palatine tonsils, decreasing the chances of upper respiratory infections in children where these tonsils are fibrotic or removed [8–10].

The controversy whether tonsillectomy affects the immune system is still a topic of debate among the scientific community [11, 12]. In an attempt to help clarifying the outcome of that debate, we present a study where we have analysed whether tonsillectomy affects the long-term levels of total serum IgG, IgA and IgM, and consequently the immune system in general.

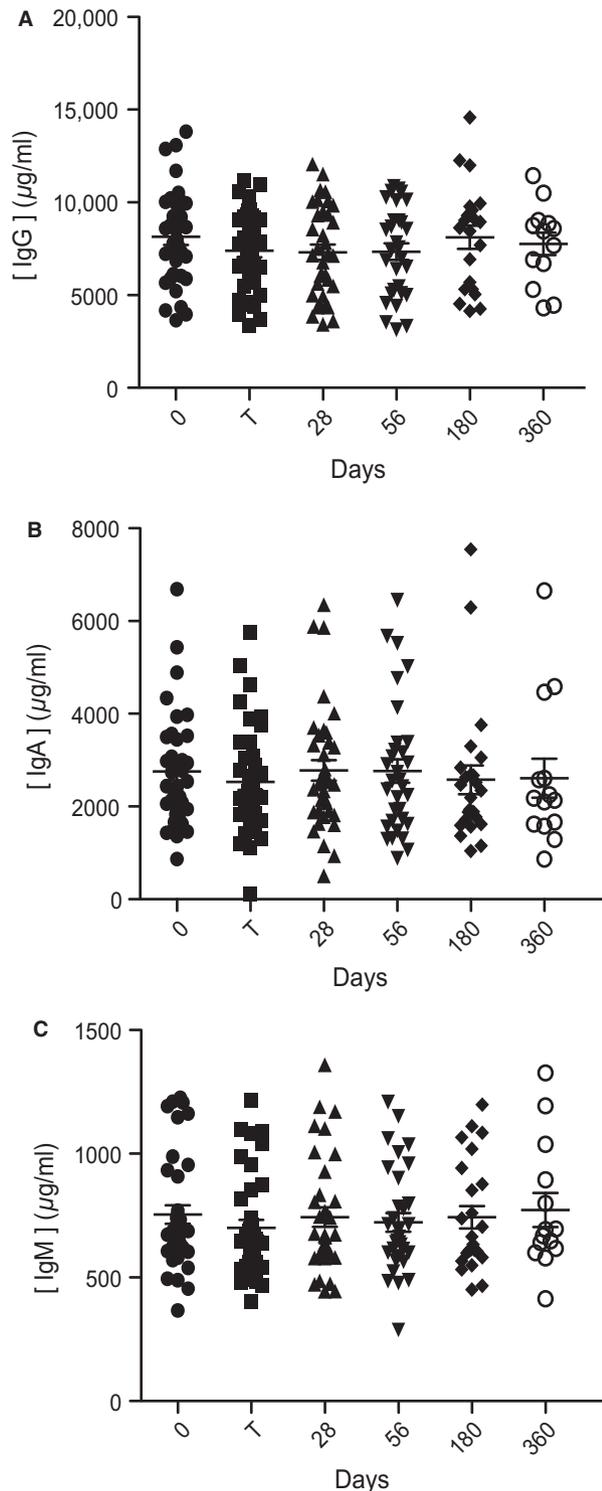
We measured the total IgG, IgA and IgM levels in serum collected from 45 children (3–17 years old) with recurrent tonsillitis or tonsillar hypertrophy at various time points, before and up to 1 year after tonsillectomy. Plasma samples were collected at the Department of Oto-Rhino-Laryngology, Head and Neck surgery, Haukeland University Hospital (Bergen, Norway) during the 2012–2013 influenza season. These patients were enrolled in a clinical trial of Fluenz© (AstraZenica, London, UK), a live attenuated Influenza vaccine (LAIV) [13]. The study was approved by the Regional Ethics Committee and the Norwegian Medicines Agency (EUDRACT # 2012-0028 4824).

Analysing the total serum IgG, IgA and IgM levels (Fig. 1), we found no significant alteration throughout the study period, which comprised baseline (prevaccination), vaccination day, tonsillectomy day and follow-up at 28, 56, 180 and 360 days post-vaccination (ANOVA; GraphPad Prism, La Jolla, CA, USA). IgG, IgA and IgM had a baseline serum concentration of  $8.2 \pm 2.6$ ,  $2.8 \pm 1.2$  and  $0.8 \pm 0.2$  mg/ml, respectively. Their concentrations remained stable through pre- and post-operation and at both the short- and the long-term follow-up, suggesting that tonsillectomy does not compromise systemic humoral immunity.

Although the vaccination response was not the main focus of this study, we have also monitored the anti-influenza-specific serum titres from these patients. As an example, the serum anti-H3N2 titres rose significantly after LAIV vaccination independently of tonsillectomy and were maintained up to 1 year after vaccination, suggesting that tonsillectomy does not influence the humoral response to LAIV vaccination (unpublished results, R.J. Cox). Our data are also in line with previous studies, where patients received a parenteral influenza vaccine [14, 15].

The stability of humoral immunity after tonsillectomy has earlier been reported in studies, but did not include vaccinated subjects. Pires Santos *et al.* [16] reported a non-significant decrease of IgG 1–2 months after surgery in children under 4 years of age, and a statistically significant decrease of IgG and IgA 12–14 months post-tonsillectomy, although the values were within the normal range. Dai *et al.* [17] observed decreased levels of IgG, IgA and IgM 1 month after tonsillectomy, but returning to normal levels 3 months post-surgery. However, they suggest partial tonsillectomy rather than conventional tonsillectomy as the best procedure as they found a lower impact on short-term humoral immunity when partial tonsillectomy was performed.

Importantly, others have found significant alterations of immunoglobulins earlier in short-term studies. Nasrin *et al.* [4] found IgG levels to decrease significantly 3 months post-operation compared with preoperative data but remained similar to the normal range. However, IgA and IgM did not show significant differences in this study, lasting 3 months. Similarly, Kaygusuz *et al.* [5] found a significant decrease of serum IgG, IgA and IgM 1 month post-operation compared to preoperation, although the post-operation levels did not differ significantly from those of the control group. However, the same research group



**Figure 1** The total levels of serum IgG (A), IgA (B) and IgM (C) were measured by capture ELISA. Goat anti-human Ig (H+I) was used as the capture antibody (Southern Biotech, cat. no. 2010-01) and goat peroxidase-conjugated anti-human IgG, anti-human IgA or anti-human IgM immunoglobulins for detection (Sigma, cat. no. A0293, A0295, A0420, respectively). Total serum levels were measured at day 0 (the vaccination time point), at the time of tonsillectomy (T, day 3–20), and time 28, 56, 180 and 360 post-vaccination.

found a different outcome when performing a long-term follow-up study [18] collecting data from 54 months post-tonsillectomy. At that time, the levels of IgG, IgA and IgM from tonsillectomized patients were not significantly different from those found in healthy controls.

The outcome of several studies suggests that humoral immunity may be slightly impaired short term, that is the first month after tonsillectomy, due to a minor decrease in especially IgG and IgA serum levels, although these values return to normal levels after a few months. Hence, the long-term humoral immunity is not compromised.

The recovery of humoral immunity may be due to redundancy, with other tonsils from the Waldeyer's ring acquiring the function of the palatine tonsils and compensating for their removal. Another important issue is when tonsillectomy is indicated due to chronic tonsillitis. The recurrent inflammation of the palatine tonsils focuses the immune system to be extremely active in this area. Tonsillectomy removes this important focus of infection, redirecting the immune system towards other ENT areas potentially infected by airborne or foodborne pathogens.

In our study with 45 very young children, serum levels of IgG, IgA and IgM did not change significantly after tonsillectomy in either the short term or long term. Our paediatric clinical trial adds to the evidence that tonsillectomy does not compromise systemic humoral immunity nor the specific immunoglobulin response to LAIV vaccination. Hence, both surgery and LAIV vaccination can be performed within a short time period.

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