Immunogenicity and safety of inactivated vaccine in preoperative children

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[Background]

It has been a common belief that surgical stress and anaesthesia suppress immune responses. However, there has been no report on changes in antibody titres and associated immunity to vaccines administered before surgery with general anaesthesia¹⁾ .

Thus, we examined 1) whether anaesthesia modifies T lymphocyte populations, 2) whether the antibody responses to a vaccine administered before surgery are impaired, in children who undergo minor surgery with general anaesthesia.

[Subjects and methods]

Subjects were preschool children aged ≥1 year old who underwent minor surgery with general anaesthesia and were received inactivated trivalent influenza vaccine 5-7days before the surgery (Group An). Age-matched healthy children who received the vaccine in the same season served as control (Group C). Total lymphocyte count, CD4/CD8 ratio and hemagglutination inhibition (HI) titer were measured before and 1 month after the vaccination. Total lymphocyte count and CD4/CD8 ratio were also measured 1 and 7 days after the surgery in Group An. The effects of the influenza vaccine was evaluated based on the standard of European Medicines Agency. Adverse events were also recorded. Mann–Whitney U test, repeated measure ANOVA, student’s *t*-test and an analysis of variance.

[Results]

Fifteen subjects in Group An and 30 in Group C were enrolled in the study (Table 1). There were no significant difference in the lymphocyte count and the CD4/CD8 ratio at entry between the 2 groups (p = 0.22, p=0.28)(Fig 1,2). There were no significant changes in the lymphocyte count, CD4/CD8 ratio during pre- and post-operative period in Group An and Group C.

HI titers to influenza H1N1, H3N2 and B were significantly elevated after vaccination in both groups and there was no significant differences in the titers between the 2 groups(Fig 3-5).

No significant adverse events were observed.

[Conclusions]

Minor paediatric surgery had no major impact immune status of young children.
Inactivated influenza vaccine is safe and immunogenic for children who undergo minor surgery.

Table1 Patient characteristics

	Group An (n=15)	Group C (n=30)	P value
Age (months)	46.5±22.1	47.4±17.5	0.88
Height (cm)	96.6±12.8		
Weight (kg)	15.1±4.2		
Male/Female	9/6	19/11	0.83
Duration of anaesthesia (min)	75±37		
Duration of surgery (min)	49±33		
Total dose of intraoperative Remifentanyl (ml)	3.3±2.7		
Sevoflurane (ml)	22.7±12.9		

(mean±SD)

Fig 1 Change of lymphocyte count

Fig 2 Change of CD4/CD8 ratio

Fig 3 HI titers to influenza H1N1

	criteria	Group An	Group C
seroconversion	>40%	38%	29%
seroprotection	>70%	92%※	92%※
GMT ratio	>2.5	3.4※	2.0

Seroconversion: the proportion of persons with pre-vaccination HI antibody titer of <1:10 and post-vaccination titer of ≥1:40 or ≥4-fold post-vaccination rise in antibody titer.
Seroprotection: the proportion of persons satisfying the protective level of antibody titer (HI antibody titer of ≥1:40)
※ significantly elevated

Fig 4 HI titers to influenza H3N2

	criteria	Group An	Group C
seroconversion	>40%	62%	46%
seroprotection	>70%	100%※	100%※
GMT ratio	>2.5	3.5	3.1※

Seroconversion: the proportion of persons with pre-vaccination HI antibody titer of <1:10 and post-vaccination titer of ≥1:40 or ≥4-fold post-vaccination rise in antibody titer.
Seroprotection: the proportion of persons satisfying the protective level of antibody titer (HI antibody titer of ≥1:40)
※ significantly elevated

Fig 5 HI titers to influenza typeB

	criteria	Group An	Group C
seroconversion	>40%	63%※	69%※
seroprotection	>70%	63%	92%※
GMT ratio	>2.5	4.4※	5.0※

Seroconversion: the proportion of persons with pre-vaccination HI antibody titer of <1:10 and post-vaccination titer of ≥1:40 or ≥4-fold post-vaccination rise in antibody titer.
Seroprotection: the proportion of persons satisfying the protective level of antibody titer (HI antibody titer of ≥1:40)
※ significantly elevated

1) Siebert JN, Posfay-Barbe KM, Harbe W, et al.: Influence of anesthesia on immune responses and its effect on vaccination in children: review of evidence. *Pediatr Anaesth* 17:410-420,2007
2) The European Agency for the Evaluation of Medicinal Products. Committee for proprietary medicinal products (CPMP). Note for guidance on harmonisation of requirements for influenza vaccines. 1-18, 1997 (CPMP/BWP/ 214/96)