

A346

TITLE: THE EFFECT OF PROLONGED ADMINISTRATION OF SEVOFLURANE ON SERUM CONCENTRATION OF FLUORIDE ION IN PATIENTS

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INTRODUCTION: The fluoride excretion induced by 1 or 2 hours sevoflurane anesthesia has already been examined and been safe in clinical use like enflurane. It has been used in practice last year in Japan. However, the serum fluoride ion level in prolonged sevoflurane anesthesia (more than 4 hrs.) has not yet been examined in humans and it has still possibility to cause renal insufficiency.

In this present study, we address following questions in prolonged sevoflurane anesthesia; 1) is the peak of serum fluoride ion concentration exceeded to the 50 $\mu\text{mol/l}$ that may nephrotoxicity. 2) how long does the high level of serum fluoride ion continue after prolonged sevoflurane exposure.

METHODS: Eleven patients, age 55-71 years, ASA I or II, scheduled for long term elective surgery (more than 4 hrs.) were studied after approval from our Human Subject Review Committee.

Anesthesia was induced with thiopental 3-5 mg/kg and vecuronium 0.12 mg/kg, followed by intubation and maintained with N_2O 60% in oxygen and sevoflurane. The end-tidal concentration of sevoflurane, measured by mass spectrometry, was controlled from 0.3% to 4.0% depending on surgical stimulation. The serum fluoride ion concentration was measured every two hours during anesthesia and 1, 2, 3, 6, 12, 24, 36 hours post exposure.

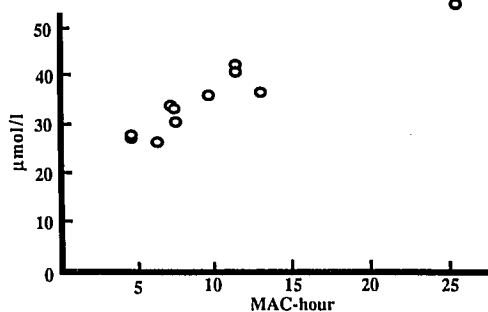
RESULTS:

1) The period of exposure with sevoflurane was 4.7 hours to 23.5 hours.

2) In one case, the peak serum fluoride ion concentration exceeded 50 $\mu\text{mol/l}$ at two hours after 23.5 hours sevoflurane exposure (Fig. 1).

3) The high level of serum fluoride ion continued for 12 hours post exposure and declined a half of it next 12 hours. 4) No renal insufficiency was induced clinically by prolonged sevoflurane anesthesia.

DISCUSSIONS AND CONCLUSIONS: The induced peak serum fluoride ion level by prolonged sevoflurane inhalation was sustained for 12 hours post exposure. This is observed in short duration of sevoflurane anesthesia as well. Less than 15 MAC-hours sevoflurane inhalation in prolonged anesthesia will be safe as the short duration of anesthesia.

Serum peak F^- 1-2 hours post-anesthesia

A347

TITLE: SERUM INORGANIC FLUORIDE AFTER EXTENDED EXPOSURE TO SEVOFLURANE IN PATIENTS

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Sevoflurane is metabolized and serum inorganic fluoride (F^-) concentration increases¹. A previous report on the effect of prolonged exposure to sevoflurane on serum F^- is limited in its clinical significance because only 0.5 MAC sevoflurane was administered². However, sevoflurane is likely to be used at higher concentrations. Therefore, it is necessary to confirm that a higher concentration (a concentration that sevoflurane would likely to be used at) of sevoflurane does not cause an increase of serum F^- to a further extent in surgical patients.

Fourteen patients (ASA PS I-II) scheduled for more than 8 hours of surgery were entered into this study with institutional approval and informed consent. The patients were anesthetized with either 1 MAC sevoflurane (S-group; N=7, age 45 ± 18 (mean \pm SD) yr) or 1 MAC isoflurane (I-group; N=7, age 60 ± 11 yr), both in 50% nitrous oxide. Patients having signs of liver or kidney damage pre-operatively were excluded. Thiамylal was used for induction and vecuronium or pancuronium was used for muscle relaxation. End tidal concentrations of sevoflurane or isoflurane and carbon dioxide were monitored by a Datex Capnomac. Ventilation was controlled to maintain normocapnea. Blood samples were collected immediately before induction of anesthesia (Pre), at every 4 hours during anesthesia, and at 2, 6, 12, 24 and 48 hours after termination of administration of anesthesia to measure serum F^- concentrations with a fluoride specific electrode. Serum urea nitrogen (UN) and serum creatinine (Cr) were measured before anesthesia and 4-7 days after anesthesia. Analysis of variance for repeated measures and Newman-Keuls test was used for multiple comparison within the groups and Student's t-test was used for comparison between groups considering $P < 0.05$ as significant.

Exposures to sevoflurane and isoflurane were 10.6 ± 1.0 and 9.1 ± 1.8 MAC-hours, respectively. As expected, serum F^- concentration was higher in the S-group than in the I-group (Figure). Mean peak serum F^- concentration for the S-group was $9.7 \pm 2.9 \mu\text{M/l}$. Neither UN nor Cr increased after anesthesia in both groups.

Serum F^- concentration did not reach critical levels even with prolonged exposure to 1 MAC sevoflurane. In fact, serum F^- concentrations of this study were lower than those previously reported with a lower dose of sevoflurane². In summary, in regard to serum inorganic fluoride concentration, 1 MAC sevoflurane may be used safely in long cases.

References

1. Anesthesiology 54:100-106, 1981
2. Anesth Analg 72:S298, 1991

Serum Inorganic Fluoride Concentration

