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TITLE: Serum and urinary inorganic fluoride levels after prolonged inhalation of sevoflurane in man

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Sevoflurane (Sevo) is a new anesthetic agent. One of its metabolite which might be responsible for nephrotoxicity is inorganic fluoride (inorg-F). This study was undertaken to investigate the serum and urinary inorg-F levels following the prolonged inhalation of Sevo in man.

Ten patients without hepato-renal disease, ASA physical status I or II scheduled for long time surgery (over 10 hours) were studied for the serum and urinary concentrations of inorg-F before and after inhalation of Sevo. The study was approved by the ethical committee of the hospital and also obtained Informed from patients. Serum inorg-F was determined before inhalation, every 6 hours during inhalation and 0, 2, 4, 24, 48, 72 and 96 hours after inhalation. Urinary inorg-F concentration and excretion rate were measured before inhalation and 24, 48, 72 and 96 hours after inhalation. Fluoride ion in serum and urine were measured by ion-chromatograph.

Clinically no adverse renal effect was observed postoperatively. The peak mean level of serum inorg-F reached about 42.5 +/- 4.5 μM at the end of anesthesia. Figure (1) illustrates serum F levels against %-hours. A positive correlation between serum F and anesthetic dosage was demonstrated. The mean urinary excretion of inorg-F peaked at 1804 +/- 378 μM/day in Ist postoperative day after cessation of Sevo inhalation and it decreased significantly thereafter.

Peak fluoride level was higher after Sevo anesthesia than after enflurane or isoflurane, reported previously [1]. This is because Sevo is metabolized more per unit time. In our study peak serum fluoride level and urinary excretion were reached shortly after the end of anesthesia and declined rapidly. To explain for this result, Sevo is less lipid and blood soluble than other inhalational agents, and is subjected to metabolism for a shorter time. Therefore in the case of Sevo less time is need for the inorg-F to decline to control level. The present study showed no adverse effects on renal or hepatic functions. Further clinical study is required to clarify the effect of Sevo to induce nephrotoxicity.

Reference

1. Acta Anaesth Scand, 28: 412-418, 1984

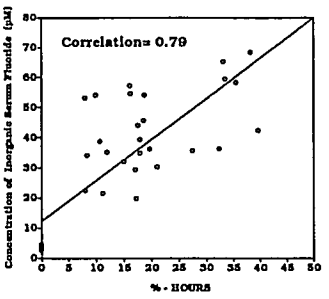

Figure (1) Relationship between serum inorganic fluoride level and %-hours

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TITLE: INORGANIC FLUORIDE PRODUCTION FOLLOWING SEVOFLURANE IN HEALTHY SURGICAL PATIENTS.

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Introduction: Sevoflurane has been shown in animal investigations to undergo biotransformation producing inorganic fluoride ions but no evidence of hepatic or renal toxicity. In this study we compared the fluoride production following surgical anesthesia with the new anesthetic sevoflurane with a comparison group receiving isoflurane.

Methods: Fifty ASA I and II patients received sevoflurane anesthesia with a control group of 25 patients receiving isoflurane. Approval by the institutional Human Subjects Committee and informed patient consent were obtained. Sevoflurane or isoflurane was administered in 100% O_2 for durations of 1 to greater than 7 MAC hours for surgical anesthesia. Preoperative and postoperative BUN, creatinine and liver function tests were done. Blood samples were obtained during and after anesthesia from an arm vein in both groups for anesthetic blood level and plasma inorganic fluoride analysis. Samples for fluoride determination were obtained prior to anesthesia, hourly during anesthesia, at anesthetic end and then 1,2,3,8 and 24 hrs post anesthesia. Anesthetic blood levels were assayed by GC and plasma fluoride concentration determined by ion selective electrode analysis. Renal and hepatic function studies were compared using 2 way AHOVA anesthetic blood concentrations were compared using Students T-Test.

Results: Sevoflurane biotransformation produced a mean inorganic fluoride concentration of 29.3μM 2 hours after anesthetic discontinuation, which declined rapidly to 18μM by 8 hrs post anesthesia (Figure 1). Isoflurane anesthesia produced a mean peak plasma fluoride concentration of 3.9μM 8 hours after anesthesia. Peak fluoride concentration correlated with anesthetic duration with sevoflurane (r=.65) but did not with isoflurane anesthesia. There were no changes in postop BUN, creatinine or liver function tests in either group. Sevoflurane blood concentrations were significantly lower than those for isoflurane 15 min after anesthesia.

Conclusion: Biotransformation of sevoflurane produced inorganic fluoride levels with a mean peak less than 30μM. Rapid pulmonary elimination of sevoflurane appears to prevent further metabolism of the drug such that fluoride levels do not remain elevated and decline rapidly. No changes in renal or hepatic function was evident in patients studied.

FIGURE 1