

Monitoraggio biologico dell'esposizione professionale a sevoflurane

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KEY WORDS

Sevoflurane; biological monitoring; occupational exposure

SUMMARY

«Biological monitoring of occupational exposure to sevoflurane». Sevoflurane has been used in the last few years in brief surgical operations, either alone or in combination with nitrous oxide. Occupationally exposed groups include anesthesiologists, surgeons and operating room nurses. In 1977 the National Institute for Occupational Safety and Health (NIOSH) recommended that occupational exposure to halogenated anesthetic agents (halothane, enflurane, and isoflurane), when used as the sole anesthetic, should be controlled so that no worker would be exposed to time-weighted average concentrations greater than 2 ppm during anesthetic administration. When halogenated anesthetics are associated with nitrous oxide, NIOSH recommends that the limit value should not exceed 0.5 ppm. We think these recommendations can be extended to sevoflurane. Metabolism of sevoflurane is catalyzed by cytochrome P-450; this involves oxidation of the fluoromethyl side chain of the molecule, followed by glucuronidation. Two urinary metabolites of sevoflurane have been identified: inorganic fluoride (which, however, is not specific) and a non-volatile compound that yields hexafluoroisopropanol (HFIP) when digested with the enzyme beta-glucuronidase. In order to investigate the role of urinary HFIP as an indicator of occupational exposure to sevoflurane (CI, ppm), CI was measured in 145 members of 18 operating room staffs. The measurements of the time-weighted average of CI in the breathing zone were made by means of diffusive personal samplers. Each sampler was exposed during the whole working period. Sevoflurane was desorbed with CS₂ from charcoal and the concentrations were measured on a gas chromatograph (GC) equipped with a mass selective detector (MSD). The GC was equipped with a 25 meter cross-linked phenylmethylsilicon column (internal diameter 0.2 mm). GC conditions were as follows: injector column temperature=200°C; column temperature=30°C; carrier gas=helium; injection technique of samples=splitless. The analytical conditions for the MSD were the following: ion mass monitored=131 m/e; dwell time=50 msec; selected ion monitoring window time=0.1 amu; electromultiplier= 400 V. Urine samples were collected near the end of the shift and were analyzed for HFIP by head-space gas chromatography after glucuronide hydrolysis. 0.5 ml of urine and 1.5 ml of 10 M sulfuric acid were added to 21.8 ml headspace vials. The vials were immediately capped, vortexed, and loaded into the headspace autosampler. Samples were maintained at 100°C for 30 min, after which glucuronide hydrolysis was 99% complete. Analyses were performed on a GC equipped with a MSD. The analytical conditions for urine analysis were as follows: cross-linked 5% phenylmethylsilicon column

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(internal diameter 0.2 mm, length 25 m); column temperature=35°C; carrier gas=helium. The analytical conditions for the MSD were: monitored ions=51.05 and 99; dwell time=100 ms; selected ion monitoring window time=0.1 amu; electromultiplier voltage=2000 Volt. With our analytical procedure, the detection limit of HFIP in urine was 20 µg/L. The variation coefficient (CV) for HFIP measurement in urine was 8.7% (on 10 determinations; mean value=1000 µg/L). The median value of CI was 0.77 ppm (Geometric Standard Deviation=4.08; range=0.05-27.9 ppm). The correlation between CI and HFIP (Cu, µg/L) was: $\text{Log Cu } (\mu\text{g/L}) = 0.813 \times \text{Log CI (ppm)} + 2.517$ ($r=0.79$, $n=145$, $p<0.0001$). On the basis of the equation it was possible to establish tentatively the biological limit values corresponding to the respective occupational exposure limit values proposed for sevoflurane. According to our experimental results, HFIP values of 488 µg/L and 160 µg/L correspond to airborne sevoflurane concentrations of 2 and 0.5 ppm respectively.