Pharmacokinetics of Desflurane, Sevoflurane, Isoflurane, and Halothane in Pigs

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We tested the prediction that the alveolar washin and washout, tissue time constants, and pulmonary recovery (volume of agent recovered during washout relative to the volume taken up during washin) of desflurane, sevoflurane, isoflurane, and halothane would be defined primarily by their respective solubilities in blood, by their solubilities in tissues, and by their metabolism. We concurrently administered approximately one-third the MAC of each of these anesthetics to five young female swine and determined (separately) their solubilities in pig blood and tissues. The blood/gas partition coefficient of desflurane (0.35 ± 0.02) was significantly smaller ($P < 0.01$) than that of sevoflurane (0.45 ± 0.02), isoflurane (0.94 ± 0.05), and halothane (2.54 ± 0.21). Tissue/blood partition coefficients of desflurane and halothane were smaller than those for the other two anesthetics ($P < 0.05$) for all tissue groups. As predicted from their blood solubilities, the order of washin and washout was desflurane, sevoflurane, isoflurane, and halothane (most to least rapid). As predicted from tissue solubilities, the tissue time constants for desflurane were smaller than those for sevoflurane, isoflurane, and halothane. Recovery (normalized to that of isoflurane) of the volume of anesthetic taken up was significantly greater ($P < 0.05$) for desflurane (93% ± 7% [mean ± SD]) than for halothane (77% ± 6%), was not different from that of isoflurane (100%), but was less than that for sevoflurane (111% ± 17%). The lower value for halothane is consistent with its known metabolism, but the lower (than sevoflurane) value for desflurane is at variance with other presently available data for their respective biodegradations.

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Washin and washout of isoflurane and halothane have been measured and found to be predicted by their respective solubilities in blood except that metabolism of halothane accelerates its terminal elimination (1). The smaller (0.42) blood/gas partition coefficient (2) and tissue/blood partition coefficients (3) of desflurane compared to those of sevoflurane, isoflurane, and halothane indicate a more rapid washin and washout of desflurane. Furthermore, studies of fluoride serum levels and excretion in enzyme-induced rats indicate a minimal metabolism of desflurane compared with that of isoflurane, halothane, or methoxyflurane (4). Similarly, fluoride levels are increased minimally or not at all after prolonged anesthesia with desflurane in swine (5). Thus, metabolism of desflurane should not limit its washin or accelerate its washout.

Metabolism of sevoflurane is known to occur (6). However, the level of metabolism (e.g., the percent of anesthetic taken up that is recovered as urinary metabolites, or the peak serum inorganic fluoride levels) is comparable to the minimal metabolism of enflurane. If the metabolism of sevoflurane is small, it is not likely to influence the washin or washout of sevoflurane.

To define the relative metabolism and rates of washin and washout among these anesthetics, we investigated the simultaneous washin, and, similarly, the simultaneous washout, of desflurane, sevoflurane, isoflurane, and halothane in swine. We conducted a mass balance study to determine whether the low levels of fluoride in plasma and urine after anesthesia with desflurane reflect a minimal metabo-

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