Title: SOLUBILITY OF I-653, SEVOFLURANE, ISOFLURANE, AND HALOTHANE IN HUMAN TISSUES

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Introduction. Tissue/blood partition coefficients define the difference among anesthetics in the rate of tissue anesthetic washin and washout; washin and washout are determinants of the rates of induction of and recovery from anesthesia. In the present study of human tissues, we simultaneously determined tissue/blood partition coefficients for the new inhaled anesthetic, I-653, and for sevoflurane, isoflurane, and halothane.

Methods. Specimens of adult human brain, heart, liver, kidney, muscle, and fat were obtained at autopsy (consent for the research use of human tissues is part of the autopsy consent given by the patients relatives and is accepted by our IRB) and homogenized in saline within 48 hours of death. Tissue/gas partition coefficients were determined at 37°C with standard techniques (1). The gases added (simultaneously) to each homogenate were 1.09% I-653, 0.42% sevoflurane, 0.39% isoflurane, and 0.49% halothane. Each tissue measurement was run in duplicate. We discarded values which deviated from the mean of the duplicate by more than 10%. The duplicate values for each specimen were averaged. Paired t-tests with Bonferroni corrections were used for statistical analysis and a P value of < 0.05 was considered as significant.

Results. Specimens were obtained from 11 patients (average age 65 ± 16 years; mean ± standard deviation). Not all specimens were obtained from all patients (6 brains, 6 hearts, 5 livers, 5 kidneys, 8 muscles, 5 fat). The order of tissue/gas partition coefficients was halothane > isoflurane > sevoflurane > I-653 (table). The order of tissue/blood partition coefficients was halothane > sevoflurane > isoflurane > I-653. Differences in tissue/gas partition coefficients among anesthetics were all significant. Similarly, tissue/blood partition coefficients were significantly different except for comparisons between sevoflurane and halothane.

Discussion. The tissue/gas and tissue/blood partition coefficients for I-653 are lower than those for sevoflurane, isoflurane, and halothane. Of the modern inhaled anesthetics, only nitrous oxide has lower tissue/blood partition coefficients.

It is known that recovery from I-653 is more rapid than that from the other potent inhaled anesthetics (2). In part, this more rapid recovery is due to the known lower solubility of I-653 in blood (3). In addition, our data indicate that the more rapid recovery also results from a lower solubility in tissues.

References.

1. Lerman J, Schmitt-Bantel BI, Gregory GA, Willis MM, Eger EI II. Effect of age on the solubility of volatile anesthetics in human tissues. Anesthesiology 65: 307-311, 1986.
2. Eger EI II, Johnson BH. Rate of awakening from I-653, halothane, isoflurane, and sevoflurane in rats: A test of the effect of anesthetic concentration and duration. Anesth Analg 66: 977-982, 1987.
3. Eger EI II. Partition coefficients for I-653 in human blood, saline, and olive oil. Anesth Analg 66: 971-973, 1987.

Human Tissue/Gas Partition Coefficients

tissue	tissue/gas			
	I-653	sevoflurane	isoflurane	halothane
brain	0.54±0.02	1.1±0.1	2.1±0.1	4.8±0.4
heart	0.54±0.07	1.2±0.2	2.1±0.3	4.6±0.8
liver	0.58±0.06	1.2±0.1	2.3±0.3	5.1±0.5
kidney	0.43±0.06	0.84±0.13	1.5±0.3	3.2±0.4
muscle	0.97±0.37	2.4±1.0	4.5±2.1	9.9±4.7
fat	13±2	37±6	70±12	150±30

Values are shown as mean ± SD

Human Tissue/Blood Partition Coefficients

tissue	tissue/blood			
	I-653	sevoflurane	isoflurane	halothane
brain	1.3±0.1	1.7±0.1	1.6±0.1	2.0±0.2
heart	1.3±0.2	1.7±0.2	1.6±0.3	1.9±0.4
liver	1.4±0.1	1.8±0.2	1.8±0.2	2.1±0.2
kidney	1.0±0.1	1.2±0.2	1.2±0.2	1.2±0.2
muscle	2.3±0.9	3.6±1.6	3.4±1.6	4.0±2.0
fat	30±5	55±9	52±10	62±12

Values are shown as mean ± SD