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Double-injection method for sequentially measuring cerebral blood flow with N-isopropyl-(^{123}I)p-iodoamphetamine

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We investigated the accuracy of a double-injection method for sequentially measuring cerebral blood flow (CBF) with N-isopropyl-(^{123}I)p-iodoamphetamine (IMP) in simulation studies based on patient data and in clinical studies. The unidirectional clearance of IMP from the blood to the brain (K_1; nearly equal to CBF) in the first and second sessions was calculated by means of a microsphere model. The K_1 values in the first session (K_1^I) were calculated from $C_b(5)/\text{Int\_}C_a^I$, where $C_b(5)$ and $\text{Int\_}C_a^I$ are values for brain radioactivity 5 min after the first injection and for arterial blood radioactivity obtained by 5-min continuous sampling. The K_1 values in the second session (K_1^{II}) were calculated by means of the following four methods. Method 1: $[C_b(t_z + 5) - C_b(t_z)]/[\text{Int\_}C_a^{II} - C_a(t_z) \times 5]$, where $C_b(t_z+5)$ and $C_b(t_z)$ are the brain radioactivity levels 5 min after the second injection and at the time the second session was started (t_z), respectively. $\text{Int\_}C_a^{II}$ and $C_a(t_z)$ are the arterial blood radioactivity levels obtained by 5-min continuous sampling after the second injection and at t_z, respectively. Method 2: $[C_b(t_z + 5) - C_b(t_z)]/[\text{Int\_}C_a^I \times R]$, where R is the injection dose ratio. Method 3: $[C_b(t_z + 5) - C_b(t_z) \times \exp(-K_1^I \times 5/\lambda)]/\text{Int\_}C_a^{II}$, where λ is the population averaged partition coefficient. Method 4: same as Method 3 except that K_1^I was replaced by K_1^{II} obtained by means of Method 2. Theoretically, Method 4 appeared to be the best of the four methods. The change in K_1 during the second session obtained by Method 1 or 2 largely depended on R and t_z, whereas Method 3 or 4 yielded a more reliable estimate than Method 1 or 2, without largely depending on R and t_z. Since Method 2 was somewhat superior to other methods in terms of noninvasiveness and simplicity, it also had the potential for routine clinical use. The reproducibility of two sequential measurements of K_1 was investigated with clinical data obtained without any intervention. The response of CBF to acetazolamide challenge was also assessed by the above four methods. The knowledge gained by this study may assist in selecting a method for sequentially measuring CBF with a double injection of IMP.

Key words: double-injection method, N-isopropyl-(^{123}I)p-iodoamphetamine, cerebral blood flow, SPECT