Note

Effect of Sodium Citrate on the Blood
Disappearance of $^{67}\text{Ga}^\dagger$

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The effect of sodium citrate on the blood disappearance of ^{67}Ga was examined in rats. The half life value of the alpha phase and the initial AUC value (0-60 min) were dose-dependently decreased by sodium citrate. The binding of ^{67}Ga to serum proteins was also dose-dependently inhibited by sodium citrate.

Key Words: gallium-67, sodium citrate, pharmacokinetic analysis, protein binding, rats

1. Introduction

Radionuclide ^{67}Ga which is widely used for detection of tumor^{1),2)} and inflammation³⁾, has been demonstrated to bind easily to serum proteins, chiefly transferrin⁴⁾⁻⁷⁾. The binding capacity of ^{67}Ga to serum proteins has been reported to be decreased by sodium citrate^{8),9),10)}. In addition it has also been reported that commercially available ^{67}Ga -citrate containing different dose of sodium citrate shows different physicochemical behavior each other¹⁰⁾. However, there are no detail reports concerning the effect of sodium citrate on the blood disappearance rate of ^{67}Ga . Then we examined the effect of sodium citrate on the pharmacokinetics of ^{67}Ga in this report.

2. Experimental

2.1 Pharmacokinetic study

$^{67}\text{GaCl}_3$ was diluted with physiological saline to 925 kBq (25 μCi)/ml and a volume of 0.2 ml (185 kBq) containing various doses of sodium citrate was administered to the femoral vein, then a 20 μl volume of the blood was repeatedly taken *via* the catheter inserted into the external jugular vein¹¹⁾. The radioactivity of the blood was counted in a well-type NaI-scintillation counter and its value was represented as a ratio in order to correct the body weight of each rat by the equation: (blood radioactivity (cpm)/blood weight (g))/(injected radioactivity (cpm)/body weight (g)). The pharmacokinetic parameters of ^{67}Ga were calculated based on a 2-compartment model using a pharmacokinetic analysis program (MULTI) for a microcomputer¹²⁾.

2.2 Protein binding study

The binding capacity of ^{67}Ga to serum proteins was determined by ultrafiltration using Centrifo membrane cones (type CF50A) with

[†] ^{67}Ga の血中消失に及ぼすクエン酸ナトリウムの影響。河野弘之, 大久保恭仁, *久保寺昭子: 東北薬科大学放射薬品学教室, 983 仙台市小松島4-4-1, *東京理科大学薬学部放射薬品学教室, 162 東京都新宿区市谷船河原町12。

Fig. 1 Effect of sodium citrate on the blood disappearance of ^{67}Ga .

Each value represents the mean and SEM of 4 rats.

Table 1 Pharmacokinetic parameters of ^{67}Ga following intravenous administration with various doses of sodium citrate

Dose ($\mu\text{mol/ml}$)	Half life (min)		AUC (ratio min)	
	α -phase	β -phase	0 - 60 min	60 - 120 min
0	30.0 ± 2.0	408.2 ± 68.0	481.7 ± 16.7	243.9 ± 6.2
4	31.4 ± 0.5	490.3 ± 53.8	473.1 ± 6.9	254.1 ± 5.8
8	26.5 ± 2.5	475.6 ± 62.9	467.6 ± 18.9	247.3 ± 13.5
16	23.5 ± 0.8	373.5 ± 50.2	433.2 ± 7.5	226.4 ± 4.0
32	18.5 ± 3.0	405.6 ± 13.9	357.7 ± 13.3	232.9 ± 11.1

Each value represents the mean and SEM of 4 rats.

a more than 95% retention for molecules above 50 000 MW. Gallium-67 (18.5 kBq/50 μl) was incubated in the rat serum (950 μl) with various doses of sodium citrate for 20 min at room temperature. An aliquot (800 μl) of each sample was then transferred to the membrane cone and centrifuged at 1 000 g for 10 min at room temperature. Another aliquot (50 μl) was transferred to a counting tube and served as a total radioactivity. After centrifugation the radioactivity of the filtrate was counted in a well-type NaI-scintillation counter. Data were represented as % filtration calculated by the following equation: (radioactivity filtrated/total radioactivity applied) $\times$ 100.

3. Results and Discussion

The effect of sodium citrate on the blood

disappearance curve and the pharmacokinetic parameters of ^{67}Ga are given in Fig. 1 and Table 1, respectively. Sodium citrate accelerated the disappearance rate of ^{67}Ga only in the early phase after the injection. The half life value of the alpha phase was dose-dependently shortened, but the one of the beta phase was not shortened by sodium citrate. The area under the time-ratio curve of ^{67}Ga during 60 min after the injection of ^{67}Ga was also diminished dose-dependently, but one between 60 and 120 min was not influenced by sodium citrate. This transient action of sodium citrate on the blood disappearance of ^{67}Ga seems to be due to its rapid degradation, about 60% of citrate has been reported to be metabolized to CO_2 by 60 min after intravenous injection¹⁹⁾. It is unable to relate the result of pharmaco-

Fig. 2 Effect of sodium citrate on the ^{67}Ga binding to serum proteins. Each value represents the mean and SEM of 4 determinations.

kinetic study with that of *in vitro* study directly, since the concentration of sodium citrate in the blood seems to be considerably low compared to that in the solution used in the binding study. Nevertheless, this facilitating action of sodium citrate on the blood disappearance of ^{67}Ga is probably due to the action on the protein binding of ^{67}Ga , because the protein binding rate of ^{67}Ga also decreased almost proportionally to the dose of sodium citrate (Fig. 2).

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