Survival of Red Blood Cells in Rabbits after Acute Administration of Unlabeled Stannous Pyrophosphate: Concise Communication

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We investigated the possibility that acute administration of unlabeled stannous pyrophosphate may adversely affect red blood cells in the rabbit. Our method was similar to the in vivo labeling of RBCs with technetium-99m for blood-pool scanning. The investigation showed that dosages recommended in the literature produce no demonstrable difference between pre- and postdose RBC survival, which strongly suggests that the stannous content of the pharmaceutical is not harmful to red blood cells.


In vivo labeling of red blood cells (RBC) with Tc-99m Sn(II) pyrophosphate is a simple, effective method of obtaining an intravascular label for blood-pool scanning (1–3). The method generally involves the i.v. injection of unlabeled stannous pyrophosphate [Sn(II)PPI] followed, after an appropriate interval, by an i.v. injection of sodium [\(^{99m}\text{Tc}\)] pertechnetate. Doses of Sn(II)PPI have ranged from 5 mg to 15.4 mg (0.07 mg to 0.22 mg for 70 kg of body weight) containing from 0.662 mg to 2.08 mg Sn(II). Although toxicity studies of orally administered stannous and stannic salts (4,5) and intravenously administered stannous pyrophosphate (6) show that these dosages have a large margin of safety so far as the LD\(_{50}\) is concerned, no studies to date have addressed the effect of Sn(II)PPI on RBC survival. We have looked for such effects in rabbits.

The study population consisted of 28 rabbits of mixed sex, weighing from 2.5 to 3.5 kg, divided into four groups of seven animals each. Two rabbits from each group first underwent splenectomy. A 3-ml sample of heparinized blood was then drawn from each animal, and the RBCs were tagged with 50 \(\mu\)Ci of sodium chromate (Cr-51) in the usual manner (7). At 2- to 3-day intervals over the next 30 days, 14 one-ml heparinized blood samples were drawn and 0.5-ml aliquots counted in an automatic gamma well counter. The data were corrected for background, plotted on two-cycle semilog graph paper, and a least-squares regression line was fitted to the data using a pocket calculator. The slope of the regression line was used to determine the halflife of the RBCs. Concurrent with the determination of the RBC survival, reticulocyte counts, hematocrit, and hemoglobin tests were done on days 1, 10, and 22 following Cr-51 labeling and on days 1, 7, and 11, following Sn(II)PPI administration.

After the determination of the RBC survival for

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each animal, the groups of animals were injected with commercial stannous pyrophosphate* in varying amounts ranging from 0.02 mg/kg to 0.16 mg/kg of body weight (Table 1). Eight 1-ml blood samples were then drawn over the next 13 days, counted as above, and the half-lives of the cells compared with the predose values.

Five rabbits, to which nothing had been administered, were used as controls for reticulocytes, hemoglobin, and hematocrit. Samples were taken from the controls at the same times as from the test animals. The results shown in Table 1 are "normal" values.

All 22 samples for each animal were counted in sequence on the same day to eliminate the need for decay correction.

RESULTS

The slopes of the regression lines for all the samples were essentially the same as the slope of the predose survival curve.

The control RBC survivals for the 20 normal rabbits and the six splenectomized rabbits were 11.41 ± 1.3 and 11.0 ± 1.7 days, respectively. After administration of the Sn(II)PPi in the doses indicated in Table 1, the RBC survival times for both groups of animals were 11.4 ± 1.4 days.

DISCUSSION

The use of stannous pyrophosphate for in vivo labeling of RBCs provides an efficient and easy way to obtain blood-pool images (I-3). Individual doses suggested in the literature range from 0.07 to 0.22 mg of Sn(II)PPi per kilogram body weight (5-15.4 mg for a 70-kg man). The dosage range in our study (0.02-0.16 mg/kg) was chosen to determine a) whether doses used at present shorten RBC survival time, and b) the threshold dose of Sn(II) ion if RBC survival time is affected.

Comparison of RBC survival, hematocrits, and reticulocyte counts for the four groups of rabbits showed no statistical differences between groups, nor between pre- and post-doses within groups (Table 1). These results indicate that the use of Sn(II)PPi for the in vivo labeling of red blood cells with Tc-99m in rabbits in no way affects red-blood-cell survival when used in doses of less than 0.16 mg/kg body weight, an amount close to the maximum used for in vivo labeling of RBCs in humans for blood-pool imaging.

Although it is likely that Sn(II)PPi similarly does not affect human RBC survival, further investigation is necessary to establish the safety of this promising technique in man.

FOOTNOTE

* Mallinckrodt Nuclear Corporation, St. Louis, MO.

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