INTERNAL CONTAMINATION WITH SEVERAL RADIONUCLIDES AND METHODS OD THERAPY

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INTRODUCTION

In cases of accidental exposure in the environment, internal contamination is likely to include several radionuclides. Special concern should be given to radioactive strontium, caesium, iodine and to highly radiotoxic transuranium elements. Efficient therapeutic agents for reducing retention of single radionuclides are already in use for radiological protection purposes i.e. alginate for radiostrontium (Skoryna et al., 1964), ferrihexacyanoferrate(II) for radiocaesium (Madshus et al., 1966), potassium iodide for radioiodine (Ramsden et al., 1967) and diethylenetriaminepentaacetic acid (DTPA) for transuranium elements (Catsch and Harmuth-Hoene, 1979). It would be desirable to devise a therapeutic regimen which would reduce the body burden not only of one but of all the radionuclides that present a hazard and which at the same time is simple to apply. Such treatment involving necessarily simultaneous administration of several different therapeutic agents could modify the efficacy of each agent or cause other adverse effects due to interactions between them. Studies presented here are related to the problem of internal contamination with several radionuclides and therapeutic treatment administered.

ANIMAL STUDIES

MATERIALS AND METHODS

The experiments were performed on 6-8-week-old female albino rats (about 150 g body weight). The animals were divided into three groups according to the therapeutic treatment administered. The first group, CONTROL, was fed standard rat diet; the second, MIXTURE + Ca-DTPA, was given food supplemented with the mixture of 15 g calcium alginate *, 2.5 g ferrihexacyanoferrate(II)§ and 0.015 g KI# per 100 g of diet and received also chelating agent Ca-DTPA intraperitoneally (380 µmol/kg body weight); the third group, MIXTURE + Zn-DTPA, received the aforementioned mixture of therapeutic agents in food together with 3.3 mmol Zn-DTPA per 100 g of diet. On the second day of the experiment, the animals received 74 kBq Sr-85, 37 kBq Cs-137, 740 kBq I-131, 1850 kBq Ce-141 orally or 37 kBq Ce-141 intraperitoneally.

The complexing agents Ca-DTPA or Zn-DTPA were prepared by dissolving diethylenetriaminepentaacetic acid⊕ in distilled water

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§Radiogardase-Cs, Heyl and Co., West Berlin, FRG.
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⊕Fluka, A.G., Buch, S.G., Switzerland.

in the presence of an equimolar amount of calcium or zinc chloride and neutralizing it with 20% NaOH to pH 6.4. Ca-DTPA was administered intraperitoneally while Zn-DTPA was added to standard rat diet which was ground and already mixed with calcium alginate, ferrihexacyanoferrate(II) and KI. The therapeutic agents were administered in food during the first three days of the experiment (one day before and two days after radionuclide administration) and afterwards the animals were fed standard rat diet.

Radionuclides of Sr-85, Cs-137 and Ce-141 were supplied from New England Nuclear, Dreieich°, as chlorides of high specific activity. Radioiodine was supplied from the Institute "Boris Kidrič"- Vinča€, as natrium iodide of high specific activity. All the animals except those which received Ce-141 orally were killed six days after radionuclide administration. Those which received Ce-141 orally were killed after 24 hr because of its low intestinal absorption. The radioactivity in the whole body, carcass and gut was determined in a single-channel, twin-crystal scintillation counter (3X3" cylindrical NaI(Tl) crystals) and of the organs in an automatic well-type scintillation counter∞. All values are expressed as percentage of the administered dose and presented as arithmetic means and standard error of the means.

RESULTS

Oral administration of alginate, ferrihexacyanoferrate(II) and KI together with intraperitoneal application of Ca-DTPA reduced the whole body retention of orally administered Sr-85 about 5 times, Cs-137 retention was reduced about 56 times and I-131 retention about 8 times while retention of intraperitoneally administered Ce-141 in liver and bone was reduced about 10 times. In case of simultaneous oral administration of all therapeutic agents (calcium alginate, ferrihexacyanoferrate(II), potassium iodide and Zn-DTPA), the retention of orally administered Sr-85, Cs-137 and I-131 was reduced 9, 40 and 11 times respectively while retention of intraperitoneally administered Ce-141 was reduced 1.4 times. The very low retention of orally administered Ce-141 was significantly increased by administration of the mixture and Zn-DTPA. Compared to controls the whole body and bone retention were increased 2.5 and 10 times respectively.

DISCUSSION

Simultaneous oral administration of the mixture of calcium alginate, ferrihexacyanoferrate(II) and KI with intraperitoneal (Ca-DTPA) or oral (Zn-DTPA) administration of chelating agent did not diminish the efficacy of the single antidotes. The retention of intraperitoneally administered Ce-141 was less reduced by

°New England Nuclear, 6072 Dreieich, FRG.
€Boris Kidrič Inst. for Nucl. Sci., Vinča, Beograd, Yugoslavia.
∞Nuclear Chicago, 2000 Nuclear Drive, Des Plaines, IL 60018.

orally administered Zn-DTPA than by intraperitoneally administered Ca-DTPA. The difference in effectivenes in our experiment is probably due to the lower efficacy of Zn-DTPA in comparison to Ca-DTPA when it is administered immediately after the radionuclide (Seidel, 1976). Increased values of Ce-141 retention after its oral administration together with chelating agent are due to the fact that oral chelation therapy enhances intestinal absorption of ingested transuranium elements for which chelation proves to be an efficient therapy. However, it also enhances the elimination of the chelated metal. The ultimate body burden may therefore be only slightly higher than if the chelating agent had not been employed. In our experiment measurements were done 24 hr after Ce-141 oral administration i.e. at a time when most of the chelated Ce-141 was not yet eliminated. We therefore assume that cerium retention values in these animals would be much lower if allowing enough time for cerium elimination.

The results obtained indicate that Ca-DTPA or Zn-DTPA did not cause a loss of efficacy of antidotes from the mixture nor did the antidotes from the mixture alter the effect of chelating agents. All four therapeutic agents can be used together without undesirable interactions. Very high efficacy of parenterally administered Ca-DTPA can not be reached by much higher oral doses of Zn-DTPA, especially in cases of their immediate administration after radionuclide entry in the body (Taylor and Volf, 1980). However, Zn-DTPA has substantially lower toxicity than Ca-DTPA and its oral administration would greatly simplify the therapy especially in cases of prolonged treatment

HUMAN STUDIES

In order to obtain relevant information in humans we used a similar therapeutic treatment and examined its effect on I-131 and Sr-85 uptake in four adult volunteers (one man and 3 women). Three of them received two oral doses of radioactive iodine I-131 (185 kBq each). The second dose of I-131 was administered 13 days after the first one. The subjects fasted 10 hr before and 4 hr after radionuclide administration. Uptake values after the antidote treatment were measured after the first radioiodine administration and normal uptake values for each subject were taken after the second I-131 dose. Measurements were made 2, 4 24 and 48 hr after each radioiodine administration. The antidote treatment consisted of 10 g calcium alginate, 3 g ferrihexacyanoferrate(II), 130 mg potassium iodide and 5 g Zn-DTPA in a volume of about 150 ml water. The antidote treatment was given 30 minutes before the first I-131 administration. Normal I-131 thyroid uptake values 24 hr after radionuclide administration were 26, 42, 30% in three subjects. After antidote treatment the respective I-131 values were 0.5, 1.3, 0.9 % indicating the almost complete block of thyroid uptake. This indicates that simultaneous administration of other antidotal agents do not cancel or decrease the effect of potassium iodide on I-131 thyroid uptake.

In the separate study one of the volunteers received the same therapeutic treatment as in aforementioned study but the

radionuclide administered was Sr-85. Two oral doses of Sr-85 were administered within the interval of 8 days. The first dose was given together with the therapeutic treatment while after the second dose no treatment was given. The plasma radioactivity level was used as indicator of radiostrontium absorption.The results were expressed as percentages of the oral dosage per liter of plasma. Plasma radioactivity was 0.1%/L after the first and 1.8%/L after the second Sr-85 administration. The therapeutic treatment reduced radiostrontium absorption by a factor of 18. This is in agreement with the results of Hodgkinson and collaborators (1967) obtained in subjects who were without a treatment (control values) or received 4 g of sodium alginate. Presence of other therapeutic agents had no effect on the efficacy of alginate to reduce radiostrontium absorption.

The results obtained deserve attention since simultaneous administration of several therapeutic agents (alginate, ferrihexacyanoferrate(II), KI and chelating agent) might present a convenient method for early and delayed therapy of internal contamination with biologically dangerous radionuclides.This may be importand in cases of increased exposure in the environment in situations where radionuclide identification is difficult or impossible to make before administration of the therapy.

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