Reduction of Iodine Transfer to Milk of Cows after Perchlorate Ingestion

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Abstract

These experiments quantitate the relation between amount of perchlorate ingested and radioiodine transferred to milk of the cow when radioiodine is fed daily or after radioiodine administration ceases.

When radioiodine was given daily, graded doses of perchlorate, from 10 to 4,000 mg/day, increased plasma iodine in accord with $Y = 88.1 X^{0.52}$. (Y = % of control value and X is the daily dose of perchlorate in milligrams.) Curves for iodine-125 in milk and ratio of milk to plasma iodine-125 between the limits of 50 and 1,000 mg perchlorate daily were fitted by $Y = 794.8 X^{-0.52}$ and $Y = 1,046.5 X^{-0.601}$; these same curves between 10 and 50 mg perchlorate daily were fitted by $Y = 85.6 + .37 X$ and $Y = 82.3 + .28 X$. Between 1,000 and 4,000 mg perchlorate, these curves had a slope of 0. These data indicate that perchlorate can inhibit the iodide-transfer mechanism of the mammary gland of the cow and that a ratio of milk to iodine of .2 indicates complete blockage of this transfer.

Administration of 1 g of perchlorate daily leads to 55% less radioiodine being transferred to milk after administration of iodine 125 has ceased.

Introduction

Anions that inhibit the uptake of iodide by the thyroid can also reduce the transfer of iodine into milk. Among the anions effective at the mammary gland are I-, SCN-, ClO₄⁻, BF₄⁻, IO₃⁻, NO₃⁻, BrO₃⁻, and Cl⁻ (1, 2, 3, 4, 5, 7, 8, 9, 10). The relative effectiveness of these inhibitors is about the same for thyroid and mammary gland and suggests a similarity of iodide concentrating mechanisms (2, 11). Perchlorate is one of the most potent inhibitors and for this reason was chosen for this study.

The study of substances that can reduce transfer of iodine into milk can provide basic information about the transfer mechanisms and can lead to the development of procedures useful when pasture or other feedstuffs become contaminated with radioiodine. In most studies a single large dose of the inhibitor substance is given, and so little information is available about the minimum and maximum amounts that can reduce iodide transfer to milk. One of the experiments reported here used a series of graded daily doses of NaClO₄ to determine the amounts needed to effect a reduction in radioiodine transfer into milk of cows.

In the second experiment cows that had attained a steady state of radioiodine in the milk from daily oral administration of ¹²⁵I were studied to determine the effectiveness of perchlorate in accelerating the decline of milk radioiodine after ingestion of radioiodine stopped.

Methods

The eight cows in this study were purebred Ayrshire, Holstein, Jersey, or Brown Swiss cows, nonpregnant, past midlactation, and free of all obvious diseases. The cows ranged in weight from 390 to 640 kg and produced from 7 to 22 kg of milk daily. Cows 161 and 163 were in the first and second experiments while the other six cows (157, 158, 162, 164, 165, and 167) were only in the second experiment.

For the first experiment cows 161 and 163 were kept in metabolism stalls for several days before and throughout the experiment. The animals were given water and alfalfa hay ad lib. and 6.8 kg of a 16% crude protein commercial grain mixture daily. Radioiodine, as Na ¹²⁵I, was given twice daily in gelatin capsules for the entire experimental period; all capsules were made at the start of the experiment and contained 80 µCi of ¹²⁵I each.

Milk samples were collected each morning for the first 10 days and analyzed for ¹²⁵I to verify the establishment of steady state. Actual sampling began at 0800 on the 11th day. For 5 days, milk (twice a day) and blood samples...
were collected to represent the control state. On the evening of the 15th day the cows received the first of the twice daily capsules containing sodium perchlorate. These capsules were given for 5 days. Sampling was as for the control period. After this perchlorate test period the animals were returned to a no perchlorate supplementation status. The perchlorate-free periods served as the control period for the subsequent perchlorate period. The levels of perchlorate were 10, 50, 100, 300, 500, 1,000, 2,000, and 4,000 mg per cow per day. Data of only the last 3 days of each 5-day period were averaged; any changes in milk and plasma as a result of perchlorate supplementation were judged to be complete by this time. Milk and plasma $^{125}$I of a particular perchlorate feeding period were calculated as a percentage of the respective control period.

For the second experiment cows were given $^{125}$I twice daily from 20 to 60 days. After $^{125}$I administration stopped, milk collections continued from 11 to 15 days. Four cows (157, 158, 161, and 163) were given twice daily doses of $0.5$ g ClO$_4$- (as sodium perchlorate) during the phase of declining milk $^{125}$I. The milk $^{125}$I concentrations were expressed as percent of the steady state radioiodine in milk. Data for cows receiving perchlorate were compared with those of cows not so supplemented.

**Results**

Data of the first experiment are in Fig. 1. This is a log-log plot of percent change in $^{125}$I concentration in plasma and milk vs. the daily intake of perchlorate. Previous experiments have shown that inhibitors of iodide transfer increase plasma iodide at the same time that of milk iodide decreases (3, 5, 6). In agreement, plasma iodine of the cows in this study increased steadily as perchlorate intake increased. The equation for plasma iodine is $Y = 88.1X^{0.222}$ where $Y$ is the percent of the control and $X$ is the daily dose of perchlorate in milligrams. Plasma iodine consists of both bound and nonbound (mostly iodide) iodine. The major action of perchlorate on plasma is to increase the nonbound iodine rather than the bound-iodine fraction (3, 5). No attempt was made in this study to distinguish between bound and nonbound iodine. It is reasonable to expect that bound-iodine would increase with time as more and more iodide is organized by the thyroid and released into blood. This increase of bound-iodine has been minimized by expressing the data of a perchlorate test period as the percent of the preceding control period, and so the rise in Fig. 1 mostly represents an increase in nonbound iodine. Total plasma iodine underestimates the change occurring in plasma nonbound iodine (3).

It was not possible to express the changes of milk $^{125}$I as influenced by perchlorate as a single curve. The curve is triphasic with little or no response of milk $^{125}$I to perchlorate doses below 50 mg and no further response to amounts above 1,000 mg per day. Daily doses of perchlorate ranging from 50 to 1,000 mg reduced $^{125}$I in milk; the data required a log-log plot to be expressed as a straight line. The equation for the function is $Y = 794.8X^{-0.52}$. As noted, increasing dose size of perchlorate resulted in an increase of plasma nonbound radioiodine, most of which was probably in the form of inorganic iodine (3). Increases in plasma iodide can lead to more radioiodine moving into milk by diffusion. As a result the decrease in milk radioiodine from perchlorate dosing could understate the effectiveness of perchlorate on the concentration mechanism. To correct for this the ratio of milk to plasma $^{125}$I (M/P $^{125}$I ratio) also is plotted in Fig. 1. This second plot is similar to the plot of the decrease in $^{125}$I concentration of milk. The ef-
ficiency of the M/P ratio is shown by the closer clustering of the data points around the line
\[ Y = 1.0465X - 0.01 \] when contrasted to the milk
\(^{125}\text{I}\) concentration data; moreover, the slope
of the line for M/P \(^{125}\text{I}\) is steeper because the
effect of increase in plasma iodine with time
has been eliminated.

Actual values for M/P \(^{125}\text{I}\) ranged from
1.65 for the control portion of the 10 mg C\(_{10}^4\)-
test period to .20 for the test period when cows
were given 4,000 mg of C\(_{10}^4\)- per day. For
\(^{125}\text{I}\) in milk the actual values for the respective
test periods were 1.30 and .26% of the daily
dose per liter of milk and for plasma .80 and
1.30% of the daily dose per liter.

Data for the second experiment, effect of
perchlorate on the rate of falloff of \(^{125}\text{I}\) in milk
after long term dosing has ceased, are in Fig.
2. The upper curve presents data of six cows
given perchlorate. The lower curve is data
of four cows that began to receive perchlorate
at the time radioiodine administration ceased.
Perchlorate administration accelerated falloff
of milk iodine. Over the 15 days only 55% as
much radioiodine appeared in the milk when
perchlorate was given to the cows as when the
animals were not so supplemented; by day 15
both groups had achieved the same radioiodine
in milk. Since the cows had been receiving
radioiodine for a long time, this effect of per-
chlorate is the maximum that can be expected.

Discussion

Twice daily dosing for extended periods is
an attempt to simulate the long-term radionu-
clide ingestion pattern after contamination of
pastures by fallout. With long-term ingestion
of radionuclides, the level of these in milk rise
for several days and then decline with a half-
time dependent upon the half-life of the radio-
active nuclide and the residence half-time of
the nuclide on pasture grasses. The first experi-
ment shows that perchlorate supplementation
reduces up to 80% the amount of radioiodine
transferred to milk even though the amount of
radioiodine ingested has not changed. When
ingestion of the radioiodine ceases and the
only source of the radioiodine of milk is that
stored in the tissues of the cow, perchlorate can
accelerate the rate of falloff of radioiodine in
milk. The success of perchlorate administration
suggests its use as a countermeasure in event
of pasture contamination by radioiodine. Be-
fore such an action can be recommended, how-
ever, the transfer of perchlorate to milk and its
effect upon health of the human population
consuming milk must be considered. Little is
known about transfer of perchlorate into milk
of cows and goats.

A study of the effect of perchlorate upon
transfer of radioiodide into goats' milk has
been reported from this laboratory (3), and
so it is possible to compare cow and goat. For
both species perchlorate exerts its effect within
12 h. The site of action of perchlorate is the
mammary gland as judged by the fact that re-
duction in M/P radioiodine ratio is able to ac-
count for all changes in milk radioiodine. If the
weight of the average cow is 500 kg, the 1,000
mg of C\(_{10}^4\)- daily is equivalent to 2 mg/kg/-
day; this amount of perchlorate reduced the
M/P \(^{125}\text{I}\) ratio to 18% of the control value for
the cows and to 28% for the goats. Four or 8
mg C\(_{10}^4\)-/kg/day had no additional effect in
the cow whereas in the goat the M/P \(^{125}\text{I}\) ratio
decreased to 18% and 13% of the control val-
ue (3).

Different milk iodine levels suggest a greater
sensitivity of the cow than the goat to per-
chlorate. If the comparison is based upon the
dose of perchlorate per kg of metabolic body
weight (mg/kg W\(^{3/4}\)), however, the cow and
goat show equal responses. Using metabolic
body weight, an intake by the cow of 2 mg of
perchlorate/kg/actual body weight/day is
equivalent to 4 mg/kg/day for the 50-kg goat.
At these levels iodine transferred to milk by
both species was equal to 18% of the control

Fig. 2. The decline of \(^{125}\text{I}\) in the milk of cows
after cessation of radioiodine intake. The lower
curve is for cows receiving 1 g of perchlorate daily
(2 x .5 g) while the upper curve is for cows not
receiving perchlorate.
value. A difference between cow and goat is evident in that iodine in milk of the goat could be reduced still further by increasing perchlorate whereas this was not true for the cow (3).

The effect of perchlorate supplementation is to cause increases in plasma radioiodine in both cow and goat. This probably is due to an increase in iodide as in the goat study (3). Increased plasma iodine is probably the result of major reductions in clearance of radioiodide by thyroid and mammary gland without compensatory increases in excretion of radioiodine by kidney and intestinal tract. This present paper demonstrates that plasma radioiodine increased before milk radioiodine starts decreasing, suggesting that the iodide concentrating mechanism of the thyroid of the cow is more sensitive to perchlorate than is that of the mammary gland. The plasma $^{125}$I curve suggests that for perchlorate less than 10 mg/day, plasma radioiodine might be depressed; this would be in accord with observations on the goat (3).

From curves for $^{125}$I in milk and M/P $^{125}$I (Fig. 1) at least two different mechanisms are operative in transfer of iodine into milk. The amount of iodine transferred to milk is an inverse function of amount of perchlorate when daily intake of perchlorate ranges from 50 to 1,000 mg. When perchlorate reaches 1,000 mg per day, there are no further reductions. Since perchlorate is a recognized inhibitor of the thyroid iodide concentrating mechanism, the descending portion of the milk iodine curve can be attributed to inhibition of a concentrating mechanism in the mammary gland. The flat portion of the curve, from 1,000 to 4,000 mg daily, could be interpreted as that portion of milk iodine that enters via diffusion. This suggests that in studies of the transfer of iodine into milk, a M/P ratio greater than 0.2 rather than 1 should be regarded as indicating activity of an iodide concentrating mechanism.

The first portion of the curve in Fig. 1 is flat between 10 and 50 mg ClO$_4$-/day. This suggests that perchlorate was not interfering with iodide transfer. There is no obvious explanation for this except for the possibility that while perchlorate can successfully compete with iodide for the transfer mechanism, there may be sufficient sites of transfer available so that the amount of iodide moving into milk is not curtailed. Perchlorate necessary to reduce iodine transfer into milk are from three or more times greater than the amount of iodine commonly supplied in the diet of the cow. There is a lack of knowledge of the absorption of perchlorate from the intestine and its proportionate transfer to milk. More will be known about the iodide transfer mechanism when the metabolism of perchlorate is determined.

References


