Uranium Gastrointestinal Absorption in Humans: A Chronic Exposure Study

M. Limson Zamora, B.L. Tracy, J.M. Zielinski, D.P. Meyerhof, G.B. Moodie, and R. Falcomer
Radiation Protection Bureau
Department of Health
Ottawa, Canada K1A 1C1

ABSTRACT

To estimate gastrointestinal (GI) absorption \( f_1 \) of uranium in humans where exposure is through chronic ingestion, a study was conducted of a rural community in Canada where the residents relied on drilled private wells that delivered water with uranium levels ranging from 2 to 780 µg/L. A comparison was made with an urban centre whose drinking water was supplied by a municipal system and had a uranium content of <1 µg/L. Fifty subjects participated in the study. To estimate daily intake from both water and food as accurately as possible, the duplicate diet approach was used where individuals collected and set aside a duplicate amount of beverage and food that they had ingested over a three-day period. Total intakes from water and through food varied from 0.03 to 570 µg/day. The \( f_1 \) values obtained ranged from 0.001 to 0.06, with a mean of 0.012 and a median of 0.009. Variation of \( f_1 \) values correlated poorly with gender, years of residence and age at the time of study. Contrary to expectations, the values were found to be in reasonable agreement with values obtained in previous human studies whether the pattern of exposure was acute or chronic.

INTRODUCTION

Despite the numerous studies conducted in both animals and humans it has been difficult to estimate an appropriate value for \( f_1 \), due to the wide range of results reported, the questions concerning the reliability of some of these results, or the relevance of the protocol and uranium levels used. Values reported in the literature [1,2] have varied from less than 1% to greater than 32%. A number of human studies have been reported more recently, but were conducted under conditions of acute [3,4] or sub-chronic [4] conditions of exposure. However, with the exception of accidents, most ingestion exposures, whether environmental or occupational, are chronic in nature.

In Canada, the federal Department of Health, in collaboration with the provinces and the Territories, establishes the uranium guideline for drinking water. The present investigation was undertaken to determine the most appropriate value for the gastrointestinal (GI) absorption rate (the \( f_1 \) value) to use in setting the uranium exposure guideline.

METHODS

Adult male and female participants, with as good a spread in age between 20 and 70 years as possible, were recruited from both the rural and urban communities. Teenagers were also included in the study. All participants were in good health and not subject to kidney or other complicating pathology.

Uranium intake in both food and water and excretion in urine and faeces were measured in samples collected concurrently from the same individuals over a three-day period. The duplicate diet method was used to monitor uranium intake in water and through food. Inductively coupled plasma mass spectrometry (ICP/MS) was used to measure uranium levels in food, beverages, and urine and faecal samples. The detection limit for this analytical technique was 6 x 10^4 ng/mL for aqueous solutions analysed after sample preparation of food, tea, coffee and other beverages, and 2 x 10^3 ng/mL for the urine samples which only required dilution so that total solids would be less than or 1%. The significance level chosen to reject the null hypothesis was \( p \neq 0.10 \).
The $f_1$ factor was estimated as follows:

$$f_1 = \frac{\text{Urinary uranium/3-day period}}{\text{Total uranium intake/3-day period}} \times \frac{1}{f_u}$$

where $f_u$ = the fraction of absorbed uranium that appears in urine.

The value of $f_u = 1$ is used in all calculations for $f_1$, based on the assumption that the subjects were in a steady state with respect to the uptake and urinary excretion of uranium.

RESULTS AND DISCUSSION

Volunteers from the rural community included 10 males and 20 females. This population depended mostly on home-grown staples and vegetables for their food. Volunteers from the urban centre included 7 males and 13 females. Participants included 10 teenagers. Years of residence varied from 3 to 59 years in the rural community and from 17 months to 33 years in the urban centre.

The frequency distribution of $f_1$ values obtained from the 50 participants is shown in Figure 1. Values ranged from 0.009 to 0.06 with fifty-two percent of the values being less than 0.01 and seventy-eight percent, less than 0.02. All but one of the other values obtained were less than 0.04. For the one value ($f_1 = 0.06$) that exceeded the ICRP 30 recommended value of 0.05, the intake was less than 1 ug/day. Because the distribution of values was non-Gaussian, the median (0.009) rather than the mean (0.012 ± 0.01) is considered the appropriate central value for the results obtained from this study.

As shown in Table 1, the $f_1$ values are in good agreement with those reported in the more recent human studies whether the exposure pattern was acute[3,4], sub-chronic [4], or chronic as in the Japanese environmental studies [5,6] and Fisher’s study [7] of occupationally exposed uranium mill crushersmen.
Acute exposure studies

<table>
<thead>
<tr>
<th>Investigator</th>
<th>Year</th>
<th>Exposure pattern</th>
<th>$f_1$ values:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wrenn et al.</td>
<td>1989</td>
<td>Acute</td>
<td>Mean: 0.006</td>
</tr>
<tr>
<td>Harduin et al.</td>
<td>1994</td>
<td>Acute; Subchronic (15 days)</td>
<td>Acute: 0.015 to 0.02 Subchronic: 0.01 to 0.015</td>
</tr>
</tbody>
</table>

Chronic exposure studies

<table>
<thead>
<tr>
<th>Investigator</th>
<th>Year</th>
<th>Exposure pattern</th>
<th>$f_1$ values:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Masuda et al.</td>
<td>1971</td>
<td>chronic (environmental)</td>
<td>Mean: 0.016 ± 0.005</td>
</tr>
<tr>
<td>Yamamoto et al.</td>
<td>1974</td>
<td>chronic (environmental)</td>
<td>Range: 0.010 to 0.031</td>
</tr>
<tr>
<td>Fisher et al.</td>
<td>1983</td>
<td>chronic (occupational)</td>
<td>Mean: 0.008</td>
</tr>
</tbody>
</table>

Table 1. Summary of recent human $f_1$ studies

The $f_1$ values were found to correlate poorly with gender ($p = 0.13$) or duration of exposure ($p = 0.74$) which was taken to be equal to years of residence at the participant’s address during the time of study.

Ages for the forty adults ranged from 21 to 87 years. For the 10 participants who were in their teens, ages varied from 13 to 17 years. When data from all the adult participants were pooled with data from the teenagers, $f_1$ values correlated poorly with age ($p = 0.98$).

Thirteen of the adults were 45 years or older. All but one were women. It is a widely accepted fact that all normal humans gain bone early in life and during growth, reach a plateau, then experience bone loss, with women losing bone at a greater rate than men following menopause [8]. Indeed, older individuals may be in negative calcium metabolic balance. Uranium mimics calcium in skeletal biokinetics. In a previous paper [9], we mentioned the need to test if older participants are in negative uranium metabolic balance. If they are, the method of obtaining $f_1$ values from urinary excretion may not give completely valid information regarding the true $f_1$ value for these individuals. Thus, we examined the variation of the ratio of the mass of uranium excretion to the mass of uranium intake, which is equal to the $f_1$ value in this study (see Methods Section), with age. If these individuals are in negative uranium balance, their $f_1$ values would increase as their ages increase. However, this group’s $f_1$ values did not correlate positively with age ($r = 0.13, p = 0.68$).

Further, if this group is in negative uranium balance, their $f_1$ values would be greater than $f_1$ values of those participants that can be reasonably expected to be in uranium balance. ICRP 69 [10] applies to uranium the generic model for alkaline earths described in ICRP 67 [11]. In the model, because bone formation rates remain elevated until the early part of the third decade of life, transfer rates for the adult apply to ages 25 years.

The reference group used for the comparison was thus drawn from participants who were 25 years to < 45 years old. The $f_1$ values for the two groups, however, were not found to be significantly different at p $\neq 0.10$. 

3
It is also assumed in ICRP 69 that the deposition of uranium in urine is reduced in minors due to the elevated uptake by bone. We tested this concept of greater deposition and retention for uranium among the younger participants as it might also affect the value of $f_1$, calculated from urinary uranium collected from these individuals. Participants were divided into two groups: Subjects who were less than 25 years of age and individuals who were 25 years or older. The younger group was made up of the ten teens whose ages varied from 13 to 17 years and five subjects whose ages varied from 21 to 24 years. Since the participants $45$ years of age were not found to be in negative uranium balance, they were included in the second group. The $f_1$ values for subjects younger than 25 years were found to be not statistically different from those obtained with subjects 25 years or older ($p = 0.21$). As members of the younger group approach age 25 and the elevated uranium uptake by bone decreases, there should be a corresponding increase in uranium excretion in urine. However, the expected positive correlation with age with the $< 25$ years group was not found to be statistically significant ($r = 0.26$, $p = 0.35$).

CONCLUSIONS

The estimate for the central $f_1$ value from this study is 0.009. ICRP 69 recommends the use of 0.02 as the appropriate $f_1$ value for adults and children over $> 1$ year old. In a study on kidney toxicity study$[12]$ of the population investigated in the present investigation, 21 ug/ day was the intake at which the most sensitive bio-indicator for kidney toxicity exceeded the normal range. The median for participants with daily intakes of 21 to 570 ug of uranium is 0.007. The kidney toxicity study together with the present study provide support to the ICRP 69-recommended value of 0.02 as a conservative estimate for GI absorption of uranium for adults. Our results do not allow us to comment on the age dependence of $f_1$ for individuals younger than 13 years old. However, since our results did not reveal significant changes of $f_1$ values with ages 13 to 24 years old, the same $f_1$ value can be used for this particular age group, as also recommended by ICRP 69. Further, since the central value of $f_1$ does not appear to be sensitive to gender, this value can be appropriately used for females as well as males.
REFERENCES


