

Medical Treatment and Dose Estimation of a Person Exposed to Tritium

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Abstract

In this study, we aimed to investigate the damaging effects and clinical therapy of internal contamination with tritium to provide information and gain experience for medical treatments in case of an emergency due to a nuclear accident. Histories were taken by several doctors who observed and recorded the clinical symptoms of the patient described herein. The general health situation was evaluated by laboratory and equipment analyses. Tritium concentrations in the urine were estimated according to relevant standards during the monitoring period using a liquid scintillation counting method. Clinical observation revealed that the patient had symptoms of mild asthenia and sleep disorder with improvement after appropriate treatment. The last committed effective dose was determined through measurement of the urine tritium concentration and dose estimation and was estimated to be 0.123 mSv; the total effective dose was 14.536 mSv. The medical treatment and dose estimation in this patient with tritium contamination were successful and can provide a reference for similar cases in the future.

Keywords

tritium, medical treatment, dose estimation, internal contamination

Introduction

Tritium is an important nuclide produced by a light nuclear fusion reaction and is also one of the major nuclides that negatively impact workers in radiation plants. With the continuous development of nuclear energy, the levels of tritium in the environment are increasing, and considering that tritium is affecting the health of humans, it is gaining more attention.¹⁻³ In particular, with the development of controllable thermonuclear fusion research at home and abroad, the commercial operation of controllable thermonuclear fusion reaction devices in the near future is also within sight. Such reactors produce approximately 10^4 times the amount of tritium produced by the fission reactors currently used in nuclear power plants; consequently, even if only some of this tritium is released into the environment, tritium emissions would still increase by hundreds of times. However, tritium facilities often have good protective preparations and strict management. However, in the process of producing tritium and using the maintenance equipment, accidental exposure or irradiation caused by an accident can still occur; thus, it is very important to seek timely and effective medical treatment for affected individuals. In recent decades, domestic and foreign scholars have conducted a series of studies on the biological

effects and toxicity of tritium,^{4,5} which has led to the accumulation of valuable experience for follow-up research. However, most of these studies have focused on laboratory animals, and tritium contamination in humans is still rare. We now report a case in our hospital of tritium contamination caused by an accident as follows.

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Materials and Methods

General Information and Accident History

“Jia,” male, 42 years old, entered the maintenance department of a nuclear power plant 2 years ago, mainly conducting various welding operations; he had no previous exposure to radioactive materials. On February 25, according to the work plan, a working group added heavy water pipeline access to the system in a room. The working group consisted of 5 members: 1 work leader, 1 welder (Jia), 2 plumbers (responsible for cutting and grinding pipes), and 1 guard. The site construction started at approximately 10:30 on February 25. The work leader and 2 plumbers entered the negative-pressure shed and polished the holes in the pipeline. During the work, they wore plastic clothes and rubber gloves and used a ventilation hood. The drilling operation lasted approximately 15 minutes, during which approximately 11 L of residual heavy water in the pipe was collected. After polishing and reaming, there was still residual heavy water dripping at the opening. According to the chemical analysis results, the concentration of tritium in the spilled heavy water was 6.48×10^8 Bq/mL. After the completion of polishing and reaming, “Jia” began to weld the spot. Since it was difficult to carry out welding within the ventilation hood, “Jia” only wore an ice box filter. The welding work was completed at 13:15. At noon on February 26, the health physics staff found through a urinary tritium analysis of the workers that one worker (namely, “Jia”) had received unplanned tritium irradiation. The final effective tritium dose was 14.536 mSv after on-site medical decorporation. For further treatment, “Jia” was sent to our hospital at 19:30. Diuretic drainage and rehydration therapy were administered from the next day (February 26) to March 5, and he was discharged on March 7. After discharge, “Jia” continued to drink plenty of water and resumed normal work, but his urine sample monitoring continued until March 28.

Clinical Observation and Treatment

After admission to our hospital, several doctors evaluated “Jia” and took note of accidents, clinical symptoms, and so on. A comprehensive physical examination was performed to determine whether the mucous membrane of the skin was ruptured and inflamed. “Jia” was advised to drink a lot of tea, about 5 to 10 L per 24 hours and was administered a 40-mg furosemide injection for daily diuresis. Vitamins and electrolytes were provided, and sleep and blood circulation improved during hospitalization. The following laboratory and instrument inspections were performed: blood cell analysis, urine and stool routine, and electrolyte and biochemical examination; analysis of tumor markers (α fetal protein, carcinoembryonic antigen, carbohydrate antigen CA125 and CA199, prostate-specific antigen); T-cell subgroup analysis and thyroid function detection (triiodothyronine, thyroxine, thyrotropic hormone); chest X-ray; and abdominal B ultrasound examination. Meanwhile, changes to renal function (mainly blood creatinine) and electrolytes (mainly serum sodium and serum

potassium) were monitored during hospitalization. A psychological assessment was carried out with the 16-personality factor (16PF) test.

Preparation and Analysis of Chromosome Samples

First, 0.5 mL of venous blood was taken from the patient and inoculated into a culture flask containing 4 mL of mixed culture medium and cultured at $37^\circ\text{C} \pm 0.5^\circ\text{C}$ for 24 hours. Colchicine was added at a final concentration of 0.05 $\mu\text{g/mL}$, and the culture was continued for 48 to 52 hours, harvested, pelleted, and stained with Giemsa. The stained slides were scanned with a low-power microscope to observe the mitotic index and the degree of chromosome dispersion. Then, a good fission phase was selected, and all identifiable chromosomal aberrations were observed through microscopy. The distortion rate was calculated for fragments, dicentrics, centromeric rings, and translocations.

Reagents and Instruments

A 1220 QUANTULU liquid scintillation counter, manufactured by Perkin Elmer (Waltham, Massachusetts, USA); an OptiPhase HiSafe 3 scintillation fluid, manufactured by Perkin Elmer (Waltham, Massachusetts, USA); a 202A-S2 digital display thermostatic drying oven, manufactured by Shengwei Experimental Instrument Factory (Changzhou, China); a BP221S electronic balance, manufactured by Sartorius (Goettingen, Germany); and potassium permanganate (purity $\geq 99.5\%$) and sodium hydroxide (purity $\geq 96.0\%$), provided by Shanghai Reagent Factory (Shanghai, China), were used in the treatment process.

Sampling and Sample Preparation

For each urine sample, the middle segment of the urine was taken (~ 30 mL mark in the sample cup), and the number and time was recorded. The first urine sample was taken on February 26 at 19:30, and all urine samples were collected for sample preparation and testing during the hospitalization period (February 26 to March 7); one urine sample was taken daily during the week after discharge (March 8 to March 14), and one urine sample was taken every 3 days after that (March 15 to March 28).

The urine samples were treated with potassium permanganate using a dip color distillation method: A 30-mL urine sample plus 0.04-g potassium permanganate and 0.04-g sodium hydroxide were taken and distorted after shaking for approximately 20 minutes; the former 2 mL distillate was discarded, and 8 mL distillation liquid and 12 mL scintillation fluid was placed in 20 mL potassium-free glass bottle, oscillated for approximately 3 minutes, and placed in a liquid scintillation counter sample chamber for 12 hours.

Sample Measurement

First, the counting efficiency of a liquid flash counter for the urine sample was measured (the specific process is

abbreviated), and the prepared urine samples were put into a liquid flash counter for measurement. The concentration of tritium in the urine was determined by software provided with the instrument and the following formula (1):

$$C = \frac{N}{E \times V \times 60} \quad (1)$$

where C is the urine tritium concentration, Bq/mL; N is the net count rate of the urine sample, min^{-1} ; E is the counting efficiency of the instrument for the sample; and V is the urine sample volume, mL.

Dose Estimation and Dynamic Observation

According to GBT16148-2009 "Rational radionuclide intake and internal radiation dose estimation specifications,"⁶ the 95% confidence level during the effective dose monitoring period can be calculated using the following formula (2):

$$E = \frac{(C_i + C_{i+1})(t_{i+1} - t_i)}{2} \times 4.8 \times 10^{-11} \quad (2)$$

where E is the effective dose produced by 2 adjacent periods (usually 1 day), Sv; C_i is the urine tritium concentration measured by t_i day, Bq/L; C_{i+1} is the urine tritium concentration measured by t_{i+1} day, Bq/L; and 4.8×10^{-11} is the dose coefficient of tritium, Sv/(Bq/L), which is calculated from the total dose of 1.15×10^{-12} Sv \times standard reference of a person's water intake of 42 L/d/Bq.

Between 1% and 3% of tritium water (HTO) will be bound by the metabolite on carbon and become the organic-bound tritium (OBT). The half-life of this part of tritium is generally set to 40 days, and its contribution to the effective dose is approximately 10% during the entire cycle. If OBT is calculated, the dose coefficient in the above formula should be corrected by approximately 10%; then, formula (2) is corrected to formula (3) as follows:

$$E = \frac{(C_i + C_{i+1})(t_{i+1} - t_i)}{2} \times 5.3 \times 10^{-11} \quad (3)$$

The last effective dose in the monitoring period can be calculated by formula (4). In the absence of other evidence, the reference data of International Commission on Radiological Protection (ICRP) are selected for the biological half-life in this study, which is 10 days.

$$E = \frac{C_n}{\ln(2/10)} \times 5.3 \times 10^{-11} \quad (4)$$

Results

Clinical Manifestations

"Jia" did not appear to have obvious discomfort after the accident, but after admission into our hospital, he presented symptoms of mild fatigue; no obvious dizziness, headache, nausea, and vomiting; and mild sleep disturbance at night. Meanwhile,

Table 1. Renal Function and Electrolyte Results.^a

Date	Serum Creatinine ($\mu\text{mol/L}$)	Serum Potassium (mmol/L)	Serum Sodium (mmol/L)
February 26	72	4.68	141.5
February 27	68	4.34	140.2
February 28	74	4.28	138.2
March 1	74	4.15	135.6
March 2	70	3.92	135.8
March 3	72	4.09	138.4
March 4	75	4.21	137.9

^aThe normal range of serum creatinine in the clinical department of our hospital is 45 to 84 mmol/L, the normal range of serum potassium is 3.50 to 5.50 mmol/L, and the normal range of serum sodium is 135.0 to 145.0 mmol/L.

Table 2. Chromosomal Aberration Results.

Cell Numbers	Centric				Aberration Rate (%)
	Fragment	Dicentric	Ring	Translocation	
200	2	0	0	0	1

due to a large amount of water consumption, which was approximately 5 to 10 L/24 hours, the urine volume per 24 hours was approximately 10 to 13 L, with an average of 12.2 L. The results of the 16PF questionnaire administered to "Jia" showed that his performance was basically normal without obvious neuropsychiatric symptoms.

Laboratory and Instrument Inspection

T-cell subgroup analysis showed that the proportion of natural killer cells was 12.7%, which was slightly lower than the normal lower limit (13.0%). Biochemical examination showed that the blood glucose was high, and considering the past history of "Jia," it was possible to consider a diagnosis of diabetes. Abdominal B-mode ultrasound showed enhanced echogenicity in the liver area, and because of this result combined with the blood lipid examination, he was considered to have a mild fatty liver. No obvious abnormalities were observed in the remaining examinations.

During hospitalization, serum creatinine, serum potassium, and serum sodium were monitored, and the results fluctuated within the normal range. The data are presented in Table 1.

Chromosomal Aberration Analysis

Results are presented in Table 2. The biological dose could not be estimated because the results were within the normal range.

Results of Urine Tritium Concentration

In addition to the first urine tritium concentration data measured at the nuclear power plant on the day of the accident, the remaining data were measured during hospitalization and after discharge by looking at concentrations of tritium in the urine.

Table 3. Results of Tritium Concentration Levels on Specified Dates.

Date	Tritium Concentration (Bq/mL)	Date	Tritium Concentration (Bq/mL)
February 25	6.61E+04	March 8	2.33E+03
February 26	5.85E+04	March 9	2.10E+03
February 27	4.97E+04	March 10	1.53E+03
February 28	3.68E+04	March 11	1.23E+03
March 1	2.59E+04	March 12	1.04E+03
March 2	1.85E+04	March 13	9.82E+02
March 3	1.20E+04	March 14	8.43E+02
March 4	8.43E+03	March 17	5.97E+02
March 5	5.96E+03	March 21	2.57E+02
March 6	4.04E+03	March 24	2.28E+02
March 7	3.10E+03	March 28	1.48E+02

Table 4. Effective Dose on Specified Dates.

Date	Effective Dose on Specified Date (mSv)	Date	Effective Dose on Specified Date (mSv)
February 26	3.606	March 9	13.737
February 27	6.738	March 10	13.843
February 28	8.869	March 11	13.924
March 1	10.397	March 12	13.992
March 2	11.464	March 13	14.050
March 3	12.180	March 14	14.103
March 4	12.681	March 17	14.228
March 5	13.033	March 21	14.327
March 6	13.275	March 24	14.369
March 7	13.458	March 28	14.413
March 8	13.609	Last dose	0.123

On the first day of hospitalization (February 26), the urine concentration was 5.85×10^4 Bq/mL; it was 3.10×10^3 Bq/mL when discharged (March 7) and 1.48×10^2 Bq/mL during the last day of monitoring (March 28). The data are presented in Table 3; only values measured for the first urine sample per day are listed.

Dose Estimation

Based on the daily urine tritium concentration data, the effective dose produced by the daily dose can be estimated using formulas (3) and (4). The effective dose on the last monitoring day on March 28 was 14.413 mSv, and the last dose is estimated to be 0.123 mSv. Therefore, the final effective dose was 14.536 mSv. Daily specific data are provided in Table 4.

Discussion

Because of the low β energy of tritium, the maximum range in soft tissue is only 5 μ m, which is less than the thickness of the stratum corneum of the skin. Therefore, the external radiation damage by tritium is minor, and acute damage to the human body is mainly caused by internal radiation. Previous studies

have shown that the symptoms of low-dose tritium exposure are more likely to occur in the early stages and are often relieved without special treatment. The main symptoms are dizziness, fatigue, loss of appetite, and sleep disorders.⁷ The clinical manifestation in “Jia” was consistent with the literature, but the symptoms were relatively mild, which may be related to the dose and individual differences. In addition, these symptoms may also be related to the psychological effects on patients. A prolonged period of tritium exposure in vivo can cause a cumulative radiation effect due to the release of β rays, resulting in mutations and DNA damage to cells and possibly leading to malignant tumors. Although case reports of the carcinogenicity of tritium among humans have not been reported, a large number of animal studies have shown that the dose of tritium is positively correlated with the incidence of leukemia.⁴ “Jia” was in the normal range of tumor targets, and it remains to be seen whether cancer will occur in the future. In normal individuals, the urine volume is approximately 1 to 2 L/24 hours, with an average of approximately 1.5 L. “Jia” consumed a lot of water, and after diuretic treatment, the urine volume per 24 hours was above 10 L, with an average of 12.2 L. This output is more than 8 times that for normal individuals, which had an obvious effect of diuresis and was conducive to rapid discharge of tritium in vivo. However, it is also important to note that excessive urination can lead to the loss of fluids and electrolytes, which can cause dehydration and electrolyte disturbances and even acute renal insufficiency. If the urine volume is increased, note that 10% of potassium chloride (20 mL/d) should be given intravenously to prevent hypokalemia. Therefore, attention should be paid to maintaining the balance of water and electrolytes, especially for renal function. In this study, the renal function and electrolytes of “Jia” were monitored during hospitalization, and their concentrations fluctuated within the normal range, possibly due to the intravenous supplementation of electrolytes. In recent years, Zuo X et al⁸ carried out research on the toxicology of HTO and developed a traditional Chinese medicine compound named “Chahuangjing.” This composition, which requires further promotion and application, not only is diuretic and promotes the elimination of HTO but also removes free radicals in vivo to protect against HTO injury.

Tritium in the urine is mainly composed of HTO and OBT. For reference, 97% of tritium is HTO, which is balanced with body water and is excreted in vitro with a biological half-life of 10 days; the remaining 3% of tritium are combined with organic molecules to form OBT and is excreted in vitro with a biological half-life of 40 days. The concentration of tritium measured by distillation refers only to the concentration of HTO, and OBT is often difficult to measure alone.⁹⁻¹¹ Lanxin¹² analyzed samples of 72 people exposed to tritium and concluded that the OBT concentration was the average of the HTO concentrations ($5.4\% \pm 3.7\%$). In this study, factors of OBT were taken into account in dose estimation, the corresponding coefficients were modified appropriately, and the results were more objective. However, it was recommended by ICRP reference data for this location that the results could be due to the

different environmental temperatures, the intensity of labor, age, and volatility, especially for patients who received medical treatment. Yong et al¹³ studied a case of tritium contamination in a patient who received medical treatment. Through analysis of a large amount of urine tritium concentration results, the metabolic data of the individual were obtained, and the effective dose was estimated. The result was more accurate than the reference data, but the estimation process was more complex and still needs to be refined further and applied.

In conclusion, the medical treatment of tritium contamination should be carried out as soon as possible. The final effective tritium dose of the present patient was 14.536 mSv, which exceeded the company's maximum personal effective dose value (12 mSv) but was lower than the company's management target value (15 mSv) and the national limit value (50 mSv). The early effects in the patient were consistent with the clinical manifestations of internal contamination of low-dose radionuclides, and the later effects remain to be observed after further follow-up. We plan to continue to monitor the results of routine blood tests, urine tritium levels, and chromosomal aberration analyses of the patient. The patient had a good prognosis after effective medical treatment, which provides experience for the management of similar cases. However, the level of occupational and environmental exposure during future fusion reactor operations is still unpredictable, but it is certain that the health problems and ecological impacts caused by tritium will remain a focus of concern. Therefore, it is still necessary to carry out in-depth studies on the mechanism of the toxic effects and ecological toxicology of tritium and to accumulate case data on human contamination with tritium to obtain an objective evaluation of the radiation toxicity of tritium.

Authors' Note

Weibo Chen and Houwen Li contributed equally to this work. Yulong Liu and Houwen Li conceived and designed the experiment. Fengmei Cui, Kongzhao Wang, and Qiu Chen performed the experiments. Huahui Bian and Youyou Wang analyzed the data. Weibo Chen and Houwen Li wrote the article.


Declaration of Conflicting Interests


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