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Evaluation of the therapeutic effect of deuterium-depleted water on 131I- induced radiation gastroenteritis in patients with thyroid cancer

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Abstract: Objective To investigate the efficacy of oral deuterium-depleted water on 131I -treated thyroid cancer-induced radiation gastroenteritis. Methods A total of 50 patients with papillary thyroid carcinoma (hereinafter referred to as thyroid cancer) who were treated with 131I in the Department of Nuclear Medicine of Changshu Second People's Hospital from May 2022 to February 2023 were collected and divided into a control group and an experimental group, with 25 cases in each group. The control group was given oral omeprazole enteric-coated capsules and 660 mL of purified water tid for 5 consecutive days; the experimental group was given oral deuterium-depleted water 660 mL tid for 5 consecutive days on the basis of the same medication as the control group. Fisher's exact test and Kaplan-Meier analysis were used to observe and compare the incidence of radiation gastroenteritis after taking 131I and the relief of gastrointestinal clinical symptoms between the two groups of patients. Results From the first to the fifth day after taking 131I , the number of patients with gastrointestinal inflammation in the experimental group was 2 (8%), 5 (20%), 2 (8%), 1 (4%), and 0 (0%), respectively; and the number of patients in the control group was 2 (8%), 8 (32%), 4 (16%), 3 (12%), and 1 (4%). The difference in the incidence of gastroenteritis between the two groups was statistically significant (ÿ2 =4.064, P=0.044). After 5 days of treatment, the total effective rate of the experimental group was 96%, which was higher than 76% in the control group, and the difference between the two groups was statistically significant (ÿ2 =9.105, P=0.025). Conclusion Oral deuterium-depleted water has a certain effect on the relief of clinical symptoms of 131I-induced radiation gastroenteritis in thyroid cancer. It is recommended to further explore its application in clinical practice. Keywords: deuterium-depleted water; thyroid cancer; radiation gastroenteritis; efficacy evaluation; 131I

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Evaluation of the therapeutic effect of deuterium depleted water on gastroenteritis induced by 131I radiation in thyroid cancer treatment

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Abstract: *Objective To investigate the therapeutic effect of oral administration of deuterium depleted water on gast-roenteritis induced by 131I radiation in thyroid cancer treatment.*

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Methods: *Fifty patients with papillary thyroid cancer treated with 131I in the Departmentof Nuclear Medicine of Changshu No.2 People's Hospital from May 2022 to February 2023 were divided into control group and experimental group (25 patients in each group). Data were continuously collected throughout the study duration. The control group was orally administered omeprazole enteric-coated capsules and purified water at 660 mL tid for 5days. The experimental group received the same basic treatment as the control group except that deuterium depleted water was used instead of purified water. The incidence and alleviation of 131I radiation-induced gastroen-teritis were observed and compared between the two groups using the Fisher's exact test and Kaplan-Meier analysis.*

Results: *The number of gastroenteritis cases from day 1 to day 5 after 131I administration was 2 (8%), 5(20%), 2(8%), 1(4%), and 0 (0%), respectively, in the experimental group, and 2(8%), 8 (32%), 4(16%), 3(12%), and 1(4%), respectively, in the control group. The incidence of gastroenteritis was significantly different between the two groups (ÿ 2=4.064, P=0.044).*

After 5days of treatment, the overall response rate of patients in the experimental group was 96%, which was significantly higher than 76% in the control group (ÿ2=9.105, P=0.025).

Conclusion: *Oral administration of deuterium depleted water is effective in the relief of clinical symptoms of 131I radiation-induced gastroenteritis in thyroid cancer treatment. The clinical application of deuterium depleted water should be further investigated.*

Keywords: *Deuterium depleted water; Thyroid cancer; Radiation-induced gastroenteritis; Evaluation of therapeutic effect; 131I*

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Thyroid cancer is a common malignant tumor in clinical practice, among which differentiated thyroid cancer is the most common histopathological type. 131I is one of its important treatment methods [1-2]. However, patients treated with 131I have a large oral radiation dose [3], a large amount of 131I remains in the gastrointestinal tract for a long time [4], and significant gastrointestinal adverse reactions in a short period of time [5], which directly affects the treatment compliance and efficacy of some patients. In clinical practice, 40% to 80% of patients experience varying degrees of gastrointestinal discomfort within 1 to 5 days after 131I treatment. The clinical diagnosis was radiation gastroenteritis. The clinical diagnosis was radiation gastroenteritis. The symptoms of gastrointestinal discomfort can cause anxiety and accelerate the metabolism of residual radiation in the body, so the prevention and protection of gastrointestinal damage is particularly important. Studies have reported that deuterium-depleted water (DDW) can protect mice from radiation exposure to X-rays and x-rays, significantly increasing their survival rate after irradiation [6-7]. In recent years , many literatures have also reported that deuterium-depleted water has biological effects such as activating immune cells, improving the body's basal metabolism, inhibiting cell mutations, and endogenous synthesis of lipids. The aim of this study is to explore the effect of oral deuterium-depleted water on the treatment of thyroid disease as follows.

The clinical efficacy and prognostic impact of adenocarcinoma-induced radiation gastroenteritis are reported as follows.

1 Materials and methods

1.1 General information Continuously collected from May 2022 to 2023

In February, the nuclear medicine department of Changshu Second People's Hospital used 131I to treat 50 patients with thyroid cancer were divided into a control group and an experimental group, with 25 cases in each group. The experimental group had 12 males and 13 females, aged 20 to 60 years old, with an average age of (40.84±10.70) years old. 13 cases; aged 21 to 62 years old, average age (40.56±12.43).

None of the patients had received systemic chemoradiotherapy one month before receiving 131I treatment. Inclusion criteria: Patients aged 20 to 65 years, with complete clinical data and pathologically confirmed as papillary thyroid cancer. Patients with thyroid cancer treated with oral 150 to 200 mCi 131I . Patients who cooperated with follow-up and had normal speech and communication. Exclusion criteria: Patients who underwent other major surgeries within six months. Patients with severe heart, liver, kidney and other diseases.

This study was approved by the hospital ethics committee (ethics review number: 2021-KY-04), and all subjects participated voluntarily and signed informed consent.

Consent letter.

1.2 Methods

1.2.1 Treatment methods 131I treatment dosage and usage for thyroid cancer:

After the patients in both groups were enrolled, they were treated with 150-200 mCi 131I orally after the condition was evaluated. Deuterium-depleted water intervention method: The patients in the control group were given oral omeprazole enteric-coated capsules (20 mg 14 capsules/bottle, Hainan Haitian) 20 mg bid combined with purified water (Jiangsu Aotequan Super Light Water Beverage Co., Ltd., Food Production License No. SC10632058101493,

The patients in the experimental group took omeprazole enteric-coated capsules 20 mg bid and deuterium-depleted water (Jiangsu Aotequan Ultralight Water Beverage Co., Ltd.,

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food production license number SC10632058101493, 50 PPM, 330 mL/bottle) 2 bottles tid for 5 consecutive days. All patients were prohibited from iodine diet.

1.2.2 Evaluation of therapeutic efficacy Cured:

Within 5 days, the patient's symptoms (nausea, vomiting, abdominal distension, abdominal pain) completely disappear, and the patient can eat normally and recover to the amount of food before treatment; Significantly effective: Within 5 days, the patient's self-perception of symptoms is significantly relieved, but the patient's appetite has not yet recovered to the level before treatment; Effective: Within 5 days, the symptoms are slightly relieved. Lowered, but still uncomfortable, can eat small meals more often, and still need drug intervention;

None Effectiveness: Within 5 days, the patient's abdominal discomfort symptoms are not relieved, and he still has no appetite, abdominal distension, nausea and other discomfort symptoms. The total effective rate = (cured cases + markedly effective cases + effective cases).

1.3 Statistical methods SPSS 19.0 software package was used for data processing. Clinical count data were expressed as (n%). The differences between the groups were compared using Fisher's exact test. Kaplan-Meier analysis was performed on the occurrence of gastrointestinal inflammation (with the occurrence of gastrointestinal inflammation as the outcome event). Log-rank test was used to compare ***the differences in the time distribution of gastrointestinal inflammation between the two groups. P < 0.***05 indicated that the difference was statistically significant.

2 Results

Based on clinical experience, patients are treated with oral administration of 150-200 mCi 131I. After 5 days, the symptoms of gastrointestinal reactions were significantly relieved. Therefore, this article uses 5days as a treatment evaluation period.

The results showed that from the first to the fifth day after taking 131I , the patients in the experimental group The number of cases of gastrointestinal inflammation was 2 (8%), 5 (20%), 2 (8%), 1 (4%), 0 (0%), and the control group was 2 (8%), 8 (32%), 4 (16%), Kaplan-Meier analysis was performed on the occurrence of gastrointestinal inflammation in groups 3 (12%), 1 (4%), and 2. The Kaplan-Meier curve in Figure 1shows that the incidence of gastrointestinal discomfort on the first day in the experimental group was 8%, 28% on the second day, 36% on the third day, and 40% on the fourth day; the incidence of gastrointestinal discomfort on the first day in the control group was 28% on the second day, 36% on the third day, and 40% on the fourth day. The incidence of discomfort was 8% on the first day, 40% on the second day, and 56% on the third day. The rate was 68% on the 4th day and 72% on the 5th day. The difference in the incidence of gastrointestinal discomfort between the two groups was statistically significant (ÿ2 =4.064, P=0.044). The data are shown in Table 1 and Figure 1.

After 5 days of treatment, according to the above 1.2.2 efficacy judgment: the total effective rate of the experimental group was 96.00%, which was higher than 76.00% of the control group, and the difference was statistically significant (using Fisher's exact test, ÿ 2 =9.105, P=0.025). The data are shown in Table 2.

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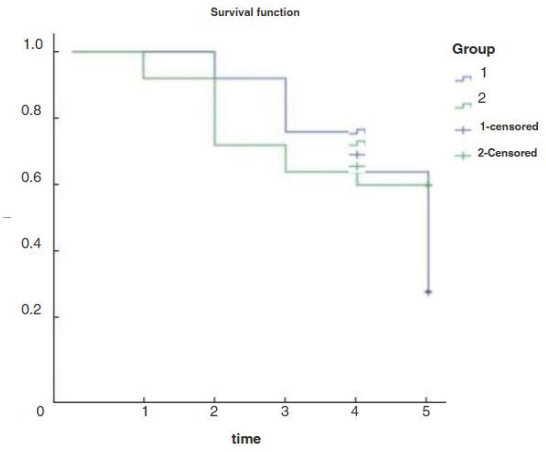
3 Discussion

Radiotherapy reports have shown that the gastrointestinal mucosa belongs to the radiosensitive group



Note: Group 1 is the control group; Group 2 is the experimental group.

Fig.1 KM survival curve analysis of the incidence of gastrointestinal inflammation in the two groups

Table 1 Comparison of the incidence of gastrointestinal inflammation in the two groups of patients after taking 131I (n%)

Number of cases in each group (n)	Time of onset of gastrointestinal inflammation after taking 131I					Overall incidence
	1d	2d	3D	4d	5d	
Experimental Group 25	2 (8)	5 (20)	2 (8)	1 (4)	0 (0)	10 (40)
Control group 25	2 (8)	8 (32)	4 (16)	3 (12)	1 (4)	18 (72)
$\ddot{y}^2$						4.064
P-value						0.044

Table 2 Comparison of total effective rate between the two groups (n%)

Number of cases in each group (n)	Treatment Outcomes				Total Effectiveness
	Cured, effective, ineffective				
Experimental Group 25	17 (68)	5 (20)	2 (8)	1 (0)	24 (96)
Control group 25	7 (28)	7 (28)	5 (20)	6 (24)	19 (76)
$\ddot{y}^2$					9.105
P-value					0.025

The radiation tolerance dose of tissue is 45 Gy, and the radiation dose exceeding 55 Gy Radiation gastroenteritis may occur, with clinical manifestations of abdominal pain, abdominal Distension, poor appetite, nausea, vomiting, and in severe cases, gastrointestinal bleeding [10]. As athyroid gland receiving oral high-dose open radiation preparation 131I In patients with adenocarcinoma, the 131I remaining in the esophagus, gastrointestinal tract and other organs will inevitably Causes a certain dose of direct radiation to surrounding tissues [11], resulting in radiation-induced at present, oral 131I is used clinically to treat gastrointestinal inflammation of thyroid cancer. The treatment methods for patients with gastrointestinal inflammation are mainly acid suppression and mucosal protection, but these treatments cannot reduce moderate to severe radiation exposure quickly and promptly. The digestive tract discomfort symptoms of patients with gastroenteritis are to a certain extent in the short term. This affects the patient's treatment mood and clinical efficacy.

Oral administration of deuterium-depleted water can change the D/H ratio in the gastrointestinal tract and quickly Dilute gastrointestinal contents, which is beneficial to the digestion and absorption of food by the gastrointestinal tract It activates the activity of digestive enzymes in the body and promotes the digestive function of the gastrointestinal tract. Animal studies have also shown that low Deuterium water promotes the healing of ulcer wounds in diabetic rats [13].

It can stimulate the proliferation of peripheral blood cells, activate cellular immunity, and enhance mouse immune it can reduce the sensitivity of mice to lethal doses of whole-body irradiation with gamma rays [6]. Immunity Défense [14-15], suggesting that deuterium-depleted water has an anti-radiation damage effect.

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Support the results and viewpoints of the above literature. The results of this paper show that:

From the first day to the fifth day after 131I, the incidence of gastrointestinal inflammation in the two groups was the difference in body weight was statistically significant (ÿ2 = 4.064, P = 0.044). The difference was statistically significant (ÿ2 **=** 9.105, ***P*** = 0.025). After 5 days of treatment, the total effective rate of the experimental group was higher than that of the control group. The difference was statistically significant (γ2 **=** 9.105, ***P*** = 0.025). The mechanism of deuterium water relieving clinical symptoms: The author believes that it may be related to deuterium-deficient water. It helps to activate the activity of digestive enzymes in the body and promote the digestive function of the gastrointestinal tract. can reduce the digestive pressure of the gastrointestinal tract; at the same time, it can also Radiation damage immediately activates the patient's humoral and cellular immune functions in particular; it can inhibit the secretion of pro-inflammatory cytokines and effectively reduce the progression of inflammation and early relief of clinical symptoms. The hospitalization period of patients with radiation gastroenteritis after intervention with deuterium-depleted water the symptom relief and recovery degree of the patients in the control group were significantly better than those in the control group.

In summary, the deuterium-depleted water studied in this paper is not a drug, but a new approach has been shown in the intervention of gastrointestinal inflammation caused by 131I therapy in prostate cancer as for the exact mechanism of efficacy response and its related benefits. The benefits and disadvantages of this study need to be further studied after the sample size is increased in clinical practice. In-depth discussion, in order to apply it more scientifically and widely in clinical practice.

Conflict of interest This research was conducted independently by the named authors according to the following contribution statement.

The article does not involve any conflict of interest.

Author contribution statement Zhu Jing was responsible for designing the research ideas and implementing the research plan.

Zhang Xiaoyi was responsible for reviewing the paper; Shen Chao was responsible for patient information

Xu Zhihong was responsible for participating in the design of the project framework; Chen Wei was responsible for literature sorting and statistical analysis

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References

[1] Wang Yan, Zheng Rong, Fan Rong, et al. Prognosis and influencing factors of bone metastasis of differentiated thyroid cancer

[J]. Chinese Journal of Radiation Health, 2023, 32 (1): 46-51, 61. DOI: 10.13491/j.

issn.1004-714X.2023.01.010.

Wang Y, Zheng R, Fan R, et al. Outcomes and prognostic factors of differentiated thyroid cancer with bone metastasis[J]. Chin J Radiol Health, 2023, 32(1): 46-51,61. DOI: 10.13491/j.issn. 1004-714X.2023.01.010.

[2] Zampella E, Klain M, Pace L, et al. PET/CT in the management of differentiated thyroid cancer[J]. Diagn Interv Imaging, 2021, 102(9): 515-523. DOI: 10.1016/j.diii.2021.04.004. Chen Chunhui, Jia Ru, Chen Biao.

[3] Hospitalization management and radiation protection status of 131I thyroid cancer patients Survey[J]. Chinese Journal of Radiation Health, 2022, 31(1): 64-69. DOI: 10.13491/j. issn.1004-714X.2022.01.012. Chen CH, Jia R, Chen B. An investigation of hospitalization management and radiation protection in 131I treatment for thyroid cancer[J]. Chin J Radiol Health, 2022, 31(1): 64-69. DOI: 10. 13491/ j.issn.1004-714X.2022.01.012.

[4] Zhang F. Study on the effective half-life of postoperative 131I therapy in patients with differentiated thyroid cancer and its influencing factors[D]. Dalian: Dalian Medical University, 2022.

[5] Mirzababaee M, Shafiei B, Seifollahi S, et al. Management of gastrointestinal complaints in differentiated thyroid cancer patients treated with 131I: comparison of the efficacy of pantoprazole, metoclopramide, and ondansetron - a randomized clinical trial[J]. Nuklearmedizin, 2014, 53(5): 186-189. DOI: 10.3413/Nukmed- 0654-14-03.

[6] Laissue JA, Altermatt HJ, Bally E, et al. Protection of mice from whole body gamma irradiation by deuteration of drinking water: hematologic findings[J]. Exp Hematol, 1987, 15(2): 177-180.

[7] Corneanu GC, Corneanu M, Crÿciun C, et al. The radioprotective effect of deuterium depleted water and polyphenols[J]. Environ Eng Manag J, 2010, 9(11): 1509-1514. DOI: 10.30638/eemj.2010.204.

[8] Bayrak BB, Kulak GY, Yanardag R, et al. Short term deuterium depletion in drinking water reduced tumor induced oxidative stress in mice liver[J]. Pathol Res Pract, 2022, 240: 154186. DOI: 10. 1016/ j.prp.2022.154186.

[9] Simonato M, Ricci F, Catozzi C, et al. Deuterium-depleted water: A new tracer to label pulmonary surfactant lipids in adult rabbits[J]. Mass Spectrom, 2022, 57(2): e4808. DOI: 10.1002/jms.4808.

[10] Dai Juan, Zhuang Yun, Ding Yanbo, et al. Endoscopic combined with drug treatment of radiation gastritis complications a case of hemorrhage[J]. Chinese Journal of Digestive Endoscopy, 2019, 36(3): 212-214. DOI: 10.3760/cma.j.issn.1007-5232.2019.03.014. Dai J, Zhuang Y, Ding YB, et al. Endoscopy combined with medication in the treatment of radiation gastritis complicated with refractory bleeding: acase report[J]. Chin JDig Endosc, 2019, 36(3): 212-214. DOI: 10.3760/cma.j.issn.1007-5232.2019.03.014.

[11] Shu Jinxia. Radiation protection methods for patients with thyroid cancer undergoing 131I treatment after surgery[J]. Radiology, 2017, 26(3): 299-301. DOI:10.13491/j.cnki.issn.1004-714X.2017.03.015. Shu JX. Thyroid cancer patients with postoperative method of radiation protection[J]. Chin JRadiol Health, 2017, 26(3): 299-301. DOI: 10.13491/j.cnki.issn.1004-714X.2017.03.015.

[12] Luo Anling, Zheng Youli, Cong Fengsong. Research progress on biological effects of

Funding project: National Key Laboratory of Radiation Medicine and Radiation Protection (GZK1202109) Author profile: Zhu Jing (1981-), female, from Changshu, Jiangsu, associate chief physician, engaged in clinical diagnosis and treatment of nuclear medicine and related basic research. E-mail: 5311355@qq.com Corresponding author: Zhang Xiaoyi, E-mail: 16370743@qq.com

deuterium-depleted water[J]. Journal of Shanghai Jiaotong University (Medical Edition), 2018, 38(4): 467-471. DOI: 10.3969/j.issn.1674-8115.2018.04.022. Luo AL, Zheng YL, Cong FS. Research progress of biological effects of deuterium-depleted water[J]. JShanghai Jiao Tong Univ (Med Sci), 2018, 38(4): 467-471. DOI: 10.3969/j.issn.1674-8115.2018.04.022.

[13] Wang Xiangqi, Zhao Chaoran, Xiong Aibing. Effect of deuterium-depleted water combined with platelet-rich plasma on diabetes mellitus in rats the influence of disease on ulcer wound healing[J].Journal of Shanghai Jiaotong University (Medical Edition), 2020, 40(3):326-332. DOI: 10.3969/j.issn.1674-8115.2020.03.008. Wang XQ, Zhao CR, Xiong AB. Effect of deuterium depleted water combined with platelet-rich plasma on wound healing of diabetic ulcer in rats[J]. JShanghai Jiao Tong Univ (Med Sci), 2020, 40(3): 326-332. DOI: 10.3969/j.issn.1674-8115.2020.03.008.

[14] Bild W, Stefanescu I, Haulica I, et al. Research concerning the radioprotective and immunostimulating effects of deuterium-depleted water[J]. Rom J Physiol, 1999, 36 (3/4): 205-218.

[15] Grigorenko DY. Peculiarities of the cellular composition of splenic lymphoid tissue in mice after long-term use of light water and irradiation[J]. Morfologiia, 2015, 148(4): 19-23.

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