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APPLICATION OF HEALTH EDUCATION BASED MEDICAL SOCIAL MEDIA IN INITIAL THERAPY OF RADIOACTIVE IODINE FOR PATIENTS WITH GRAVES'S DISEASE, A RANDOMIZED CONTROLLED TRIAL

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ABSTRACT

Background: Although radioactive iodine (RAI) has been used to treat Graves' disease (GD) for more than 70 years, patients have little knowledge of thyroid diseases and are concerned about radiation, leading to poor clinical compliance and resistance to RAI therapy in most patients. **Objective:** The purpose of this study was to evaluate the value of health education mode based medical social media in the first RAI treatment of GD, and to enhance patients' clinical compliance, improve patients' awareness of related thyroid disease knowledge. **Patients:** One hundred and twenty-six GD patients were treated with RAI for the first time. **Methods:** Patients were randomized into one of two groups: (1) experimental: medical social media was performed for health education, including We-chat, QQ and Weibo. Each GD patient is required to join the We-chat group established by our research institution; (2) comparison: Traditional health education was implemented, and patients did not join We-chat group. Our outcomes are clinical compliance score (CCS) and thyroid diseases awareness score(TDAS) in 6 months. **Results:** Of the 121 GD patients, 111 (91.7%) were effective with RAI, and 10 were ineffective or recurrent. The efficacy of RAI in GD was similar in the experimental group and the comparison group (91.7% vs 91.8%, P=0.978). The CCS and TDAS were higher than the baseline level in the two study groups (P <0.05). High school and higher

(HSAH) patients in the experimental group had higher CCS than those in the comparison group (*P*=0.013).There was no significant difference in CCS between middle school and lower (MSAL) patients in the two study groups (*P*>0.05). The TDAS of both experimental group and comparison group were higher than the baseline level (*P<0*.05). After 6 months, the TDAS of experimental group was significantly improved by 92.9%, while the comparison group was slightly improved by 52.7% (*P* <0.05). The awareness of radiation safety was increased from 2 to 52 in the experimental group, but only 7 in comparison group. The TDAS of HSAH and MSAL patients in the experimental group were significantly higher than those in the comparison group after 6 months (*P*<0.01). **Conclusions:** The health education mode based medical social media can enhance the clinical compliance of GD and improve the patients' understanding of thyroid disease and radiation safety of RAI. This method of health education can be popularized and applied in clinics.

KEYWORDS: Graves' disease; radioactive iodine; health education, medical social media; patient compliance.

INTRODUCTION

Graves' disease (GD) was first recognized as a syndrome in the 19th century, including enlarged and overactive thyroid gland, accelerated heart rate, and eye abnormalities.[1] The clinical manifestations of GD depend on the patient's age, severity and duration. Currently, the therapies for GD include anti-thyroid drug (ATD), surgery, and radioactive iodine(RAI).[2] Without complication, ATD is still the first line of treatment in Europe. In North America, more and more people tend to use ATD rather than RAI.[1] Patients with hypothyroidism due to ablative therapy of RAI or thyroidectomy may require lifelong replacement of thyroid hormones. After adequate counseling, patients' preferences remain a key factor in treatment decisions.

The treatment of hyperthyroidism with RAI has a history of more than 70 years,[1] which has been widely accepted by patients and clinicians due to its advantages of high cure rate, small side effects, low cost and quick effect. However, because of most people do not understand the physical properties of RAI, they are terrified of its radiation and keep it away. Therefore, few hyperthyroidism patients in China are willing to use RAI as a first-line therapy, despite its many advantages. The main reason for this situation is that medical workers do not enough educate to patients, so that patients do not understand the advantages of RAI in

hyperthyroidism, and even have some prejudice against ARI. In fact, the success rate of RAI in hyperthyroidism is high and the remission rate was more than 90% after the first treatment,[3] The final outcome of RAI in hyperthyroidism is mostly hypothyroidism. If hypothyroidism is not controlled as soon as possible, it will affect patients' quality of life. The patient's clinical compliance is of great significance in improving the patient's quality of life.[4,5]

It is widely accepted that patients are active partners in health care and not merely passive subjects for diagnostic tests and medical treatment. Providing information to patients is considered a key issue and a central focus in patient education activities. There is a strong need to educate patients about the nature of treatment outcomes, the benefits and risks of treatment, involve them in the decision-making process and give them fully informed consent. Information materials must contain scientifically reliable information and be presented in a form that is acceptable and useful to patients.[6,7]

Traditional health education, that is, face-to-face conversation between doctors and patients, doctors tell patients what they know and what patients need to learn as much as possible. It has to face the potential barriers of storage, access problems and the need to keep content materials up to date. As the health education model is limited by time and place, and relatively fixed and rigid, the effect is not satisfactory.

With the rapid development of the Internet era and the rise of medical social we-media, a new way of health education has emerged, which is convenient for doctors and patients. On social we-media platforms, such as Weibo, We-chat, Subscription account, We-chat service number, Toutiao and Zhihu in China, doctors can submit popular science content about related diseases in the form of video, audio or cartoons. Readers who browse these platforms can read relevant content, which has the advantages of widespread, fast speed and high efficiency. Zachary et al.[8] Studied that patient education interventions based on social media can be able to promote breast cancer survivors to increase physical activity and improve their health indexes. However, most patients do not actively learn about thyroid disease unless they had a history of thyroid disease themselves. In addition, differences in education level can affect patients' understanding of relevant content. At present, due to the lack of research on the application of health education mode based medical social media in initial therapy of radioactive iodine for patients with Graves's disease.

Therefore, the purpose of this study was to evaluate the application value of health education mode based medical social media in the first RAI treatment of GD, and to enhance patients' clinical compliance, improve patients' awareness of related thyroid disease knowledge, and better manage their own health.

PATIENTS AND METHODS

Study Design and Subjects

The CONSORT guidelines for reporting of randomized trials were refereed while drafting this manuscript.[9] This study included all eligible GD patients receiving the first RAI therapy in our hospital from October 2019 to March 2020. Patients were followed up for at least half a year until September 2020.

All patients met the following inclusion criteria: patients were 18 or older years of age; patients were diagnosed with GD for no more than 4 weeks; first RAI and had not received surgical treatment; patients with ATD and course not exceeding 4 weeks and withdrawn ATD; patients were able to correctly use smart phones. The following were the main exclusion criteria: pregnant and breast-feeding women; patients who have undergone surgical treatment or ATD therapy for over 4 weeks; patients cannot correctly use smart phones.

The medical ethics board of First people hospital of huaihua approved the study, and all patients provided their written informed consent after full discussion of the inclusion-exclusion criteria, study protocol, and potential risks. A total of 126 eligible patients were randomly assigned to the experimental or comparison groups.

Procedure of Gd therapy

Determination of thyroid mass(TM),[3] Thyroid three-dimensional ultrasound examination was performed to measure thyroid mass. Volume of each thyroid lobe was determined by the Ellipsoid formula: Volume (ml) = Length (cm) × Width (cm) × Thickness (cm) ×π/6.[10] Total volume was obtained as the sum of two thyroid lobes. The thyroid mass is converted from specific gravity 1.0 to volume.

Radioactive iodine treatment activity (RAITA)

Individualized therapy,[3] The RAITA of each GD patient was calculated base on TM and radioactive iodine uptake (RAIU). The normal range of planned activity (PA) per gram of

thyroid tissue is 2.59 to 4.44 M Bq. The calculation formula is as follows: RIATA (M Bq)=[PA(M Bq/g) ×TM(g)]/[$RAIU_{max}$ or $RAIU_{24h}$ (%)].

Radioactive iodine treatment activity will be adjusted according to different factors. It needs to be added to the list of factors: (1) large and hard thyroid; (2) older age or long duration; (3) short effective half-life; (4) patients with severe complications such as hyperthyroidism heart disease and hyperthyroidism myopathy.

It needs to be reduced to the list of factors: (1) Young age or short course of disease or small thyroid volume; (2) no treatment; (3) longer effective half-life.

All patients were treated with disposable therapy. In order to ensure that RAI can be fully absorbed by the thyroid gland, patients need an empty stomach and should drink an appropriate amount of water after taking RAI.

Grouping and Intervention

Patients were randomly assigned to experimental and comparison groups by drawing lots according to the differences in health education methods. All GD patients should be informed in writing of post-treatment precautions before RAI treatment.

Health education mode based medical social media was performed in the experimental group, including We-chat, QQ and Weibo. Firstly, each GD patient is required to join the We-chat group established by our research institution. The administrator holds weekly seminars on thyroid disease in the We-chat group. For example, the importance of clinical compliance to patients. How to improve patients' clinical compliance. How to deal with the adverse reaction after taking radioactive iodine. What are the symptoms of early hypothyroidism. When is the best time to go to doctor. Secondly, doctors pay attention to patients through We-chat group continuous and dynamic, improving the continuity of medical intervention. For example, the doctors understand whether patients follow the doctor's advice after treatment, whether there is a regular diet or quit smoking. Third, we post some health knowledge and the latest research progress of thyroid to the We-chat group every week. Patients can independently understand and learn relevant knowledge. And doctors guide patients and patients to communicate with each other, promote them to actively participate in the discussion and enhance peer education. Administrators can properly evaluate and encourage the discussions between patients and supplement appropriate knowledge content, so as to achieve the purpose

of interactive health education. Fourth, doctors obtain the psychological status of patients through conversation, dredge the bad psychology of patients, strengthen them to correctly understand GD and actively face their own diseases, and enhance their confidence in treatment.

In order to facilitate new patients who can be able to obtain information, the relevant content will be sent repeatedly.

Traditional health education was implemented in the comparison group, that is, only spread the relevant medical knowledge to the GD patients before RAI treatment, and did not join We-chat group.

Clinical outcome measures and GD assessment

Baseline assessment included clinical history, duration of GD and complications, weight of thyroid, RAITA, education. The course of GD begins with the patient's first description of symptoms or signs of hyperthyroidism. All GD patients were fully evaluated 6 months after first RAI treatment.

Outcomes of therapeutic effects

The reference criteria for evaluating the efficacy of GD are as follows [11]: (1) complete remission (CR): The symptoms and signs of GD patients disappeared completely, and the values of serum total triiodothyronine(TT_3), total thyroxine(TT_4), free triiodothyronine (FT_3) and free thyroxine(FT_4) were in the normal range. (2) partial remission(PR): The symptoms of GD patients were relieved, the physical signs partially disappeared, and the values of serum TT_3, TT_4, FT_3 and FT_4 decreased significantly, but not to the normal range. (3) ineffectiveness: The symptoms and signs of GD patients were not improved or aggravated, and the values of TT_3, TT_4, FT_3 and FT_4 were not significantly decreased. (4) recurrence: The symptoms and signs of hyperthyroidism and the values of TT_3, TT_4, FT_3 and FT_4 increased again after meeting the standard of CR. (5) hypothyroidism: After RAI treatment, GD patients showed symptoms and signs of hypothyroidism which the values of TT_3, TT_4, FT_3 and FT_4 were lower than normal, and the value of thyroid stimulating hormone(TSH) was higher than normal. In general, (1), (2) and (5) are considered to be "Effectivity" for RAI treatment.

Outcome of clinical compliance score (CCS)

All patients answered 10 questions about the questionnaire (supplementary materials). For the first 9 questions, the answer "yes" gets 1 point, and the answer "no" does not score. In question 10, the answer "no" gets 1 point, and the answer "yes" does not score.

Outcome of thyroid diseases awareness score（TDAS）

Patients' awareness of thyroid disease was obtained by issuing questionnaire when they visited patients face to face (supplementary materials). The content of the questionnaire includes 20 questions, each with a score of 0.5, with a total score of 10.

Statistical analysis

Continuous variables were expressed as the Mean ± Standard Deviation (SD); categorical variables were expressed as frequency and percentage. Student's t test or the Wilcoxon rank sum test was used to compare the two groups in continuous variables, while categorical variables were analyzed using the χ^2 /Fisher's exact test. Nonparametric methods were used throughout where normality and χ^2 assumptions did not hold. All statistical analyses were performed using SPSS 19 (SPSS Inc, Chicago, IL, USA) software. Statistical significance was defined as $p< 0.05$.

RESULTS

The CONSORT Diagram (Figure 1) provides full information on participant flow through the study. By the end of follow-up, we had treated a total of 769 patients with GD. According to the inclusion and exclusion criteria, 130 people were eligible for this study. In the experimental group, 60 patients completed the study (92.3% retention rate), while comparison group, 61 patients completed the study (93.8% retention rate). There were no significant difference in age, sex, education level, TM, $RAIU_{24h}$, RAITA and course of GD between experimental group and comparison group (all $p＞0.05$)(Table 1).

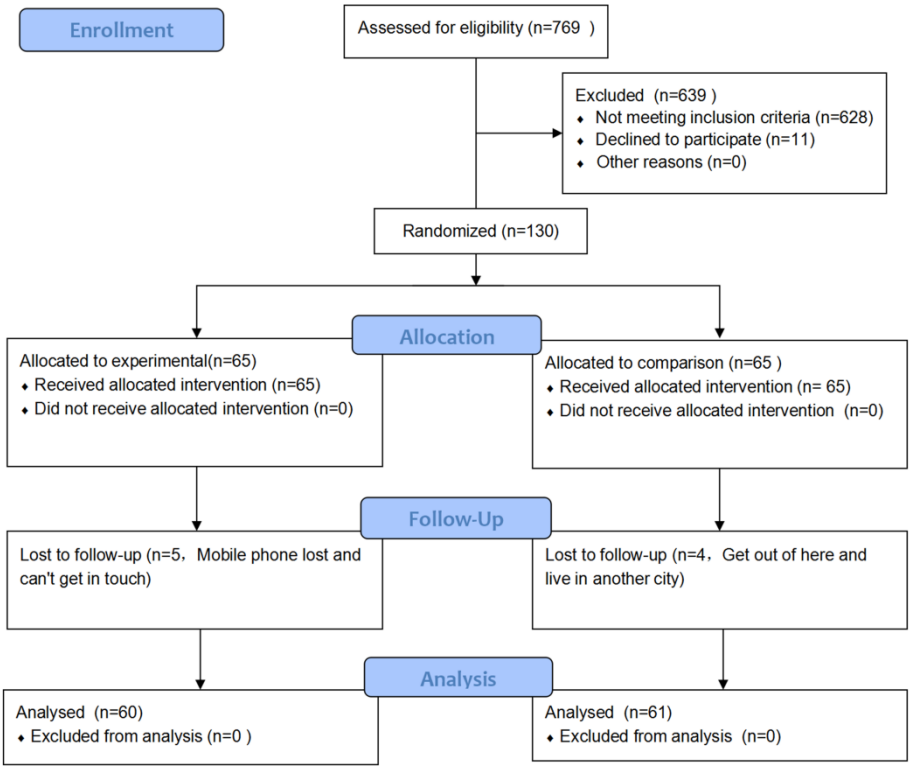

Figure 1: The diagram shows the number of Graves' disease patients screened, excluded and enrolled in the study.

Table 1: Baseline characteristics of the patients.

	Experimental (n=60)	**Comparison (n=61)**	***P*-Value**
Sex			
Females,%	43(71.7)	41(67.2)	0.595
Males,%	17(28.3)	20(32.8)	
Mean age, year (mean±SD)	39.82±13.23	40.89±13.62	0.66
Education			
High school and higher,%	36(60)	33(54.1)	0.512
Middle school and lower,%	24(40)	28(45.9)	
Duration of GD,months (mean±SD)	7.33±10.46	6.61±7.41	0.66
Complications*			
GO,%	15(25)	13(21.3)	0.631
Liver insufficiency,%	17(28.3)	19(31.1)	0.735
Heart failure,%	13(21.7)	12(19.7)	0.859
Drug Allergies,%	8(13.3)	8(13.1)	0.996
Diabetes,%	7(11.7)	4(6.6)	0.328
Leukocytopenia,%	16(26.7)	13(21.3)	0.490
Thyrotoxic periodic paralysis	6(10)	9(14.8)	0.428
Thyroid mass（g）(mean±SD)	56.23±23.38	52.87±16.55	0.27

$RAIU_{max}$ or $RAIU_{24h}$(%) (mean±SD)	75.29±13.44	73.84±12.08	0.42
Iodine-131 doses（M Bq） (mean±SD)	355.57±194.99	316.72±83.62	0.18
*Some patients have multiple complications; SD, Standard Deviation;GD,Graves' disease; $RAIU_{max,}$Maximum radioactive iodine uptake.			

Outcomes of therapeutic effects

Of the 121 GD patients, 111 (91.7%) were effective with RAI, and 10 were ineffective or recurrent. There is no significant difference in the effective rate of RAI treatment for GD in the two groups (p=0.978) (Table 2). Three patients in the experimental group and four patients in the comparison group were non-response to RAI, and they were all given the second RAI treatment on the 4th month after the first treatment. Two patients in the experimental group and one patient in the comparison group reached the standard of CR 4 months after first RAI treatment, but relapsed again 2 months later and had to be treated a second time. Patients with recurrence and inefficacy responded significantly to RAI secondary therapy. In the experimental group, 12 patients showed early hypothyroidism 3 months after RAI treatment. After thyroid hormone replacement therapy, the symptoms of hypothyroidism were quickly improved. In contrast, in the comparison group, there were 8 patients who did not have regular follow-up as required and did not find out in time that they had developed hypothyroidism, showing significant weight gain, fatigue, no spirit, lethargy and other hypothyroidism symptoms. When they first saw a doctor 5 months after RAI treatment, the results of thyroid function indicated a significant increase in serum TSH and a significant decrease in serum FT_4.

Table 2: Evaluation of efficacy of radioactive iodine in GD after 6 months.

	Experimental (n=60)	**Comparison (n=61)**	χ^2	***P***
Complete remission,%	23(38.4)	20(32.8)	0.406	0.524
Partial remission,%	12(20)	13(21.3)	0.032	0.859
Hypothyroidism,%	20(33.3)	23(37.7)	0.252	0.615
Recurrence,%	2(3.3)	1(1.6)	0.359	0.549
Inefficacy,%	3(5)	4(6.6)	0.135	0.714
Effectivity ,%	55(91.7)	56(91.8)	0.001	0.978

Clinical compliance score

The CCS of baseline level and six months later in two groups presented in Table 3. Based on the analysis of the questionnaire results of CCS in GD patients, it was found that 30(50.0%)

people got full marks in the experimental group and 18 (29.5%) people in the comparison group, with a statistically significant difference ($p<0.05$). In the subgroup analysis of education level, patients with CCS in high school and higher (HSAH) were about the same as those middle school and lower(MSAL) ($p>0.05$). However, CCS in HSAH patients in the experimental group was higher than that in the comparison group ($p=0.013$).

Table 3: Descriptive statistics for CCS and TDAS variables by group at baseline and 6months[#].

	Experimental				Comparison			
	CCS		TDAS		CCS		TDAS	
	Baseline	6 months	Baseline	6 months	Baseline	6 months	Baseline	6 months
No subgroups	4.42±1.09[a]	8.50±1.79[b]	5.07±1.29[a]	9.78±0.51[b]	4.11±1.13	7.67±1.76	4.80±1.08	7.33±1.21
Educational level								
High school and higher	4.50±1.03[a]	8.78±1.68[b]	5.81±1.06[a]	9.82±0.44[b]	4.09±0.98	7.76±1.64	5.58±0.71	7.36±1.06
Middle school and lower	4.38±1.28[a]	8.25±1.98[c]	3.96±0.62[a]	9.72±0.61[b]	4.00±1.19	7.57±1.83	3.89±0.63	7.31±1.38

[#]All values Mean±Standard Deviation; [a] Comparison of baseline level between the experimental group and the control group, all $p>005$; [b] Comparison between the experimental group and the control group after 6 months, all $p<005$; [c] Comparison between the experimental group and the control group after 6 months, all $p<005$; CCS, Clinical compliance score ; TDAS, Thyroid disease awareness score.

Thyroid disease awareness score

After 6 months of followed up, 49 (81.7%) patients in the experimental group and 5(8.2%) patients in the control group were given full marks for thyroid disease awareness, and the difference was statistically significant ($p<0.05$). The TDAS of baseline level and six months later in two groups presented in Table 3. The TDAS of experimental group was significantly improved by 92.9%, while the comparison group was slightly improved by 52.7% ($p<0.05$). Especially, the awareness of radiation safety was increased from 2 to 52 in the experimental group, but only 7 in comparison group.

DISCUSSION

In this study, GD patients selected RAI for treatment because of severe complications, such as tachycardia, atrial fibrillation, cardiac failure, drug induced liver injury, and agranulocytosis associated with hyperthyroidism.[1,2] These complications are the first indication for the treatment of hyperthyroidism with RAI.

Most GD patients have responded well to RAI therapy, and over 90% of them can get relief of related symptoms and signs after the first treatment, and some patients will develop hypothyroidism after 3-6 months. In our study, the overall response rate of the first treatment was 91.7%, and only a small number of patients chose the second treatment after treatment failure or recurrence. The failure of the first treatment may be related to the patient's large and hard thyroid gland, long course of disease, hyperthyroidism with thyroid nodules.

In addition to a wealth of medical theoretical knowledge and clinical skills, the doctors should also be able to educate and motivate, communicate with patients. Patients should also actively participate in the prevention of adverse reactions and response evaluation after treatment. Communication between patients and doctors is a pivotal factor for the success of treatment.[12] After taking RAI, patients are advised not to knead and press the thyroid gland, pay attention to rest, avoid fatigue and mental stimulation, so as not to aggravate the condition. In general, it is recommended that patients should be reviewed 1 to 3 months after treatment. Therefore, good clinical compliance is one of the critical factors for successful treatment of any disease.[12] Our study believed that nursing education could increase patients' understanding and cognition of the disease, enhance patients' compliance and actively cooperate with medical treatment plans, which would be conducive to improve the treatment effect and treatment success rate of GD patients. The reason why patients have good compliance is the trust in doctors, the fear of the complications of hyperthyroidism and the desire to control hyperthyroidism as soon as possible. Poor patient compliance may be related to patients' misunderstanding of the conditionofapatient, dissatisfaction with the improvement in health status, disappointment with the efficacy of drug treatment, and concerns about side effects.[13]

The CCS of patients in experimental group were higher than that of comparison group in this study, indicating that relevant intervention measures could enhance patients' clinical compliance and improve patients' trust in doctors. In the aspects of regular follow-up, regular medication and regular rest, especially, the compliance of patients in experimental group was significantly higher than that in comparison group. Although this study showed that there was no difference between the remission rate of GD patients with good compliance and poor compliance, the former could improve the quality of life and life happiness of GD patients.
In this study, 12 patients in the experimental group were diagnosed as early hypothyroidism 3 months after RAI treatment, and hypothyroidism was effectively controlled after timely

supplementation of thyroid hormone. In contrast, in the comparison group, there were 8 patients who did not follow the doctor's advice for regular review and did not timely find serious hypothyroidism, which seriously affected the patients' quality of life. Therefore, this phenomenon shows that health education has a very important clinical value in improving patients' clinical compliance. Patients with good clinical compliance can better and faster control the disease to develop in a bad direction. Ross et al.[13] also believed that improving the compliance of patients with hypertension could well control their blood pressure within the normal range, avoid serious complications caused by long-term fluctuations of blood pressure, and improve the survival rate and quality of life of patients. Some researchers used the new anticoagulant management system on smart phones to evaluate the clinical compliance of patients treated with warfarin, indicating that patient compliance is critical for a good prognosis.[14]

At the same time, their research suggested that good education can improve patients' clinical compliance.[14] However, our study found that there was no statistically significant difference in baseline CCS among patients with different education levels, which may be due to different patients' cognitive level of different diseases. After intervention, the scores of experimental group of HSAH were significantly higher than that of comparison group, while there were no difference in MSAL between the two groups. These results suggest that patients with well-education after receiving certain interventions can change their behavior and improve their compliance, so that they are willing to interact with doctors and accept their suggestions. However, for patients with poor-education, no matter how much external stimulation you give them, they will not change their nature of cognition. From another perspective, our results show that education level is an important factor affecting patients' clinical compliance, which is consistent with the study by Nurunniyah et al.[15] Therefore, the medical social media, as the main health education mode, is like building an invisible bridge between doctors and patients, which can promote the interaction between doctors and patients, reduce estrangement and narrow the distance between them, and avoid the emergence of doctor-patient conflicts.

In this study, there was no significant difference in baseline TDAS between experimental group and comparison group. Importantly, only patients with GD who had been diagnosed for less than 4 weeks were included in the inclusion criteria, so as to avoid the interference of patients' existing knowledge reserve before the trial on the study results. After 6 months of

followed up, the TDAS of experimental group were significantly higher than that of comparison group, indicating that health education plays an important role in improving patients' disease awareness. Patients in the HSAH group at baseline had higher TDAS than those in the MSAL group, which shown that the higher the level of basic education, the more people pay attention to their own diseases, the more people have the desire to learn medical popular science knowledge, and the higher the requirements for their own disease rehabilitation. However, there was no statistically significant difference in scores between the HSAH and MSAL groups after intervention. In other words, the health education method in this study can improve the TDAS of patients with low educational level, improve their reserve of medical knowledge. This is a significant change in the outcome because patients can communicate with each other about their stateofanillness, share their own conditions after treatment and their personal feelings on the medical social media.

The radiation safety of RAI has always been the common focus of most doctors and all patients. The vast majority of patients were unaware of the radiation of RAI when baseline radiation safety was assessed. They believe that the radiation energy released by RAI is very harmful to human tissues and organs, and most patients are reluctant to use it as a treatment for hyperthyroidism. These patients had lower scores on the radiation safety questionnaire. Therefore, in China, few patients with hyperthyroidism use RAI therapy as their first treatment because of radiation concerns. In this study, the post-intervention scores of patients with all levels of education were significantly higher than those at baseline. Therefore, it can relieve patients' tense and anxious mood, enhance patients' confidence in life and improve their quality of life by indoctrinating patients with radiation safety knowledge about the treatment of hyperthyroidism with RAI.

Limitations

This study also has some limitations, hope to be able to improve in the future. Firstly, the content of the questionnaire in this study is a little difficult, which may limit its practicability. Secondly, the number of people lost to follow-up in this study was slightly higher, although it did not affect the overall analysis of the data results. Thirdly, although a clear division was established between experimental and comparison groups, individual patients in comparison group visited their doctors privately to seek help with health education. Finally, China has a large population, uneven distribution of medical resources, and its medical development is unique. The health care situation in China may be different from that in other countries.

Therefore, the similarities and differences between China and other countries can be explored in further studies.

CONCLUSIONS

This study showed that health education mode based medical social media can enhance the clinical compliance of Graves' disease patients and improve the patients' understanding of thyroid disease and radiation safety of radioactive iodine. This mode of health education can be popularized and applied in clinic.

Abbreviations

GD: Graves' disease; ATD: anti-thyroid drug; RAI: radioactive iodine; TM: thyroid mass; RAITA: radioactive iodine treatment activity; RAIU: radioactive iodine uptake; PA: planned activity; CCS: clinical compliance score; TDAS: thyroid diseases awareness score; SD: Standard Deviation; HSAH: high school and higher; MSAL: middle school and lower.

Ethics approval

The study was approved by the Hospital Ethics Committee.

Availability of data and materials' statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

All authors contributed to the study conception and design. The literature search and data analysis were performed by Xue Liu, Tao Jiang and Huaiwei Xu. The first draft of the manuscript was written by Xue Liu and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Competing interests

The authors have declared that no competing interest exists.

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