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Comparative study on radioiodine therapy for lung metastasis of differentiated thyroid cancer in elderly and non-elderly patients.

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Abstract

This study aimed to compare the efficacy of 131I therapy between elderly and non-elderly patients with lung metastasis of differentiated thyroid cancer (DTC). Thirty-eight patients diagnosed with lung metastasis of DTC were divided into elderly group (60-80 years old; 17 cases) and non-elderly (33-59 years old; 21 cases). All patients received 131I therapy following the total thyroidectomy. After six months, the overall treatment efficacy, pulmonary function, peripheral blood indexes and salivary gland function were evaluated. The adverse reactions of treatment were observed. Results showed that, the remission rate in non-elderly group was 85.73%, which was significantly higher than 52.92% in elderly group (P<0.05). The maximum voluntary ventilation in non-elderly group was significantly higher than that in elderly group both before and after treatment (P<0.05). After treatment, the white blood cell and platelet levels in non-elderly group were significantly higher than those in elderly group, respectively (P<0.05). After treatment, the uptake indexes and secretion ratio of parotid glands and submandibular glands in non-elderly group were significantly higher than those in elderly group, respectively (P<0.05). The short-term adverse reactions in elderly group were severe than non-elderly group, and no obvious chronic adverse reaction occurred in each group. 131I therapy is an effective method for non-elderly patients with lung metastases of DTC. It is also has relatively satisfactory efficacy for elderly patients, but when applying, the effects on pulmonary function, peripheral blood indexes and salivary gland function should be paid more attention.

Keywords: Differentiated thyroid cancer, Lung metastases, 131I, Elderly.

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Introduction

Thyroid cancer is one of the most common malignant tumors of the endocrine system, which is generally considered to be a kind of malignant tumor with relatively good prognosis [1]. However, the thyroid cancer has a very high mortality after distant metastasis [2].The main pathological types of thyroid cancer are papillary carcinoma, follicular carcinoma, medullary carcinoma and undifferentiated carcinoma. Papillary carcinoma and follicular carcinoma are called differentiated thyroid carcinoma (DTC). DTC has the biological features similar to the thyroid tissue, such as uptake of iodine and secretion of thyroglobulin. The disease is more common in female. Its clinical manifestations are relatively occult, and the early detection will obtain a better prognosis. DTC has a long course and slow development, and its malignancy is lower than thyroid cancer with other pathological types [3]. In recent years, DTC has shown a rising trend in elderly patients, and has a high rate of distant metastasis (lung, bone, etc.) [4]. Due to the age factor, the physical conditions of elderly are very different from the young. The clinical feature, pathological type, treatment and prognosis of DTC are different among children, young and elderly. Surgery is the most basic treatment of thyroid cancer, and 131I therapy is the main method for the treatment of DTC with postoperative lung metastasis [5-7]. This study compared the efficacy of 131I therapy between elderly and non-elderly DTC patients with lung metastasis. The objective was to provide a basis for further application of 131I therapy to treatment of DTC.

Subjects and Methods

Subjects

Thirty-eight patients diagnosed with lung metastasis of DTC in Qilu Hospital of Shandong University from January 2005 to December 2011 were enrolled in this study. The inclusion criteria were as follows: i) after removing the residual thyroid tissue, the 131I imaging indicated the lung metastasis of DTC; ii) the chest X or CT examination indicated the lung metastasis of DTC. The exclusion criteria were as follows: i) the patients had 131I treatment contraindication; ii) the patients previously

received the received radiotherapy or chemotherapy treatment. There were 16 males and 22 females. According to the age, the patients were divided into elderly group (17 cases; 7 males and 10 females; 60-80 years old; average age of 70.5 ± 5.6 years) and non-elderly (21 cases; 9 males and 12 females; 33-59 years old; average age of 49.7 ± 8.5 years). This study was approved by the institutional review board of Qilu Hospital of Shandong University. Written informed consent was obtained from all participants.

Treatment method

The total thyroidectomy was performed on all patients, followed by the 131I therapy. Firstly, according to the uptake rate of patient, the 131I was orally administrated, with dose of 2.52-3.7 GBq/time, for cleaning the residual thyroid tissue. The clearance outcome was judged by receiving the second 131I therapy. The total dose of 131I was 14.8-22.2 GBq. The treatment cost with 3-5 courses, among which the interval was 5-6 months. After 5-6 days from treatment, the routine systemic and local 131I imaging was performed. After all the treatments, the patient was followed up for six months to observe the treatment efficacy.

Determination of overall treatment efficacy

After six months from all the treatment, the overall treatment efficacy was determined according to criteria as follows: i) complete remission (CR): both the systemic 131I scan and chest CT scan showed that the metastatic lesions disappeared, and the serum thyroid globulin (Tg) level was kept normal even in stimulated situation; ii) partial remission (PR): the systemic 131I scan or chest CT scan showed that the metastatic lesions were faded, shrunk or reduced, and the serum Tg level was gradually decreased when stimulating; iii) no remission (NR): the systemic 131I scan and chest CT scan showed that the metastatic lesions were invariant, enriched, enlarged or increased, and the serum Tg levels did not decrease or increase in stimulated situation.

Determination of pulmonary function

Before and after six months from treatment, the pulmonary function indexes including vital capacity (VC), forced vital capacity (FVC) and forced expiratory volume in the first second (FEV1) and maximum voluntary ventilation (MVV) were measured using MasterScreen™ PFT System (Jaeger & Co., Germany). The measurement of all patients was operated by the same professional doctor.

Determination of peripheral blood indexes

Before and after six months from treatment, the venous blood of the patient was taken. The peripheral blood indexes including white blood cell (WBC), neutrophils, lymphocytes, hemoglobin (Hb) and platelet (PLT) were measured using DxH 800 fully automated hematologic analyzer (Beckman Coulter Inc., USA).

Determination of salivary gland function

Six months after treatment, the salivary gland function of patient was determined using the 99mTcO4- salivary gland scintigraphy method [8]. The uptake index (UI) was calculated as follows: UI=(maximum gland radioactive count-background radioactive count)/background radioactive count. The secretion ratio (SR) was calculated as follows: SR=(maximum gland radioactive count after vitamin C taking-minimum gland radioactive count after vitamin C taking)/maximum gland radioactive count after vitamin C taking.

Table 1. *General data of patients in two groups.*

Group	Elderly	Non-elderly	P
n	17	21	
Gender (n (%))			
Male	7 (41.18)	9 (42.86)	0.8634
Female	10 (58.82)	12 (57.14)	
Histology (n (%))			
Papillary	10 (58.82)	14 (66.67)	0.6475
Follicular carcinoma	7 (41.18)	7 (33.33)	
Cervical lymph node metastasis (n (%))			
No	3 (17.65)	4 (19.05)	0.9177
Yes	14 (82.35)	17 (80.95)	
Other organ metastasis (n (%))			
No	9 (52.94)	19 (90.48)	0.0126
Yes	8 (47.06)	2 (9.52)	
Pulmonary lesion type (n (%))			
Diffuse	5 (29.41)	14 (66.67)	0.0211
Nodular	12 (70.59)	7 (33.33)	

Table 2. *Comparison of overall treatment efficacy between two groups.*

Group	n	CR (n)	PR (n)	NR (n)	RR (%)
Elderly	17	2	7	8	52.92
Non-elderly	21	7	11	3	85.73
P					0.0132

CR: Complete Remission; PR: Partial Remission; NR: No Remission; RR: Remission Rate ((CR+PR)/(CR+PR+NR) × 100%).

Statistical analysis

All statistical analysis was carried out using SPSS 13.0 software (SPSS Inc., Chicago, IL, USA). The enumeration data were presented as number and rate, and were compared using χ^2 test. The measurement data were presented as mean ± SD, and were compared using t test. $P<0.05$ was considered as statistically significant.

Results

General data of patients in two groups

General data of patients in elderly and non-elderly groups were shown in Table 1. There was no significant difference of gender, histology or cervical lymph node metastasis of DTC between two groups (P>0.05). The other organ metastasis of DTC and pulmonary lesion type had significant difference between two groups, respectively (P<0.05).

Overall treatment efficacy between two groups

As shown in Table 2, at the end of follow-up, there were 2, 7 and 8 cases with CR, PR and NR in elderly group, respectively, and there were 7, 11 and 13 cases with CR, PR and NR in non-elderly group, respectively. The remission rate in non-elderly group was 85.73%, which was significantly higher than 52.92% in elderly group (P<0.05).

Pulmonary function before and after treatment in two groups

At the end of follow-up, no radiation pneumonia or new pulmonary fibrosis was found in each group. The pulmonary function before and after treatment in two groups was shown in Table 3. In each group, the VC, FVC, FEV1 and MVV after treatment were decreased, compared with before treatment, but there was no significant between before and after treatment (P>0.05). In addition, MVV in non-elderly group was significantly higher than that in elderly group, both before and after treatment (P<0.05) (Table 3).

Table 3. Pulmonary function before and after treatment in two groups.

Group	n		VC (L)	FVC (L)	FEV1 (L)	MVV (L/min)
Elderly	17	Before	93.05 ± 13.02	93.33 ± 12.56	84.02 ± 13.01	82.51 ± 15.91
		After	88.56 ± 10.21	90.23 ± 8.67	83.61 ± 9.39	80.44 ± 11.38
Non-elderly	21	Before	94.92 ± 12.94	93.49 ± 10.66	86.29 ± 7.90	94.83 ± 11. 23[a]
		After	89.45 ± 10.34	91.11 ± 11.78	84.78 ± 12.81	92.16 ± 13.02[b]

[a]P<0.05 compared with elderly group before treatment; [b]P<0.05 compared with elderly group after treatment. VC: Vital Capacity; FVC: Forced Vital Capacity; FEV1: Forced Expiratory Volume in the first second; MVV: Maximum Voluntary Ventilation.

Peripheral blood indexes before and after treatment in two groups

In elderly group, the WBC, neutrophils, lymphocytes and PLT levels after treatment were significantly decreased, respectively, compared with those before treatment (P<0.05). The Hb level was not obviously changed after treatment (P>0.05). In non-elderly group, there was no significant difference of each index between before and after treatment (P>0.05). Before treatment, there was no significant difference of WBC, neutrophil, lymphocyte, Hb or PLT concentration between elderly and non-elderly groups (P>0.05). After treatment, the WBC and PLT levels in non-elderly group were significantly higher than those in elderly group, respectively (P<0.05) (Table 4).

Salivary gland function after treatment in two groups

In elderly group, the UI of parotid glands and submandibular glands was 5.34 ± 1.03% and 6.83 ± 1.44%, respectively, and the SR of parotid glands and submandibular glands was 13.36 ± 3.04% and 19.67 ± 3.28%, respectively. In non-elderly group, the UI of parotid glands and submandibular glands was 7.47 ± 2.01% and 8.67 ± 2.34%, respectively, and the SR of parotid glands and submandibular glands was 21.52 ± 2.99% and 24.75 ± 4.01%, respectively. There was significant difference of each index between two groups (P<0.05) (Table 5).

Table 4. Peripheral blood indexes before and after treatment in two groups.

Group	n		WBC (10^9/L)	Neutrophils (10^9/L)	Lymphocytes (10^9/L)	Hb (g/L)	PLT (10^9/L)
Elderly	17	Before	6.38 ± 1.34	4.15 ± 1.03	2.37 ± 0.56	138.05 ± 20.96	234.26 ± 33.78
		After	5.06 ± 2.56[a]	2.91 ± 0.82[a]	1.61 ± 0.34[a]	135.99 ± 30.29	200.89 ± 25.04[a]
Non-elderly	21	Before	7.17 ± 2.67	4.52 ± 0.78	2.45 ± 0.61	142.56 ± 19.62	249.43 ± 19.44
		After	6.61 ± 1.73[b]	4.08 ± 1.03	2.25 ± 0.57	133.62 ± 26.01	235.66 ± 38.03[b]

[a]P<0.05 compared with before treatment in one group; [b]P<0.05 compared with elderly group after treatment. WBC: White Blood Cell; Hb: Hemoglobin; PLT: Platelet.

Adverse reactions

On the 1 week after treatment, in elderly group, there were 7 (41.17%), 6 (35.30%), 3 (17.65%) and 9 (52.94%) cases of neck pain, gastrointestinal reaction, acute sialadenitis and fatigue, respectively. In non-elderly group, there were 8 (38.10%), 7 (33.33%), 2 (9.52%) and 8 (38.10%) cases of neck pain, gastrointestinal reaction, acute sialadenitis and fatigue, respectively. The incidences of acute sialadenitis and fatigue in elderly group were significantly higher than those in non-elderly, respectively (P<0.05). After six months from treatment, no chronic sialadenitis or secondary tumor occurred in each group.

Discussion

The clinical manifestations and behaviors have differences between the elderly and non-elderly patients with lung metastases of DTC. In elderly patients, the disease is latent, and the course is long; the patients have poor health, and see a doctor later; there are more nodular pulmonary lesions, with high incidence of distant metastases, especially for the bone metastases. In non-elderly patients, the disease course is short; the patients have relatively good health; there are more diffuse pulmonary lesions; the incidence of distant metastases is low. In this study, there was no significant difference of gender, histology or cervical lymph node metastasis of DTC between two groups (P>0.05). The other organ metastasis of DTC and pulmonary lesion type had significant difference between two groups, respectively (P<0.05). There is the comparability between the two groups.

Table 5. *Salivary gland function after treatment in two groups.*

Group	n	UI (%)		SR (%)	
		Parotid glands	Submandibular glands	Parotid glands	Submandibular glands
Elderly	17	5.34 ± 1.03	6.83 ± 1.44	13.36 ± 3.04	19.67 ± 3.28
Non-elderly	21	7.47 ± 2.01[a]	8.67 ± 2.34[a]	21.52 ± 2.99[a]	24.75 ± 4.01[a]

[a]P<0.05 compared with elderly group after treatment. UI: Uptake Index; SR: Secretion Ratio.

Most of the DTC and metastases retain the 131I uptake ability. The 131I radiation can not only remove the residual thyroid tissue, but also clear the DTC metastatic foci at the same time [6]. This is the theoretical basis of 131I treatment for lung metastases of DTC. Therefore, 131I therapy is a necessarily continued treatment for patients with lung metastases of DTC after surgical treatment. In this study, both the elderly and non-elderly groups received the 131I therapy following total thyroidectomy. After treatment, the remission rate in non-elderly group was 85.73%, which was significantly higher than 52.92% in elderly group (P<0.05). This indicates that, the overall treatment efficacy of 131I therapy for lung metastases of DTC in non-elderly patients is better than that in elderly patients. The reason may be that, the elderly patients are often complicated with other age-related diseases such as hypertension, coronary heart disease, diabetes and respiratory diseases, which not only make the patients difficult to tolerate radical surgery, but also cause distress to postoperative 131I treatment. In contrast, most non-elderly patients are not complicated with other significant underlying diseases. The surgery is less difficult, with less residual lesions, which lays a good foundation for further treatment and therapy effect monitoring. In this study, most of the elderly patients have delayed treatment and high incidence of distant metastasis. The distant metastases lesion will decrease the sensitivity of 131I treatment [9], especially for the bone metastases. The elderly group has a high incidence of bone metastasis, so that the treatment effect is decreased. In addition, the nodular lung lesions have large volume, with poor blood supply, which will cause the oxygen deficiency in the tissue [10]. In this study, the incidence of nodular lung lesions in the elderly group is higher than non-elderly group, which also affects the treatment outcome.

The irradiation treatment may cause the pulmonary injury such as radiation pneumonia and pulmonary fibrosis, leading to the changes of pulmonary function [11,12]. The reason may be that, the lung tissue is very sensitive to irradiation. The absorbed irradiation can cause the production of high-active free radicals, which leads to the chemical and biological change of lung tissue, increased alveolar capillary permeability and fibrous connective tissue fragmentation [13]. This can affect the lung function, thereby hampering the reconstruction of tissue structure and resulting in the pulmonary dysfunction and scar formation. Results of this study showed that, in each group, the VC, FVC, FEV1 and MVV after treatment were decreased, compared with before treatment, but there was no significant between before and after treatment (P>0.05). This indicates that, the 131I therapy with suitable dose cannot obviously affect the pulmonary function of patients.

It is reported that, the irradiation therapy can cause the bone marrow suppression for some DTC cases [14]. The bone marrow suppression is transient, and can be relieved without any treatment [15]. Other scholars [16] suggest that, after oral administration, 131I enters the blood circulation system, and causes the radiation damage to blood cells and bone marrow, leading to temporary decrease of peripheral blood cells. However, the long-term large doses of 131I therapy may lead to the severe bone marrow suppression. Results of this study showed that, in elderly group, the WBC, neutrophils, lymphocytes and PLT levels after treatment were significantly decreased, compared with those before treatment (P<0.05). In non-elderly group, there was no significant difference of each index between before and after treatment (P>0.05). The healthy conditions of elderly patients are worse than non-elderly patients, which may result in the relatively severe bone marrow suppression, compared with non-elderly patients.

Salivary glands are rich with sodium/iodide symporter protein in the striated ducts, which has the strong uptake ability of 131I [17]. It is reported that, the concentration of 131I in salivary glands is 30-40 times higher than that in the blood concentration. After 12 h from oral administration, the 131I

concentration in the salivary glands can reach 6 Gy [18]. In 131I treatment, the salivary glands physiologically uptakes and concentrate the 131I, and receives the unnecessary exposure, which leads to the temporary or permanent damage. In this study, after 131I treatment, the salivary gland function in non-elderly group was better than elderly group. This may be due to the worse healthy conditions of elderly patients, compared with non-elderly patients. In Addition, the short-term adverse reactions in elderly group were severer than non-elderly group, and no obvious chronic adverse reaction occurred in each group. This indicates that, the 131I therapy is a relatively safe choice for both elderly and non-elderly patients with lung metastases of DTC.

In conclusion, the 131I therapy is an effective method for non-elderly patients with lung metastases of DTC. It is also has relatively satisfactory efficacy for elderly patients with lung metastases of DTC. However, when applying, the effects on the pulmonary function, peripheral blood indexes and salivary gland function should be paid more attention. This study still has some limitations. The sample size of this study is relatively small. Larger sample size will make the results more convincing. In our next studies, the sample size should be further increased for obtaining more satisfactory outcomes.

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