

Study of the radiotherapy sensitization of retroperitoneal lymph node metastasis in patients by sodium glycididazole

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Abstract: To observe the radiotherapy sensitization effect of retroperitoneal lymph node metastasis in patients by sodium glycididazole in recent clinical efficacy and toxicity. A total of 42 patients admitted with metastasis and recurrence of retroperitoneal lymph node from September 2006 to December 2009 were classified with the method of case-control. After three dimensional conformal radiation therapy with or without sodium glycididazole (800mg/m²) for sensitization, the results of recent clinical efficacy, relief of pain, and Karnofsky score were obtained. Tumor remission rate of patients in sensitization group (with sodium glycididazole) at post-radiotherapy 3 months was significant higher than that in control group (without sodium glycididazole) (52% vs. 24%; $P < 0.05$). Oral dose of morphine daily, and Karnofsky score in anterior-posterior radiotherapy of patients in the sensitization group were significant different with those in the control group (93±12 and 42±6mg vs. 94±12 and 20±5mg and (65±4) and (90±9) vs. (64±5) and (80±10), respectively; $P < 0.01$). Sodium glycididazole has positive radiotherapy sensitization to the metastasis or recurrence of retroperitoneal lymph node for digestive tract cancer, which could obviously improve the life quality or release the pain for patients.

Keywords: Digestive system neoplasms; neoplasm metastasis; radiotherapy; three dimensional conformal radiation therapy; sodium glycididazole.

INTRODUCTION

Retroperitoneal lymph node metastasis carcinoma is a common disease in clinic, which causes pain in abdominal and lower back and fever. Usually, the patients need to use the morphine drug for the relief of pain, which seriously affects the quality of life of patients. Numerous therapy methods, such as radiotherapy, chemotherapy and radiofrequency ablation, were used to treat the patients (Gao *et al.*, 2012). But the tumor remission is short and the curative effect is not ideal. For the purpose, we admitted 42 patients with metastasis and recurrence of retroperitoneal lymph node, and observed the radiotherapy sensitization effect of retroperitoneal lymph node metastasis in patients by sodium glycididazole in recent clinical efficacy.

MATERIALS AND METHODS

Subjects

A total of 96 patients with retroperitoneal lymph node metastasis for three dimensional conformal radiotherapy were recruited for this study from September 2006 to December 2009 at PLA 404 hospital and Weihai cancer hospital. In which, 73 were only do three-dimensional conformal radiotherapy, 23 were sensitization by sodium glycididazole after three-dimensional conformal radiation therapy. All patients were diagnosed with by abdominal ultrasound followed by either CT or MRI examination.

Inclusion criteria

Patients with Karnofsky score > 60 and estimates of

survival above 3 months were not treated with radiotherapy. A total of 42 patients eventually included in the research. Among the 42 patients, 34 were male and 8 were female, aged 41 to 74, with an average age of 56.7±7.5. There were 4 cases of liver cancer, 18 cases of post-operative poorly differentiated adenocarcinoma of stomach, 8 cases of bile duct carcinoma, 6 cases of post-operative poorly differentiated squamous esophageal carcinoma and 6 cases of pancreatic cancer (2 cases without surgery). The minimum size of the tumors was 38×36×28 mm³, while maximum size was 63×61×45 mm³. All patients have different degree of abdominal and lower back pain symptoms.

Trial group

According to the case-control principle, features of age, tumor type, pathological type, and tumor size were evaluated and patients were classified into control group and sensitization group. Table 1 shows the data of the two groups are comparable.

Treatment

Except for symptomatic treatment with nutritional support these patients did not receive any chemotherapy, biological therapy or immune therapy.

For control group, 6MVX of linear accelerator (Xinhua, Shandong) and electric leafy grating (Haitai, Sichuan) were used. The treatment plan system (TPS) is three-dimensional conformal treatment planning system (Xihua, Shandong). The whole process of radiotherapy induced the fission die fixed, program design, validation and implementing the plan. Location was performed on an empty stomach in the morning with a 5mm layer

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thickness and 2 mm layer distance scanning. Images with the original data were input into the TPS workstation. The gross target volume (GTV) was confirmed by doctor from image diagnostics division, radiotherapy doctors and physician together. The planning target volume (PTV) was 1.0-1.5cm outside the GTV. 80% isodose lines covered the target according to the target lesion size and shape design of targets and conformal layout, which was set as prescription dose. The plan was assessed using dose volume histogram (DVH). The control probability of tumor and the complication probability of normal tissue provide reference for the optimization. The optimized field is usually set as 4-8 and 180 cGy of prescription dose is above the 80% isodose lines and 225cGy is 100% isodose lines. Average of total dose is 4000 cgy. After outlining the risk organs, such as spinal cord and kidney, patients were treated following the plan.

For the sensitization group, patients received sodium glycididazole (800mg/m²) in a 30-minute intravenous infusion, and treated with radiation therapy within 60 min. The sodium glycididazole was administrated three times a week (in every Monday, Wednesday, Friday) until the end of radiotherapy. Sodium glycididazole was given three times a week during radiotherapy period with an average of 4 weeks and 20 fractions.

Evaluation index

Evaluation standard of curative effect

According to the WHO evaluation standard of therapeutic effect of solid tumor (1981), the patients were categorized into 4 degrees: Complete remission (CR), partial remission (PR), stable or no change (NC) and progression (PD). The first 2 degrees were considered efficient. The change of lymph node in size was detected by MRI in patients before and 3 months after treatment.

Quality of life evaluation

The KPS score was examined in patients before and 3 months after treatment.

Evaluation of pain relief

The local pain symptoms in patients were graded using digital classification. The grade of pain and the daily dose of oral morphine for patients before treatment and 3 months after treatment were compared.

Evaluation of adverse reactions

The acute radiation reaction of normal tissue was evaluated according to the radiation injury classification standard from tumor radiotherapy group (RTOG/EORTC).

STATISTICAL ANALYSIS

SPSS13.0 was used for statistical analysis. Data of KPS score, grade of pain, and daily dose of oral morphine was

presented as mean + SE and the differences between 2 groups were compared using rank and t test. Chi-square test was used for efficient comparison between the 2 groups. $P \leq 0.05$ was considered statistically significant.

RESULTS

Evaluation standard of curative effect

In control group, there was 1 case of CR, 4 cases of PR, 10 cases of NC and 6 cases of NC and the total effective rate was 24% (5/21). In sensitization group, there were 2 cases of CR, 10 cases of PR, 8cases of NC and 1 case of PD and the total effective rate was 24% (5/21). There were significant different between the 2 groups ($X^2=4.84$, $P<0.05$).

QOL (KPS score), grade of pain and daily dose of oral morphine

The KPS score in patients after treatment of radiotherapy was significant higher than that before treatment ($P<0.01$). And the KPS score in sensitization group was much higher than that in control group ($P<0.01$). The grade of pain and the daily dose of oral morphine for patients after radiotherapy treatment was significantly decreased compared with that for patients before radiotherapy ($P<0.01$) and that for patients in sensitization group was much lower than in control group ($P<0.01$). In the end of treatment, 5 cases in control group and 11 cases in sensitization group completely stopped taking oral morphine to relieve pain and the pain symptom decreased for other patients (table 2).

Evaluation of adverse reactions

The adverse effects in digestive system were not serious during the period of radiotherapy. All patients recovered from suitable treatment without any late complications.

DISCUSSION

All patients in the study are retroperitoneal lymph node metastasis which occurred after confirmation of primary gastrointestinal tumor by clinical pathological diagnosis. Using non-surgical treatment methods was due to the patients and their family member refused reoperation or unfavorable surgical. Radiation therapy is a common and most effective clinical treatment. Because the retroperitoneal lymph node in metastasis is closed to the risk organs, such as spinal cord, kidney and intestines, the adverse reaction of conventional radiotherapy treatments was bigger and not easy to eliminate. On the other hand, existence of hypoxic cell in tumor tissue greatly influenced the radiation effect. Bigger tumor is, more hypoxic cells in tumor tissue are. Foreign scholars in recent years also focused on the research of hypoxic cell (Ghattass *et al.*, 2013). Sodium glycididazole is a novel radiation sensitization agent for hypoxia cells. It is made in China and approved in clinical work since 2002.

Table 1: Clinical data of patients in the control group and the sensitization group

Project	Control group (21)	Sensitization group (21)
Gender/case		
Man	18	16
Woman	3	5
Age/year	55±9	57±7
Lesion size/mm ³	105682±287 (39×34×29-65×59×45)	105627±225 (38×36×28-63×61×45)
The pathologic types		
Cancer of the liver	2	2
Post-operative poorly differentiated adenocarcinoma of stomach	9	9
cholangiocarcinoma	4	4
Post-operative low differentiated squamous esophageal carcinoma	3	3
Pancreatic cancer (2 cases without operation in 1 case)	3	3

Two groups were compared by X^2 or t-test: $P>0.05$

Table 2: KPS score, grade of pain, and daily dose of oral morphine in patients of 2 groups (n=21)

Group	Time	KPS score	Pain relief score	The daily dose of morphine/mg
The control group	Before radiotherapy	64±5	8.4±1.4	93±12
	3 months after radiotherapy	80±10	3.1±1.2	42±6
	Difference value	18±10c	-5.3±2.6c	-52±14c
Sensitization group	Before radiotherapy	65±4	8.3±1.6	94±12
	3 months after radiotherapy	90±9	1.2±0.8	20±5
	Difference value	26±17cf	-7.1±1.9cf	-74±17cf

The differences between before and 3 months after radiotherapy treatment were compared using rank and t test, ^c $P<0.01$; Chi-square test was used for efficient comparison between the 2 groups, ^f $P<0.01$.

Several studies (Zheng *et al.*, 2000, Li and Yang 2012, Weiwei *et al.*, 2012 and Mi *et al.*, 2012) showed that Sodium glycididazole could enhance the radiotherapy effect in some solid tumors, such as lung cancer, esophageal cancer and so on. There are few reports about the effect of sodium glycididazole on the metastasis of retroperitoneal lymph node, and also not much about that of radiotherapy sensitization of other malignant tumor. Zeng, *et al.*, studied the conventional radiotherapy sensitization of limited advance laryngeal squamous carcinoma (T3-4, N0-3, M0) (Zeng *et al.*, 2010). He divided 60 patients into the trial group (with intravenous 700mg/m² sodium glycididazole within 30min) and control group (radiotherapy alone). 1-month Follow-up evaluation of tumor size and lymph node subsidies after radiotherapy showed that the tumor remission was 92.59% and 92.59% in the trial group and the control group, respectively ($P=0.005$), suggesting that sodium glycididazole could obviously improve the recent efficacy and patient tolerance of radiotherapy for the limited advanced laryngeal cancer.

In the study, patients after radiotherapy treatment in the 2 groups was significant higher QOL (KPS score), grade of

pain, and lower daily dose of oral morphine than that before radiotherapy treatment. When treated with sodium glycididazole, patients treated with radiotherapy got much higher QOL (KPS score), grade of pain, and much lower daily dose of oral morphine, suggesting that the pain relief was obvious and that the radiotherapy with sodium glycididazole could be a valuable methods to improve the QOL of patients. The total effective rate in the sensitization group was much higher than that in the control group (57% vs. 24%). The digestive tract symptoms were observed in both 2 groups, but the tumor in patients in sensitization group were more sensitive and rapid remission. After symptomatic treatment of symptoms, did not affect the proceeding of the radiation, no obvious radiation complications.

This study shows that sodium glycididazole has positive radiotherapy sensitization to the metastasis or recurrence of retroperitoneal lymph node for digestive tract cancer, which could obviously improve the life quality or release the pain for patients. It has satisfied recent curative effect, slight adverse reaction, can yet be regarded as a new method for the treatment of the disease.

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