

Application of tegafur gimer, docetaxel and carboplatin in head and neck squamous cell carcinoma therapy

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Abstract: Squamous cell carcinoma, in the clinical manifestation, is a form of cancer derived from lesions of keratinocytes of epidermis or accessories such as sebaceous ducts, hair follicles, sweat glands, etc. The disease is more common in older men, with prone locations at patients' scalp, face, neck and arms and other exposed parts. Head and neck squamous cell carcinoma (HNSCC) causes a serious impact on patients' daily life, making patients suffer from double blow in mental and physical aspects and reducing patients' life quality. To find effective treatment method for HNSCC, our hospital studies clinical effects of combination therapy of tegafur gimer, docetaxel and carboplatin for the disease. By way of grouping research, therapeutic effect of such treatment and adverse reactions were assessed and analyzed. The study clearly and fully confirms effectiveness of combination therapy of tegafur gimer, docetaxel and carboplatin for HNSCC.

Keywords: Tegafur gimer, docetaxel, carboplatin, head and neck squamous cell carcinoma, clinical efficacy.

INTRODUCTION

Clinical studies show that HNSCC, as a malignant disease with high incidence, doesn't have obvious clinical manifestations at the beginning of illness. This disease starts from epidermis or the keratinocytes of adnexa such as sebaceous gland duct, hair follicle, and sweat duct. This disease is more often seen on elder males' exposed positions such as scalp, face, neck, and back. Almost 50% of HNSCC patients are in advanced stage once the disease is discovered. Therefore, HNSCC mortality rate is relatively high. Chemotherapy is often used in clinics to treat patients with the disease, whose effect is difficult to be satisfied. Thus, in recent years, drugs are gradually adopted in clinics to treat the disease. For example, Gao Jing, Cao Jingyan, Gao Jing et al. made analysis on the therapeutic effect of combined therapy of tegafur gimeracil oteracil ootassium capsule, docetaxel and carboplatin in treating head and neck squamous cell carcinoma, and found that such method enjoyed significant superiority and therapeutic effect over conventional chemotherapy treatment (Gao 2014; Sachdeva and Rathee, 2015; Balkhair and Ashraf 2016; Liu and Liu 2010). To fully explore scientific and clinical value of this method, our hospital selects a greater number of patients for research and analysis related to combination drug therapy, and further demonstrates effectiveness of drug therapy. See below for specific circumstances.

MATERIALS AND METHODS

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General information

Selected patients are 2,000 cases of HNSCC patients admitted in our city's five major hospitals during January 2012-May 2015. All the selected patients meet diagnostic criteria for HNSCC, with KPS scores above 80 points. Their survival time is expected to be between 3-6 months. The study excludes patients with HNSCC and other major body organs diseases. According to parity order of hospitalization date, all the selected patients are averagely divided into chemotherapy group and medication group, each 1000 cases in average. Fundamental information such as age, sex distribution, etc. of selected patients is not statistically significant and is comparable. In addition, the selected patients and their families are aware of this study and signed treatment informed consent. In addition, all selected patients and parents knew and voluntarily took part in this research, and signed informed consent. (statement: all research contents were true and reliable, tested by clinical verification, which did not involve any violation of moral principles and ethics).

Treatment Method

For medication group patients, combination therapy of tegafur gimer, docetaxel and carboplatin is used, with specific treatment methods are as follows:

In this study, the patients orally take tegafur gimer 80mg / m² / day, 2 times a day, 1 time after breakfast and after dinner respectively, continuously take for 14 days and suspend for 7 days (Liu 2015; Li 2015; Liu 2013; Al-Hazmi and TariqJaveed 2016).

Adopt intravenous administration, with single dose of 75 ~ 100mg / m². What is adopted in the country is 75mg / m², with combination use of 60~75mg/m². Take

intravenous drip for 1 hour, repeat every 3 weeks. In recent years, many scholars at home and abroad apply weekly therapy, with usual single dose of 35~40mg/m², 1 time every week, continued use of 6 weeks and suspension for 2 weeks. It is recommended that before taking docetaxel, orally take dexamethasone 8mg every day, once every 12 hours, with continued use of 3 days. This product should be dissolved in the provided solvent, and then diluted with sodium chloride injection or 5% glucose, with final concentration at 0.3~0.9mg/ml. For carboplatin drugs, also take intravenous drip, once every day, with dose of 20mg /m² and continued use of 3 days. The control group patients receive chemotherapy treatment with docetaxel, cisplatin, leucovorin and fluorouracil. For docetaxel, the same usage as that of medication group is adopted. Drug dose of dexamethasone is 40mg/m²; that of cisplatin is 20mg / m², and that of leucovorin is 200mg, continuously take 5 days (Yang, 2014); fluorouracil is pumped with micro pump, with dose of 350mg/m² and pumping is completed within 22 hours. During chemotherapy treatment, nurses need to pay close attention to the patients' response to treatment. The rendering of chemotherapy treatment for HNSCC is shown as *et al* 1.



Fig. 1: Rendering of Chemotherapy Treatment for HNSCC

Comparison of method

Evaluate the clinical effects of the two treatments after three cycles of this treatment. Clinical results of this study are divided into complete remission (CR), partial response (PR), stable (SD), progress (PD) (Zhang, 2014). Effective treatment rate of patients is percentage of total number of total remittent and partially remittent patients in total number of treated people. Observe adverse reactions of patients after treatment.

Statistical method

The clinical study on the effects of drug therapy on HNSCC adopts SPSS19.0 statistical software for data analysis and processing, count data is represented by (n,%), chi-square test is adopted. Measurement data is expressed as mean ± average ($\bar{x} \pm s$); when P<0.05, it indicates that difference is statistically significant.

RESULTS

By analyzing follow-up record of therapeutic effect of 2,000 cases of patients, it can be known that clinical effect

of medication group is more obvious, effective rate of patients' recent treatment is 54%. By contrast, effective rate of clinical treatment of patients with chemotherapy is 42%, showing that differences between groups are significantly less than 0.05, with statistical significance.

In addition, patients in both groups appeared leukopenia and thrombocytopenia, nausea, vomiting, diarrhea, abnormal electrocardiogram, elevated serum creatinine and other adverse conditions. However, frequency of complications in patients of medication group is significantly lower than that in patients of chemotherapy group. Differences between the two groups is P<0.05, statistically significant.

DISCUSSION

Numerous clinical experiences suggest that primary squamous cell carcinoma is rare. Patients in early stages usually present pimples of small size, showing tubercular state or verrucosa. Pimples project, reddish in color and with rough surface. Once appears, it will grow rapidly. If patient handle it improperly, rupture occurs and infiltrates the surrounding area. HNSCC is a relatively common type of squamous cell carcinoma disease (Sun, 2006). The CT picture of HNSCC is shown as *et al* 2. The HNSCC distribution is shown as *et al* 3.

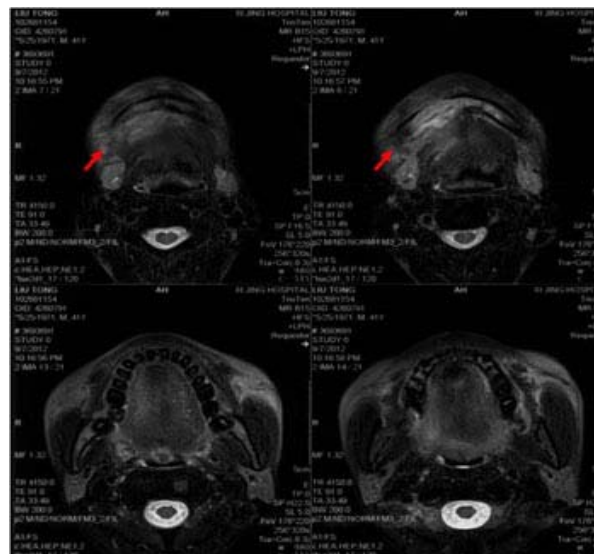


Fig. 2: CT picture of HNSCC.

Clinically, secondary squamous cell carcinoma is more common, usually caused by canceration based on chronic ulcers, scarring and other damage of the original scalp. In accordance with clinical form, there are usually two types: one is the cauliflower type, which specifically demonstrates as small plaques, nodules, ulcers in the early stages of illness, then based on this, shows upheaval of cauliflower shape and hard surface, through which angioectasis can be clearly seen. Sometimes, there are scaly scabs with sting like horny usually in the central area. This type of squamous cell carcinoma is more

common on patients' face; the other is deep type. At early stage of illness, light red hard nodules appear in patients' face, and with gradual deepening of the disease, nodules will continue to expand. Ulcers occurs when it is serious and quickly goes deep into patients' skull, regional lymph node metastasis is possible in the early stage. The main pathogenesis of squamous cell carcinoma is relatively complex. Related scholars summed up following pathogenesis through clinical research (Alshammari, 2016; Haidar *et al.*, 2016; Yao *et al.*, 2015; Nowak *et al.*, 2016). The first is ultraviolet radiation, the part with wavelength of 290 ~ 320nm in solar spectrum will easily lead to symptoms of squamous cell carcinoma. Secondly, direct contact of patients' skin with arsenic, bitumen may also lead to squamous cell carcinoma. Moreover, precancerous skin diseases and a variety of traumatic scars are likely to lead to squamous cell carcinoma (Li 2012; Chen 2012; Liu 2013; Chen and Chen 2014; Koocheki *et al.*, 2011).

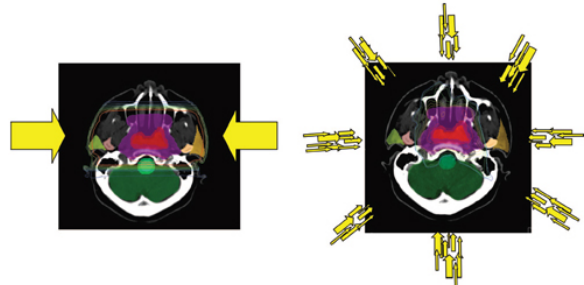


Fig. 3: HNSCC Distribution

Tegafur gimer, an oral anticancer agent derivative from fluorouracil, consists of tegafur (FT), gimeracil (CDHP), oteracil (Oxo). Wherein: FT is 5-Fu prodrug with high oral bioavailability, and can be directly converted to 5-Fu after patients take it. CDHP can suppress 5-Fu catabolism released from FT due to dihydropyrimidine dehydrogenase, which can help 5-Fu effective depth for a long time in blood and tumor tissue and thereby achieve efficacy similar to 5-Fu continuous intravenous infusion. Oxo can block the phosphorylation of 5-Fu, with a high concentration in gastrointestinal tissue after oral administration and direct impact on 5-Fu gastrointestinal tract distribution, reducing the toxicity of 5-Fu (Zhang, 2012). Thus, in the treatment course of HNSCC patients, tegafur gimer improves and maintains plasma concentration, increases anticancer activity. Moreover, tegafur gimer can reduce drug toxicity, thereby reducing the toxicity and side effect of drug therapy for squamous cell carcinoma, reduce the occurrence possibility of intercurrent diseases. The Tegafur Gimer Cancer Treatment Principle is shown as fig. 4.

The chemical name of docetaxel is 2 α R- (2 α , 4 β , 4 α β , 6 β , 9 α , (α R', β S')), 11 α , 12 α , 12 α , 12 β α) - β -1,1-dimethylethoxy carbonyl-amino - α - carbonyl phenyl propionic acid 12b- acetoxyl-12- benzoyloxy -2 α , 3,4,4 α , 5,6,9,10, 11,12,12 α , 12b- dodecahydro -4, 6,11-trihydroxy -4 α , 8, 13, 13- tetramethyl-5-oxo-7,11-methylene -1H-

cyclodecane pentaene 3,4-benzo 1,2-b oxetane-9-menthone borate (Liu, 2013). Clinical studies have shown that docetaxel has a certain effect for HNSCC treatment. But it is worth noting that docetaxel can only be used under the guidance of doctors with professional experience. During drug use period, to ensure patients' life safety, during the injection of drugs, professionals are needed to monitor main function indicators. In particular in this study, to give full play to the therapeutic effect of docetaxel, carboplatin is used at the same time, which thus should strengthen monitoring on patients' index to ensure patients' safety during treatment (Yan, 2013). During treatment, it needs to be noted that docetaxel may cause allergic reactions in patients. Such case needs timely termination of treatment. The docetaxel drug structure is shown as fig. 5.

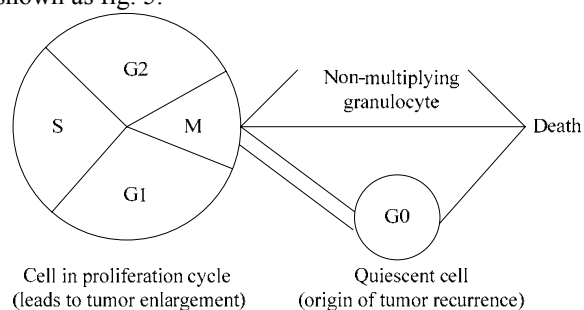


Fig. 4: Tegafur gimer cancer treatment principle

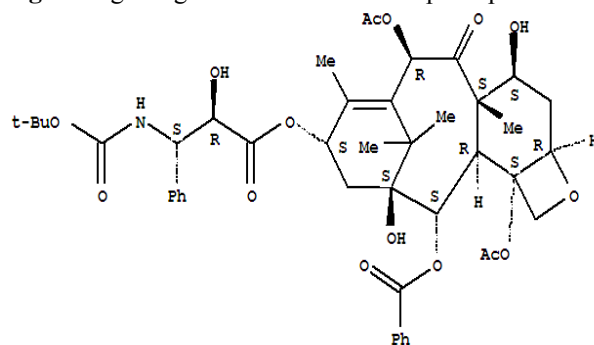


Fig. 5: Docetaxel Drug Structure

Carboplatin belongs to the second generation of platinum compound with similar biochemical characteristic as cisplatin. However, renal toxicity, ototoxicity and neurotoxicity caused by carboplatin is low, security is high. So in recent years, in clinical treatment, medicinal value of carboplatin has been more widely appreciated. Currently, carboplatin is a broad-spectrum anti-tumor drug, with an important role in HNSCC treatment. The carboplatin drug structure is shown as fig. 6.

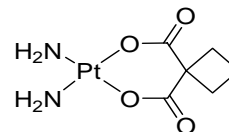


Fig. 6: Carboplatin Drug Structure

In this study, our hospital adopted tegafur gimer, docetaxel, carboplatin for drug therapy of HNSCC patients and good effect was achieved. After treatment,

patients' condition was effectively controlled, and occurrence frequency of toxic and side effect was significantly lower than that of chemotherapy patients, proving that drug therapy is safer. Therefore, this treatment method is worthy to be widely applied in clinical practice.

CONCLUSION

In all, this research fully shows that the combined therapy of tegafur gimeracil oteracil ootassium capsule, docetaxel and carboplatin can achieve sound therapeutic effect in treating head and neck squamous cell carcinoma, effectively control the disease, and have a significant smaller occurrence frequency of side effects as compared with conventional chemotherapy treatment. Therefore, it is suggested to promote such treatment into clinical practice.

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