RESEARCH ARTICLE

Clinical Study on Safety and Efficacy of JiSaiXin (Recombinant Human Granulocyte Colony Stimulating Factor Injection Manufactured in China) for Chinese Undergoing Chemotherapy

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Abstract

Objectives: To assess safety and efficacy of JiSaiXin (Recombinant Human Granulocyte Colony Stimulating Factor Injection manufactured in China, G-CSF) 150ug per day for three days and whether this regimen could reduce the incidence of febrile neutropenia caused by chemotherapy. Method: From July 2014 to December 2014 patients treated by chemotherapy in our hospital were randomly divided into two groups: Group A with prophylactic use of G-CSF (JiSaiXin) 24 hours after chemotherapy for consecutive 3 days; and Group B with G-CSF (JiSaiXin) after neutropenia. Routine blood tests were performed 7 days and 14 days after chemotherapy. Results: A total of 100 patients fulfilled study criteria, and the incidence of severe neutropenia (grade III/IV) and the incidence of febrile neutropenia in Group A were lower than those in Group B. Nine patients were found severe neutropenia (grade III/IV) in Group B, but one in Group A, three febrile neutropenia in Group B, but 0 in Group A. Conclusions: This study suggested that prophylactic use of G-CSF (JiSaiXin) 150ug per day 24 hours after chemotherapy for consecutive 3 days is safe and could be effective for preventing febrile neutropenia in patients with chemotherapy.

Keywords: Prophylactic use - JiSaiXin - chemotherapy - febrile neutropenia

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Introduction

Neutropenia is one of the most common adverse reaction, and one of the dose-limiting toxicities of chemotherapy, Subsequent febrile neutropenia (FN) is related to life-threatening infections, which would result in 7- 11% mortality rate (Caggiano et al., 2005; Kuderer et al., 2006; Lal et al., 2008), Granulocyte colony stimulating factor (G-CSF) could reduce the incidence of neutropenia, FN and infection, the risk of infection-related deaths and a variety of early death risk, and also the incidence of chemotherapy reductions and delays (Kuderer et al., 2007), G-CSF is usually recommended to be administered until neutrophil recovery after the chemotherapy-induced nadir during chemotherapy. Retrospective study showed that prophylactic use of G-CSF was associated with a one-third to two-thirds reduction in the risk of hospitalization for FN (Weycker et al., 2007). Two more recent studies on comparative effectiveness of G-CSF prophylaxis reported similar findings (Tan et al., 2010; Weycker et al., 2011). G-CSF is widely used in China to reduce chemotherapy induced neutropenia. With products manufactured in Main Land China. JiSaiXin is producted by Huabei Jintan pharmaceutical Co. each 150ug.Safety and efficacy of prophylactic use of JiSaiXin is not clear and no standardized use is established. So we designed a comparative study: one group received G-CSF prophylaxis use 24 hours afer chemotherapy for consecutive 3 days, another group received G-CSF only after neutropenia.

Materials and Methods

Patient eligibility

All patients mainly with lung or digestive tract cancers were confirmed by pathologically/cytologically diagnosis and received chemotherapy in Jiangsu Cancer Hospital & Research Institute from July 2014 to December 2014. Eligible patients were those with karnofsky performance status ≥60, aged between 18-75 years, predicted survival time ≥3 months, with adequate bone marrow (white blood cell count>4.0×109 and transaminases<1.5 times and within the upper limit of normal), no evidence of heart and kidney disease, signed an informed consent before chemotherapy.

Patients excluded from the study if they failed to complete two cycles of chemotherapy, with any serious medical or psychiatric condition, other malignancies. Pregnant or lactating women are excluded from the study.

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Table 1. General Characteristics of Patients

	GroupA	GroupB
Median age (range) years	57 (25-77)	56 (29-74)
Gender		
Male	30	29
Female	20	21
Treatment		
Without prior chemotherapy	37	33
With prior chemotherapy	13	17
Primary tumor site		
Gastrointestinal oncology	20	19
Lung cancer	16	12
Other	14	19

Treatment method

Eligible patients were divided into two groups. Patients in Group B received prophylactic use of G-CSF (JiSaiXin) 24 hours after chemotherapy for consecutive 3 days, 150ug Per day , subcutaneouly injected; while patients in Group B received G-CSF after neutropenia. Routine blood test was performed 7 days and 14 days after chemotherapy. Patients were assessed and graded for toxicities according to the National Cancer Institute Common Toxicity Criteria (version2.0) (National Cancer Institute, 1998).

Statistical analysis

SPSS13.0 statistical software was used for statistical analysis. Statistically significant difference was set at $p<0.05$. We have enough experience in conducting medical researches, and have published some results elsewhere (Deng et al., 2013; Huang et al., 2013; Yan et al., 2013; Cao et al., 2014; Cui et al., 2014 ; Gong et al., 2014; Hou et al., 2014; Liu et al., 2014; Lu et al., 2014; Tian et al., 2014; Wu et al., 2014).

Results

One hundred patients were included during the study period, 50 in Group B, and 50 in Group B. All patients received at least two systemic chemotherapy. In Group B, every patients received prophylactic use of G-CSF (JiSaiXin) 150ug per day 24 hours after chemotherapy for 3 days, while patients in Group B received G-CSF (JiSaiXin) only after neutropenia.

In Group B, the mean age was57 (25-77) years and there were 30 male and 20 female patients, including 20 with gastrointestinal, 16 with lung and 14 with other sites of cancer. No patients were diagnosed with FN, thus the incidence of FN was 0%. Seventeen patients were documented with neutropenia (grade I/II), and 1 was found severe neutropenia (grade III/ IV). In Group B the mean age was 56 (29-74) years and there were 29 male and 21 female patients. Including 19 with gastrointestinal oncology, 12 with lung and 19 with other sites of cancer. Three patients were diagnosed with FN, thus the incidence of FN was 6%. Twenty seven patients were documented with neutropenia (grade I/II), and 9 were found severe neutropenia (grade III/ IV). The difference of incidence in liver or with renal function abnormality, shock, acute interstitial pneumonia and myalgia between two groups is not statistically significant ($P>0.05$), General characteristics of patients are shown in Table 1. Adverse reactions are shown in Table 2.

Table 2. Adverse Reactions of Chinese Patients with Prior Chemotherapy and without Prior Chemotherapy

	Group A	Group B
Febrile Neutropenia	0	3
Leukocytopenia		
grade I/II	17	27
grade III/ IV	1	9
Myalgia	3	2
Liver dysfunction	7	8
Renal function abnormality	0	0
Shock	0	0
Acute interstitial pneumonia	0	0

Discussion

Bone marrow suppression is one of the main side-effects of chemotherapy and has serious impact on clinical efficacy. Granulocyte colony-stimulating factor (G-CSF) is a specific hematopoietic regulating growth factor of granulocyte lineage produced by gene recombination technique. It can cause the multipotent hemopoietic stem cells to differentiate into mature granulocytes and macrophages.

According to ASCO recommendations for white blood cell growth factors in 2006 (Smith et al., 2006) and NCCN myeloid growth factors guideline in 2012, G-CSF's primary prophylactic, secondary prophylactic and therapeutic use were stated as follows. Primary prophylaxis was recommended mainly based on the regimens' risk of FN. Secondary prophylaxis with G-CSF was recommended for patients who experienced a neutropenic complication from a prior cycle of chemotherapy outcome, Therapeutic use should be considered in patients with fever and neutropenia who were at high risk for infection-associated complications, or who have prognostic factors that are predictive of poor clinical outcomes. However, patient age, ports; administration of combined chemoradiotherapy, pneumonia, hypotension; poor nutritional status should influence G-CSF's use. So there's no standard use of G-CSF.

Our study found that the difference of incidence in severe neutropenia (grade III/ IV) in Group B who received prophylactic use of G-CSF (JiSaiXin) 150ug per day 24 hours after chemotherapy for 3 days and in Group B who received G-CSF (JiSaiXin) only after neutropenia was statistically significant ($P<0.05$), and the incidence of FN was 0% in Group B but 6% in Group B, while the difference of incidence in liver dysfunction, renal function abnormality, shock, acute interstitial pneumonia (AIP) and myalgia which may caused by using G-CSF between two groups was not statistically significant ($p>0.05$).

There are several bias and limitations inherent in the study, the data are dependent on a small sample size and hence contain errors or omissions when confounding factors exist, eg., variability of chemotherapeutic regimes, sites of cancer, complications of treatment , etc. Otherwise,

in our study G-CSF prophylaxis started 24 hours after chemotherapy and lasted for 3 days, however, the best starting time and duration is unknown Thus, we should recommend to conduct further studies to verify our results and search the best time for G-CSF prophylaxis.

In conclusion, we suggest that prophylactic use of G-CSF (JiSaiXin) 150ug per day for 3days 24 hours after chemotherapy is safe and could be effective for preventing febrile neutropenia in patients with chemotherapy.

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