

## RESEARCH ARTICLE

# Clinical Safety of Chemotherapy for Elderly Cancer Patients Complicated with Hypertension

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### Abstract

**Objective:** To access the safety of chemotherapy for elderly cancer patients complicated with hypertension. **Methods:** Elderly cancer patients who were complicated with hypertension and treated by chemotherapy were recruited. All patients were treated by chemotherapy after an intervention on hypertension by psychotherapy, exercise guidance, salt regulation and nutrition support, therapy on hypertension, as well as prevention on hypertension associated complications. **Results:** In 68 eligible patients, two suspended chemotherapy because of adverse reactions and 4 because of disease progression. The remaining 62 patients completed chemotherapy smoothly based on good hypertension control. **Conclusion:** With effective control of blood pressure, chemotherapy for elderly cancer patients complicated with hypertension is generally safe.

**Keywords:** Elderly cancer patients - hypertension complications - chemotherapy - safety

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### Introduction

Hypertension is one of the most common diseases in China. Because of the acceleration of population aging and the change of dietary habits, the number of patients is continually growing.

Hypertension is a systemic disease, associated with fat and sugar metabolic disorder, functional or physical changes in target organs, eg., heart, brain, kidney and retina. It can cause a variety of complications and seriously affect quality of life of patients. While tumor is another common clinical disease, with the development of economy and the environmental pollution, the incidence rate increases yearly. How to improve the diagnosis and treatment for elderly cancer patients complicated with hypertension, reduce the risk of chemotherapy and finally improving the prognosis is an important research topic of medical research. On this background, we investigate on clinical safety of chemotherapy for elderly cancer patients who complicated with hypertension.

### Materials and Methods

#### Patients

By definition, hypertension is present when there is a persistent elevation of either systolic blood pressure (>140 mm Hg) or diastolic blood pressure (>90 mm Hg), or when a patient is taking antihypertensive medication (regardless of the blood pressure level). Well hypertension control was defined as SBP between 130-110 mmHg and

DBP between 90-70 mmHg.

All eligible patients were required to be pathologically diagnosed with cancer, with hypertension, with Karnofsky performance status  $\geq 60$ , aged more than 65 years, predicted survival time  $\geq 3$  months. With adequate bone marrow (white blood cell count  $> 4.0 \times 10^9$  and platelet count  $> 100 \times 10^9$ ), and liver function (bilirubin and transaminases  $< 2$  times the upper limit normal), no heart and kidney disease, and signed an informed consent before chemotherapy. Patients excluded from this study if they failed to complete two cycles of chemotherapy, with any serious medical or psychiatric condition, or other malignancies. Pregnant or lactating women are excluded from the study.

#### Treatment method

Eligible patients were treated with chemotherapy combined with regimens for blood pressure control, which are constituted by following steps:

**Psychotherapy:** Doctors should have specific knowledge on basic political and cultural condition, consideration, as well as family economic status of patients so as to direct them to adjust healthy consciousness and control emotions. Doctors should also efficiently communicate with patients: stressing the importance of treatment, outlining an economic and suitable treatment plan for individual patients, solve their psychological problems and try to satisfy their needs; explaining to them eg., postoperative adjuvant chemotherapy was usually administered for 4~6 cycles, thus long periods of treatment

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could be delivered. Doctors should especially describe to patients adverse reactions of chemotherapy, eg., digestive tract reaction, hematology toxicities, skin and mucous membrane injury, alopecia as well as high medical expense, because all these adverse reactions could result in moodiness, appeared anxiet, discouraged and irritable. Hypertension could further enhance these negative emotions. Nurses in the department of chemotherapy should create a condition that it is accessible for patients to read humorous books, to view witty images, and to listen some light music so as to divert their attention. Educated nurses should cited successful treatment examples to patients in order to establish anti-cancer confidence. All healthy professionals were required to keep a neat appearance, well-educated behavior and genial attitude to make patients feel comfortable.

**Exercise guidance:** All patients were educated that proper exercise could promote muscular glucose uptake and decrease blood pressure. These proper exercises included walk, setting-up exercise, and shadowboxing etc. Exercise should be done one hour after the meal and one to two hours a day according to physical condition.

**Salt regulation and nutrition support:** Patients should be educated that reasonable salt intake and proper nutrition support are essential to elderly person with hypertension during chemotherapy. The ratio of three major nutrients to the total calories is protein 15-20%, fat<25%, carbohydrates 50-65%. Eating habits and amount of food intake was defined strictly according to dietary prescriptions from dietitians. The diet treatment is a basic treatment for hypertension. Patients with gastrointestinal cancer should pay more attention to diet. Patients should control their daily salt intakes, on the other hand, chemotherapy could cause side effects, eg., nausea and vomiting. Thus, most cancer patients have certain degree of malnutrition, hypoalbuminemia and anemia, they should increase nutrition to improve tolerance for chemotherapy. And they are encouraged to eat food rich in protein, high fiber, a moderate amount of carbohydrates, low animal fat, and avoid foods high in cholesterol. They should eat more fresh vegetables, fruits, appropriate increase of seafood, eg., kelp, seaweed, fish, etc, to improve nutritional status and control blood pressure. Food should be diversified, and well balanced. Intravenous supplement nutrients, eg., amino acid, lipid emulsion was prescribed in case of serious gastrointestinal reactions.

**Intervention on hypertension:** How to prevent cardio-cerebrovascular complications is especially important. Clinical observation on blood pressure should be strengthened and medication should be adjusted according to variation of blood pressure to prevent hypotension. The mechanism of different anti hypertension medications should be adopted strictly, because medication for elderly patients with hypertension should be very careful, hypotension could be caused by severe gastrointestinal side effects, eg., nausea, vomiting, diarrhea, etc. Thus, signs of hypotension, eg., fatigue, palpitation, nausea, vomiting, blurred vision, ochrodermia, cold sweats, etc. should be monitored closely.

**Preventing complications:** Patients are educated that

immunosuppression caused by chemotherapy leads to suppressed immune system. They are at high risk for infection, especially when they are complicated with hypertension. Therefore, measures should be taken to prevent and treat these complications. Patients should be educated that teeth brushing and gargle regularly are effective to control bacteria infection of the mouth, and dress warmly in cold season is important to prevent cold. Patients with sever gastro-intestinal side effects should have medical intervention timely to prevent gastrointestinal hemorrhage, electrolyte disturbances, and acid-base imbalance, etc.

## Results

From January 2011 to December 2012, 68 elderly cancer patients with hypertension were enrolled in this study (16 with esophageal cancer, 14 gastric cancer, 12 colorectal cancer, 14 non-small cell lung cancer, 4 breast cancer, 6 malignant lymphoma and 2 cervical cancer), men 40, women 28, aged from 56-78, each of them was diagnosed as essential hypertension of different degree before admission. There were no severe fluctuation of blood pressure in all patients. Blood pressure of 62 patients was well controlled by monitoring blood pressure and adjusting anti hypertension medications. All patients were successfully treated by chemotherapy.

Sixty patients were treated with diet control, and 8 patients of grade I hypertension treated with diet control and moderate exercise, and they all underwent chemotherapy smoothly based on good hypertension control. Through psychotherapy, exercise, diet guidance, blood pressure monitoring, anti hypertension medication, the blood pressure of 68 patients were able to be effectively controlled, only two patients suspend chemotherapy because of adverse reactions and 4 because of disease progression, the other 62 patients completed 4-6 cycles of chemotherapy smoothly based on good hypertension control. Clinical materials are shown below.

Chemotherapeutic agents included fluorouracil, capecitabine, TS-1, cisplatin, carboplatin, oxaliplatin, paclitaxel, docetaxel, and pemetrexed, etc.

## Discussion

Hypertension is a common medical condition in China. The coexistence of hypertension and cancer in China is also common, and both hypertension and cancer incidence rates have been reported to increase with age (Janssen-Heijnen et al., 1998; Yancik et al., 1998; Yancik et al., 2001; López-Encuentra et al., 2002; Janssen-Heijnen et al., 2004). Hypertension is reported regularly in cancer patients, with estimates of hypertension approaching 40% in cancer populations (Havlik et al., 1994; Satariano et al., 1994; Yancik et al., 2001; Ko et al., 2002; Piccirillo et al., 2004; Tammemagi et al., 2005; Smith et al., 2008; Pereira et al., 2012; Choi et al., 2013). The reported hypertension prevalence is even higher in elderly patients (Satariano et al., 1994; Yancik et al., 2004; Smith et al., 2008).

The onset of hypertension has been reported as an adverse event for numerous cancer therapies, with risk

estimates regularly approaching 10% and in certain instances as high as 36% (Townsend et al., 2006; Yeh et al., 2006; Jain et al., 2007; Daher et al., 2008). Hypertension rates vary greatly by cancer treatment type and dose, and increased risk of developing high-grade hypertension at severe or crisis levels has been observed with more recent cancer therapies, such as those that target vascular endothelial growth factor (VEGF), known as anti-VEGF agents (Cao et al., 2009; Ranpura et al., 2010). The mechanism(s) by which different chemotherapy agents induce hypertension is not fully understood. Potential mechanisms include vascular rarefaction (decrease in microvessel density), decreased sex hormones leading to impaired vasodilator and potentiated vasoconstrictor effects, and endothelial dysfunction causing an interference with nitric oxide (NO) signaling and thereby an increase in oxidative stress (Townsend et al., 2006; Jain et al., 2007; Izzedine et al., 2009).

As hypertension is a risk factor for coronary heart disease, stroke, heart failure, and end-stage renal disease (Izzedine et al., 2009), an improved understanding of hypertension prior to starting chemotherapy, new-onset hypertension during and after chemotherapy, and factors influencing hypertension among cancer patients is paramount. Prior studies have focused on the prevalence of hypertension in cancer patients rather than incidence (Havlik et al., 1994; Satariano et al., 1994; Yancik et al., 2001; Ko et al., 2002; Piccirillo et al., 2004; Tammemagi et al., 2005; Smith et al., 2008), but the incidence of new-onset hypertension is an important clinical outcome that requires investigation. This study uses blood pressure measurements to identify patients with hypertension to access the safety of chemotherapy for elderly cancer patients who complicated with hypertension. During this study, all patients were treated by chemotherapy after an intervention on hypertension by psychotherapy, exercise guidance, salt regulation and nutrition support, therapy on hypertension, as well as prevention on hypertension associated complications, and demonstrated that in 68 eligible patients, two suspended chemotherapy because of adverse reactions and 4 because of disease progression, the rest 62 patients completed chemotherapy smoothly based on good hypertension control. And in conclusion, it is suggested that under the effective control of blood pressure, chemotherapy for elderly cancer patients who complicated with hypertension could be safely conducted.

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