Oncoology database of drug interactions between chemotherapeutic agents and traditional Chinese medicinal herbs that are used in supportive care management

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ABSTRACT

Chemotherapy is often complicated by myelosuppression, fatigue syndrome, pain, nausea and vomiting, and alopecia. The use of traditional Chinese medicinal (TCM) herbs in cancer patients to ameliorate chemotherapy side effects has risen in popularity and these populations consume herbal remedies, often without informing their oncologists. Consequently, severe side effects and herb-drug interactions may result. The objective of this project is to create a database on potential herb-drug interactions. The information on herb parameters and herb-drug interactions was collated from Pubmed, Micromedex® Healthcare Series Version 5.1, and various well-established literatures. The data acquired were organized into table using Microsoft Excel. Among the 151 TCM herbs checked, 45 herbs are commonly used for supportive care management. 41 of these herbs interact pharmacokinetically or pharmacodynamically with chemotherapeutic agents. Ginsengs are the most popular herbs and they exhibit pharmacodynamic interactions with many anticancer drugs, especially procarbazine. Willow bark give rises to the most pharmacodynamic interactions with chemotherapy medicines due to its salicylate content. St. John’s wort induces CYP 450 3A4 enzyme and give rises to many pharmacokinetic interactions with anticancer drugs. This database provides the relevant interaction information to healthcare professionals and helps them detect the potential herb-drug interactions in oncology practice.

INTRODUCTION

Cancer is characterized by uncontrolled cellular growth, local tissue invasion and distant metastasis. Chemotherapy is commonly employed in the management of cancer patients. This approach is often complicated by adverse effects such as myelosuppression, fatigue syndrome, nausea and vomiting, pain, and alopecia (Joseph, 2005). The use of TCM herbal remedies in cancer patients has risen in popularity. These populations concomitantly use herbal remedies and chemotherapeutic agents, usually for palliative purpose (Siljie, 2007) and without informing their oncologists. Consequently, severe side effects and herb-drug interactions may result. Therefore, it is crucial for clinicians to enquire about the history of TCM herbal usage among the cancer patients.
Herbal remedies may interact with chemotherapeutic medicines pharmacokinetically or pharmacodynamically (Skalli, 2007). Pharmacokinetic (PK) interactions influence drug action quantitatively, by increasing or decreasing the plasma concentration levels of herb or drug that is required to exert a therapeutic effect, while pharmacodynamic (PD) interactions influence the action of herb or drug qualitatively, through synergistic or additive effects, antagonizing actions or sequence-dependent events (Charity, 2006).

AIMS/ OBJECTIVES

The objective of this project is to identify the potential interactions between TCM herbs that are used for supportive care and chemotherapeutic medicines from literatures, and create a database on herb-drug interactions that are clinically significant from well-established resources. Both categories of interactions between TCM herbs that are used for supportive care management and chemotherapeutic agents will be emphasized throughout this project.

METHODOLOGY

TCM herbs that are commonly used were identified and the herb parameters were then searched from credible herbal medicine sources. Common names, scientific names as well as Chinese names were checked for the herbs used in this database. Other herb parameters include the main active ingredients, various Chinese properties, mechanisms of actions, therapeutic effects, adverse drug reactions, metabolism routes, as well as various PD and PK parameters. The data acquired were organized into a table using Microsoft Excel.

TCM herbs that are mainly used in cancer patients for supportive care management were used in this database. Potential herb-drug interactions were searched from drug-herb information databases and interaction checkers. Published articles that are relevant to the interaction were also reviewed. The data on herb-drug interactions, such as interaction effects, severity, onset, evidences as well as management of the interaction, were organized into a table using Microsoft Excel.

Information on herb parameters and herb-drugs interactions were collated from Herb-Drug Interactions in Oncology 2003, Pubmed, Micromedex® Healthcare Series Version 5.1, Oncology Nursing Society, Natural Centre for Complementary and Alternative Medicines, PDR health, and various well-established literatures.

RESULTS AND DISCUSSIONS

Many TCM herbs are used in chemotherapy patients for myelosuppression management. Black cohosh, cat’s claw, dong quai, garlic and St. John’s wort are inducers of CYP450 3A4 enzyme and consequently enhance the metabolism of chemotherapeutic drugs like alkylating agent and corticosteroids. There is controversial data and it was not clear whether ginkgo affects the metabolism of these drugs by inducing or inhibiting the CYP450 3A4 enzyme. Bitter melon increases the activity of corticosteroids through additive effect, but astragalus and echinacea reduce the effectiveness of corticosteroids through antagonizing actions. Ginsengs may cause worsening of
depression if use together with procarbazine. Therefore, patients should avoid the use of any ginseng product while taking procarbazine and for several weeks after discontinuation. Bilberry fruit enhances the hypoglycemic effect of rituximab, while butcher's broom and capsaicin may increase the catecholamine secretion of procarbazine. Overall, patients should be advised to take caution when use these TCM herbs, and if possible, avoid their use with chemotherapeutic agents simultaneously.

Astragalus, Asian, American and Siberian ginsengs, dong quai, ephedra, guarana, maté, and St. John’s wort are used by chemotherapy patients to overcome fatigue syndrome. Besides dong quai, ephedra and St. John’s wort which are inducers of CYP 450 3A4 enzyme, all other herbs that are used for fatigue interact pharmacodynamically with anticancer drugs. Astragalus reduces the immunosuppressant effects of cyclophosphamide and corticosteroids, while ginsengs and guarana interact with procarbazine and cause acute headache and elevated blood pressure. Due to the theophylline content in maté, the use of maté in combination with methotrexate, procarbazine and prednisolone should be avoided.

Among TCM herbs that are frequently used for pain management, dong quai, licorice, maté and St. John’s wort may interact pharmacokinetically with chemotherapeutic drugs. It was proposed that licorice may cause corticosteroids stay in the body longer than usual. Consequently, the effects of corticosteroids might be prolonged. This may increase the risk of side effects of corticosteroids as well. Additionally, methotrexate may decrease the clearance of theophylline and caffeine contents in maté. The theophylline content in maté may cause it to interact with procarbazine and prednisolone. Concomitant use of maté and procarbazine will lead to hypertensive crisis, while low potassium levels may result from concurrent use of maté and prednisolone due to additive potassium-lowering effects. Furthermore, willow bark exhibits PD interactions with many anticancer drugs due to the presence of salicylate content. For example, patients may bruise or bleed more easily when using willow bark together with drugs like docetaxel and doxorubicin. Besides, capsaicin may increase the catecholamine secretion of procarbazine. Also, aloe vera should not be taken internally with corticosteroids.

Capsaicin and ginger are the two herbs that are usually administered in chemotherapy patients to alleviate the symptoms of nausea and vomiting. Capsaicin may increase the catecholamine secretion of procarbazine, while ginger may enhance the hypoglycemic effect of rituximab. Caution is required when co-administering capsaicin with procarbazine and ginger with rituximab.

Chemotherapy patients who experience alopecia will usually use fenugreek to counteract this problem although its actual mechanism of action is unclear (Sloan-Kettering, 2003). Fenugreek may inhibit the activity of corticosteroids and have additive hypoglycemic effect on rituximab. Owing to the amine content in fenugreek, it may potentiate the effect of procarbazine. Overall, caution should be taken when use fenugreek in concurrent with these drugs.

CONCLUSION

An oncology herb-drug interaction database was created in this study. PD interactions were found to be relatively more common compared to PK interactions. Ginsengs and willow barks
account for a high percentage of PD interactions, while St. John’s wort interacts pharmacokinetically with majority of the chemotherapeutic agents. This database may provide relevant interaction information to healthcare professionals and help them detect the potential herb-drug interactions in their oncology practice.

REFERENCES


Sloan-Kettering - About Herbs, Botanicals & Other Products. [Internet database]. New York: Memorial Sloan-Kettering Cancer Center. Updated periodically.