MI Q&A

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CAM AND CHEMOTHERAPY

Background

The use of complementary medicines (CAM) in patients with cancer is increasing and is higher than in the general population.[1, 2] Despite many CAM being considered 'safe' when taken alone, there is the potential for interactions or an increased risk of adverse effects when taken in combination with chemotherapy.[3] Given high level evidence and human studies on CAM are severely lacking, potential interactions and problems often need to be identified using in vitro or in vivo animal data, making the clinical significance difficult to establish.

What to consider

General considerations

- Many CAM products contain a number of ingredients. Useful sources of information to determine the ingredients of a product include the TGA Public Summary documents, the manufacturer, the product label and the internet.
- As many CAM are unregistered products, the quality control is not guaranteed and there may be inherent safety risks in the manufacture and/or supply process.
- Most CAM have several different names e.g. botanical name, scientific name, common name, Chinese name. This makes searching for information challenging. In addition, plant species can vary in their potency. Different parts of the plant can also contain different compounds.
- Information may not be easily located in standard resources and access to specialised resources may be required e.g. Chinese Materia Medica. Some potentially useful free resources include Memorial Sloan Kettering Cancer Center About Herbs, National Center for Complementary and Integrative Health, CAM Cancer or the Clinical Oncology Society of Australia Position statement (2013). Some potentially useful resources which require subscription include Natural Products Database (Lexicomp), Natural Medicines and UpToDate.
- Some CAM adverse effects may relate to the dose administered or the route of administration.
- Patients often take more than one product, some of which may have similar or the same ingredients, thereby potentially increasing their exposure.
- The treatment intent of the patient should be considered e.g. if a patient is being treated with palliative intent, recommendations regarding the safety of taking a CAM might differ than for a patient being treated with curative intent. An individual assessment of risk versus benefit is required.
- Certain products will be inherently unsafe e.g. apricot kernel is a source of cyanide and can be unsafe when ingested. Acute poisonings may progress to respiratory failure, coma and death within 15 minutes.[4]

Specific considerations

Potential interactions between CAM and chemotherapy can occur via several different mechanisms including:

Drug absorption

CAM can affect gastrointestinal motility thus affecting the rate or extent of absorption of orally administered chemotherapy e.g. slippery elm may theoretically slow absorption due to its mucilage content.[4]

Drug metabolism

Some CAM and chemotherapy agents are metabolised via cytochrome P450 (CYP)

isoenzymes, uridine diphosphate-glucuronosyl transferases (UGT), or transported via membrane transporters such as P-glycoprotein (P-gp). The clinical significance of theoretical interactions often cannot be established due to limited data.
e.g. turmeric in vitro and in vivo data suggests
- inhibition of CYP 1A1, 1A2, 2D6 and 3A4 isoenzymes
- inhibition of P-gp and
- induction of CYP 2A6 isoenzymes.[4-6]

Doxorubicin is known to be a major substrate of CYP 3A4, 2D6 and P-gp.[7] Therefore, turmeric may potentially increase doxorubicin serum concentrations, increasing the risk of toxicity.

Antioxidant activity

The combined use of CAM with antioxidant activity and chemotherapy agents that generate free radicals is controversial. Some data suggest that antioxidants may reduce the effectiveness of chemotherapy agents that generate free radicals[8] including the alkylating and alkylating-like agents (e.g. cisplatin, carboplatin, chlorambucil, carmustine, cyclophosphamide, busulfan and ifosfamide), anthracyclines (e.g. doxorubicin, daunorubicin and epirubicin) and podophyllotoxin agents (e.g. etoposide).

Antiplatelet/anticoagulant activity

The use of CAM with antiplatelet activity or anticoagulant activity may increase the risk of bleeding in patients who are thrombocytopenic as a result of receiving chemotherapy or their disease e.g. haematological malignancy, or who are being treated with anticoagulant or antiplatelet medicines.

Immune activity

CAM with immune activity (immunostimulatory, immunosuppressive or immunomodulatory) may affect how immunotherapy or immunosuppressive chemotherapy agents interact with the immune system. This could potentially affect activity or toxicity of the immunotherapy or chemotherapy.

Oestrogenic or other hormonal activity

CAM with oestrogenic activity or other hormonal activity may potentially interfere with hormone sensitive cancers and conditions such as breast or ovarian cancer. Consideration should be given to avoiding these CAM in patients with a current hormone sensitive cancer or a history of a hormone sensitive cancer.

Other

Other mechanisms of interaction may also be important, for example:
- resistance e.g. fish oil has been shown to contain high levels of platinum-induced fatty acid 16:4(n-3), which has been shown to induce resistance to chemotherapy in mouse models. A pre-clinical study in mice found that fish oil reduced the activity of cisplatin, irinotecan and oxaliplatin.[9]
- QT prolongation e.g. short term use of panax ginseng has been shown to prolong the QT interval.[4]
- direct inactivation e.g. green tea polyphenols including epigallocatechin gallate (EGCG) have been shown to block the proteasome inhibitory action of bortezomib reducing therapeutic efficacy.[10]

Summary

Pharmacists play an important role in enhancing patient safety and treatment efficacy by identifying potential interactions and problems associated with the use of CAM in combination with chemotherapy.

Being familiar with reputable resources for CAM information and having knowledge of the different factors that need to be considered allows pharmacists to provide clinicians and patients with evidence based information to help them to make informed decisions.

The discussion with patients around CAM use is important and the patient's choice should be respected.

References for this Q&A are available **here**

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