Herbal medications - harmless or harmful?

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"Poisons and medicines are oftentimes the same substances given with different intents"

- Peter Mere Latham (1789-1875)

Plants have been used for medicinal purposes since the Neanderthal period 60 000 years ago. Recent studies in the UK and USA have reported increasing use of herbal medication with incidences of between 4.8% and 32%. 70% of these patients did not disclose this fact during pre operative assessment, often for fear of censure of their use of alternative medical therapies. Patients perceive these medications as "natural" and therefore safe. While these remedies have been used for hundreds of years there is no clear regulation of the herbal medicine sector and the reported content and quality of some products may be questionable.

Herbal medication may be defined as a plant derived product used for health and medicinal purposes. They include a wide spectrum of substances ranging from homemade teas prepared from collected herbs to medicinal products approved by national regulatory bodies. A large number of drugs currently marketed by pharmaceutical companies have their origins in plants. Examples include ephedrine, morphine, cocaine, atropine, quinine, theophylline and aspirin. Many herbal medications include potent contents which would fall within the category of prescription only medication. Herbal remedies may therefore have the potential for significant physiological effect as well as carrying the risk of potentially serious drug interactions.

A UK survey done in 1998 noted that only 21% of herbal remedy users did so on recommendation of a health care provider. The remainder self medicated, their influences being 36% family member or friend, 12% TV/ advertisement and 36% decided on their own to start. Females in the age group 40-60 years were most likely to consider herbal therapy. One out of five patients on prescription medication were using herbal remedies and there was a strong association with over the counter medication increasing the potential for possible drug interactions.

Herbal medication actions, adverse effects and herb-drug interactions.

Herbal medications in routine use include Echinacea, garlic, ginkgo biloba, ginseng, St Johns wort, valerian, ephedra, kava, grapefruit juice and ginger.

ECHINACEA has been used by native Americans since the 1600's. It is prepared from the "above ground" parts of *Echinacea purpurea* (purple cone flower). It has immunostimulatory properties due to enhanced phagocytosis, modulation of cytokines and activation of macrophages and natural killer cells. Current evidence shows that it may decrease severity and duration of the common cold but is not useful as prophylaxis. Further randomised controlled trials (RCTs) are needed as commercial products vary in composition. It has also been used to treat chronic wounds, ulcers and osteoarthritis although there is no evidence to support this at present. Adverse effects include an unpleasant taste, GIT upset and headache and the risk of hepatotoxicity with prolonged use. It is contraindicated in autoimmune disease (HIV, SLE) and patients taking immunosuppressants, as there is a suggestion that prolonged use > 8 weeks may lead to immunosuppression.

Echinacea does not interact with traditional drugs although it is advisable not to use it with known hepatotoxic drugs – anabolic steroids, Amiodarone, Methotrexate, and Ketoconazole.

GARLIC (*Allium sativum*) has been investigated for its antihypertensive effects, although these are short-lived (<2hrs in animal studies) and is not recommended for routine use. The main interest with garlic is its anticholesterol activity. Allicin, a thiosulphate is formed when the garlic bulb is crushed and it inhibits HMG – CoA, an enzyme important in the synthesis of cholesterol. RCTs suggest possible short-term beneficial effects in lowering lipid and cholesterol levels. Adverse effects include nausea (6%), and bleeding as the allicin also inhibits platelet aggregation.

Garlic should be avoided in patients on Warfarin, aspirin and NSAIDs due to its antiplatelet effect. It also has a hypoglycaemic effect and may potentiate antidiabetic agents.

GINSENG is one of the most popular and most expensive herbs sold worldwide. Panax ginseng is the most commonly used; its biological activity is due to ginsenoside (glycosylated steroid) and it is taken as a stimulant and mood enhancer. It also lowers blood glucose levels by increasing the number of insulin receptors and enhancing insulin release. Further RCTs are needed as its efficacy unclear. It may cause bleeding with Warfarin (mechanism unclear), thus avoid use with anticoagulants and NSAIDs. Patients on MAOIs may also exhibit signs of mania.

GINKGO BILOBA extract contains several flavenoids, terpenoids and organic acids that act as free radicals and inhibit platelet activating factors, protecting vascular walls and nerve cells. It also reduces erythrocyte aggregation and blood viscosity. Ginkgo is used treat Alzheimer's and multi infarct dementia; a review of RCTs suggest it is superior to placebo. It is also used to treat claudication where it has again been shown to be more effective than placebo. Adverse effects include mild GIT upset, headache and bleeding as ginkgolide B has anti platelet activity.

Avoid use in patients taking NSAIDS and Warfarin.

ST JOHN'S WORT (*Hypericum perforatum*) is extracted from the plant flowers and leaves. It contains at least 10 pharmacologically active components. It is widely used to treat mild to moderate depression in the short term which has been confirmed with RCTs. It acts through a number of mechanisms, namely inhibition of serotonin, noradrenaline and dopamine reuptake, inhibition of Monoamine oxidases A & B as well as having a high affinity for GABA receptors. Side effects include GIT upset, fatigue, dizziness, confusion, headache and rarely photosensitivity. It increases uterine tone in animal studies and should be avoided in pregnancy.

There have been a large number of reported drug interactions. It should not be combined with anti-depressants as it may result in a serotonin syndrome with SSRIs and tricyclic antidepressants and must be avoided in patients taking MAOIs. St John's wort is a potent inducer of hepatic cytochrome P450 enzymes, notably CYP3A4 and CYP 2C9 as well as the intestinal transport protein P-glycoprotein. This may result in decreased efficacy of Warfarin, Digoxin, Theophylline as well as certain antiretroviral and anticonvulsant medications. It also may decrease the serum levels of Cyclosporin and there have been reports of rejection of

transplanted organs. As St John's wort may cause photosensitivity it is advisable to avoid other photosensitising drugs such as tetracyclines, sulphonamides and Chlorpromazine.

VALERIAN (*Valeriana officinalis*) is derived from a pink flowered perennial. It is suggested that it inhibits degradation and reuptake of GABA and is used as an anxiolytic and to aid sleeping although current data regarding its efficacy is inconclusive. Adverse effects are seen with high doses or prolonged periods of use and include tremor, headache and drowsiness.

Valerian should be avoided where sedative drugs are used, namely benzodiazepines, barbiturates and alcohol and it may cause prolonged anaesthesia. Patients may suffer from withdrawal with discontinuation of therapy.

EPHEDRA (*Ma Huang*) traditionally used to treat asthma and chronic bronchitis, it is now mainly utilised as a stimulant and diet aid. The predominant active component is ephedrine, which is both a directly and indirectly acting sympathomimetic and causes a dose dependant increase in both heart rate and blood pressure. Adverse effects include tachycardia, palpitations, hypertension, myocardial infarction, stroke and seizures. It is contraindicated in ischaemic heart disease, cerebrovascular disease, thyroid disease, diabetes and pregnancy.

Ephedra has the potential to interact with MAOI, CNS stimulants, ergot alkaloids and xanthines.

KAVA (*Piper methysticum*) also known as tonga, kava kava and intoxicating pepper is derived from the dried root of the pepper plant family. It is used as an anxiolytic and sedative with its effects being due to enhanced GABA mediated inhibitory neurotransmission. RCTs suggest superiority to placebo. Long-term use may lead to addiction and tolerance as well as kava dermopathy (reversible scaly cutaneous eruptions).

Concomitant use of Kava and sedative drugs should be avoided as well as use with levodopa as it may potentiate parkinsonian symptoms.

GRAPEFRUIT JUICE contains compounds which may decrease atherosclerotic plaque formation and inhibit cancer cell formation. It inhibits intestinal cytochrome P450 enzyme activity (CYP 3A4) which results in increased serum concentrations of calcium channel blockers, Cyclosporin, Cisapride and antihistamines. Recurrent ingestion of grapefruit juice may actually decrease CYP 3A4 protein expression in enterocytes leading to increased bioavailability of these drugs.

GINGER (*Zingiber officinale*) has been used both as a spice and medication for about 2500 years in India and China. 6-gingerol is the active component which is found in the tuberous root. It is widely used as an anti-emetic with the proposed mechanism of action either direct stimulation of the GIT or serotonin antagonism in the gut or CNS. It also has an anti-inflammatory effect produced by inhibition of arachidonic acid metabolism. No adverse effects or significant drug interactions have been reported although caution is advised with anticoagulants and antiplatelet agents due to the inhibitory effect on thromboxane synthetase.

Safety of herbal medications

While herbal medications may well be harmless, they probably pose a greater risk of adverse effects and interactions than traditional medicine due to the fact that:

1. Most are self prescribed.
2. They are usually bought over the counter or from a source other than a registered practitioner.
3. Current Western use may not reflect the traditional herbal indication.
4. These medications do not require FDA or other regulatory body approval and subsequently there are no safety guidelines regulating consistency and purity of compounds, labelling accuracy or manufacturing.
5. Most herbal medications are not patent – eligible and there is no funding for randomised controlled trials to ensure efficacy and safety.
6. Manufacturers are not compelled to report adverse reactions although these can now be reported by medical practioners via the Yellow card System to the Exeter database in the UK.

Due to the lack of regulation, it is important to be aware of undisclosed contaminants – heavy metals (lead, arsenic, thallium, cadmium), micro organisms, microbials and pesticides, as well as traditional pharmacological additives – NSAIDs, corticosteroids, hypoglycemics, Ephedrine and antihistamines. The anaesthetist must be alert not only for adverse reactions due to the herbal medications but also for undeclared substances and their possible effects.

There is an indirect risk that an herbal remedy without demonstrable efficacy may compromise, delay or replace an effective form of conventional treatment.

Peri-operative implications

1. The increasing use of herbal remedies will result in regular exposure to patients taking these medications.
2. Failure of patients to disclose their use and of practioners to inquire about their use will result in potential drug interactions and unexpected intra –operative surgical and anaesthetic complications – CVS instability
   - coagulopathy
   - sedation
   - adverse immunological effects
3. Patients undergoing anaesthesia are exposed to a large number of pharmacological agents, thus increasing the potential for interactions.
4. Anaesthetists must be aware of potential side effects of herbal medications and be prepared to prevent or manage them.
5. The ASA guidelines suggest discontinuing herbal medication 2 weeks prior to surgery, which is the estimated time for all compounds to be fully metabolised. In practice this is not always possible as many patients are not seen until 2-3 days before surgery and in daycase surgery, on the morning of surgery.

In Summary

Natural does not necessarily mean safe.

Ask your patient if they are taking herbal medication.

Much of the available information is anecdotal. More randomised controlled trials are needed. Since the active ingredients are not consistent from study to study, it is difficult to extrapolate meaningful data from many of them.

Most herbal medications are not patent eligible and there is no clear regulation of the herbal medical sector.

Good website sources of information on further herbal medications:
www.phytotherapies.org
www.herbmed.org

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