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Review Article

Potential effects of herbal medicines and nutritional supplements on coagulation in ENT practice

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Abstract

Background: Herbal remedies and other natural supplements have become popular alternative medical therapy. Patients using these products may present to ENT surgeons with epistaxis or with unexpected, excessive peri-operative bleeding.

Objective: The purpose of this review was to consolidate the available data regarding herb–drug interactions and the direct effects of herbal medicines and nutritional supplements in isolation, regarding disturbance in haemostasis, so as to emphasise their individual importance.

Method: A literature review was performed using the Medline (PubMed) and UKMi databases.

Results: Searches of these databases revealed 24 herbal products with documented interactions with anticoagulants and 98 herbal products with theoretical interactions with the coagulation system. Herbal products with effects on coagulation when given alone were also documented.

Conclusion: When encountering patients presenting with epistaxis, or in the elective surgical setting, a thorough enquiry about the use of herbal medicines is of great importance.

Key words: Herbal Medicines; Haemostasis; Epistaxis; Coagulation

Introduction

Herbal remedies and other natural supplements have become popular alternative therapy for a variety of conditions. Some patients do not consider them truly to be 'medicine', and for that or other reasons may not report use of these substances to physicians.[1] The majority of these products are unlicensed, and awareness among ENT surgeons of their side effects and interactions with prescribed medications is limited. Such an interaction can be defined as a pharmacological or clinical response to the co-administration of a 'traditional' drug or pharmaceutical preparation together with a herbal product.[2] The potential effects of these substances include bleeding, cardiovascular changes, drug metabolism changes and potentiation of sedation.[3]

The use of herbal medications can have a potential effect on haemostatic mechanisms, especially when taken concomitantly with medications known to cause disturbance in the coagulation system. In this scenario, patients may develop epistaxis or unexpected, excessive bleeding during various ENT procedures. Establishing patients' use of herbal products can assist the management of such situations, and may in particular help anticipate those patients who potentially may bleed abnormally during surgery. It is therefore prudent to take a detailed history from patients regarding their use of herbal medications.

The purpose of this review was to consolidate the available data on herb–drug interactions regarding disturbance in haemostasis, so as to emphasise their importance. We have also identified many alternative medicines and nutritional supplements that may have an effect on coagulation if given in isolation. The presented Tables may be copied for reference in ENT departments.

Method

A literature review was performed using the Medline (PubMed) database. Search terms included 'herbal medications' combined with 'bleeding', 'warfarin' and 'anti-coagulant therapy'. Data regarding various herbal medications interacting with anticoagulant treatment or having the potential to disturb haemostasis when given alone were also accessed through the UKMi database.[4] The PubMed database was searched from January 1963 to October 2006. The UKMi database was accessed between July 2006 and August 2006. The search was limited to articles written in English and excluded studies based on animals. Abstracts that met these inclusion criteria were reviewed by the authors and full articles

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were requested. Data thus obtained were tabulated to identify possible herbal–drug interactions in patients receiving anticoagulant therapy, as well as those medications likely to affect clotting on their own.

Results

Searches of the Medline and UKMi databases revealed 136 relevant papers, from which 24 herbal products with documented interactions with anticoagulants and 98 products with theoretical interactions with anti-coagulants and thus effects on the coagulation system.

In addition, many herbal products (Tables I and II) and nutritional supplements (Table III) were identified for which a potential effect on the haemostatic system has been reported when taken in isolation. (Note that such interactions are likely to be a potential problem only when the preparation in question is taken to excess.)

TABLE I

HERBAL PRODUCTS WITH DOCUMENTED OR THEORETICAL EFFECT ON PLATELET FUNCTION

Product	Effect on coagulation
Astragalus*	↓
Bilberry*	↓
Boldo*	↓
Danshen*	↓
Dong quai*	↓
*Gingko biloba**	↓
Allspice	↓
Andrographis	↓
Borage seed oil	↓
Bromelain	↓
Cat's claw	↓
Celery	↓
Dandelion root	↓
Docosahexaenoic acid	↓
Eicosapentaenoic acid	↓
Erigeron plant	↓
Evening primrose oil	↓
Feverfew	↓
Flaxseed oil	↓
Forskolin	↓
German sarsaparilla	↓
Guggulu	↓
Hawthorn	↓
Inositol hexaphosphate	↓
Jiaogulan	↓
Meadowsweet	↓
Sea buckthorn	↓
Pantethine	↓
Policosanol	↓
Poplar	↓
Reishi mushroom	↓
Resveratrol	↓
Sha shen	↓
Shinpi bark	↓
Skullcap	↓
Sweet birch oil	↓
Turmeric	↓
Willow bark	↓
Wintergreen leaf oil	↓
Wood ear mushrooms	↓
Grape seed extract	↓
Mistletoe	↑

*Products with documented interactions with anti-coagulants: ↓ = decreased coagulation; ↑ = increased coagulation.

TABLE II

HERBAL PRODUCTS WITH DOCUMENTED OR THEORETICAL EFFECT ON COAGULATION CASCADE OR WARFARIN METABOLISM

Product	Effect on coagulation
Chondroitin sulphate*	↓
Devil's claw*	↓
Fenugreek*	↓
Lycium*	↓
Melatonin*	↓
Papain*	↓
Saw palmetto*	↓
Curbicin*	↓
PC-SPES*	↓
Agrimony	↓
Alfalfa	↓
Angelica	↓
Aniseed	↓
Asafoetida	↓
Black haw	↓
Bladderwrack	↓
Bogbean	↓
Buchu	↓
Chamomile	↓
Cinchona	↓
Echinacea	↓
Gamma linolenic acid	↓
Horse chestnut	↓
Horseradish	↓
Inositol nicotinate	↓
Ipriflavone	↓
Kava	↓
Licorice root	↓
Lovage root	↓
Mesoglycan	↓
Milk thistle	↓
Passion flower	↓
Prickly ash	↓
Quassia	↓
Red clover	↓
Rue	↓
Sweet clover	↓
Sweet vernal grass	↓
Tonka bean	↓
Vanadium	↓
Wild carrot	↓
Wild cherry	↓
Wild lettuce	↓
Chlorella*	↑
Ginseng*	↑
St John's wort*	↑
Soy*	↑
Avocado*	↑
Acerola	↑
Beetroot	↑
Blond psyllium	↑
Cherokee rosehip	↑
Corn silk	↑
Di-indolylmethane	↑
Mace	↑
Nettle	↑
Nutmeg	↑
Plantain	↑
Rosehip	↑
Yarrow	↑

*Products with documented interactions with anti-coagulants: ↓ = decreased coagulation; ↑ = increased coagulation. PC-SPES = is a mixture of 8 herbs sold as a dietry supplement to treat prostate cancer and to keep the prostate healthy.

Discussion

Many patients assume that because herbal products are naturally derived they are automatically safe

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TABLE III

NUTRITIONAL SUPPLEMENTS WITH DOCUMENTED OR THEORETICAL EFFECT ON COAGULATION

Product	Effect on coagulation
Cranberry*	↓
Garlic*	↓
Grapefruit juice*	↓
Blackcurrant	↓
Capsicum	↓
Chinese rhubarb root	↓
Clove oil	↓
Cod liver oil	↓
Fish oils	↓
Ginger	↓
Parsley	↓
Peppermint oil	↓
Onion	↓
Green tea*	↑
Broccoli	↑
Cabbage	↑
Castor oil	↑
Grape juice	↑
Spinach	↑
Turnip	↑

*Products with documented interactions with anti-coagulants: ↓ = decreased coagulation; ↑ = increased coagulation.

and can therefore be used with conventional medications with impunity.[3] This common misconception of 'natural equals safe' is one of the reasons why patients do not inform their physicians or pharmacists about herbal product use.[5] In the ENT field, *Gingko biloba* has been used for tinnitus and vertigo, echinacea, andrographis and garlic for common cold, and bromelain for sinusitis.[6–12]

Many herbal medicines or alternative healthcare preparations demonstrate anti-platelet properties. Some have salicylate constituents and others contain coumarins and thus affect vitamin K or interfere with the metabolism of warfarin. Thus, inappropiate or excessive use of these products can lead to disturbance in the normal haemostatic system and can present with unexplained bleeding. Patients or healthcare professionals can mistake the effect of an interaction for a toxic adverse effect of the pharmaceutical preparation itself.

The current recommendation by the American Society of Anesthesiologists is that patients should cease herbal medicines at least two weeks prior to surgery.[13] Kaye *et al.* found that 32 per cent of adult patients presenting for elective surgery admitted to taking one or more herb-related compounds (most commonly garlic, *Gingko biloba*, St John's wort, ephedra, echinacea and aloe).[14] Different studies have suggested that between 6.8 and 22 per cent of adult pre-surgical patients report the use of herbal medications, most commonly echinacea, gingko, St John's wort, garlic and ginseng.[15,16]

The nature of ENT operative practice is such that a bloodless surgical field is often crucial to surgical success. Haemorrhage at various anatomical sites has been reported with the ingestion of *Gingko biloba* extract alone or in combination with non-steroidal therapy. Jayasekera *et al.* reported a patient who had been using a herbal medicine containing gingko, which resulted in increased post-operative haemorrhage.[17] Bent *et al.* reported a patient who had taken *Gingko biloba* for six months and who presented with epistaxis, with a bleeding time of greater than 15 minutes (the prothrombin time and activated partial thromboplastin time (APTT) were within normal limits).[18]

A case of excessive intra-operative bleeding has been reported in a patient taking saw palmetto; the bleeding time was increased to 21 minutes, with prothrombin time and APTT again within normal limits.[19]

Weinrobe and Montgomery reported the case of a 62-year-old man taking PC-SPES (is a mixture of 8 herbs sold as a dietry supplement to treat prostate cancer and to keep the prostate healthy), who presented with a history of epistaxis followed by syncope.[20] On presentation, the prothrombin time was >106 seconds and the APTT >120 seconds. The patient was managed with multiple transfusions and vitamin K. Three weeks after the herbal compound had been ceased, the prothrombin time and APTT were within normal limits.

Prolonged clotting time has also been reported in a healthy 32-year-old woman who admitted to heavy garlic ingestion in her routine diet.[21] Her clotting time dropped to normal values after ceasing garlic intake.

A similarly significant increase in bleeding time has also been reported with ingestion of cod liver oil.[22]

Anticoagulant therapy alone is well known as a cause of epistaxis.[23] Patients receiving warfarin therapy should be discouraged from taking herbal medicines, especially preparations which we have identified as having additional anti-platelet and antithrombotic effects. A possible or documented interaction with warfarin has been reported for astragalus, avocado, bilberry, boldo/fenugreek mixture, chlorella, chondroitin, co-enzyme Q-10, cranberry, danshen, devil's claw, donq quai, garlic, *Gingko biloba*, ginseng, grapefruit juice, green tea, lycium, melatonin, papain, St John's wort, saw palmetto and soy.[4]

Lam *et al.* reported a case of elevated international normalised ration (INR) in a patient taking *Lycium barbarum* together with warfarin.[24] Similarly, Wong and Chan reported a case of elevated INR in a patient taking quilinggao concurrently with warfarin.[25] Lambert and Cormier reported a disturbance in INR in a patient taking boldo/fenugreek mixture together with warfarin.[26] Other case reports describe interactions between warfarin and dong quai and danshen.[27,28]

Warfarin has a narrow therapeutic index. It is thus extremely important to emphasise to patients taking this medication which of the aforementioned preparations should be avoided.

Conclusion

When managing patients with epistaxis, or in the preoperative setting, a thorough enquiry about patients' use of herbal medicines is of great importance. The

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potential for interaction between herbal medicines and other medications (especially anticoagulant therapy) must always be borne in mind.

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