
Complementary therapies and anticoagulants

Good or bad companions?

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Airedale NHS Trust

- Covers a mixed urban/rural population of ~220k, within an area including:
 - Much of the Yorkshire Dales
 - Keighley, Ilkley and parts of Bradford
 - Parts of East Lancashire
- Pharmacy have managed the Anticoagulant clinic since 1982
- Currently have ~2100 patients, in both primary and secondary care settings
- Also dose in-patients



What are Complementary Therapies (CTs)?

- “A diverse group of health-related therapies and disciplines which are not considered to be a part of mainstream medical care”
 - *House of Lords Select Committee 2000*
 - The types of treatment patients are not always keen to tell us about!
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How big a problem?

- 19% of anticoagulant patients used some form of complementary therapy
 - 92% never discussed this with GP
 - 8.8% named herbal remedies
 - 28% thought that herbal remedies may interfere with their prescribed medicines
 - *Smith L, Ernst E, Ewings P et al. Co-ingestion of herbal medicines and warfarin. Br J Gen Pract 2004; 54: 439–41*
 - USA – 30% of patients reported as using complementary therapies
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Safety of CTs with anticoagulants

- available evidence

- Overall, at best this could be described at “patchy”
 - Frequently, it’s anecdotal
 - Occasionally, it’s adequate
 - Mostly, it’s inconclusive
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Sources of evidence

- Publications
 - Stockley's Drug Interactions
 - FACT
 - Focus on Alternative and Complementary Therapies
 - Other
 - Internet
 - Magazines
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Consider CTs in 3 groups

- No reported evidence of interactions
 - Appear to be safe
 - Some evidence of interactions
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Appear to be safe

■ Acupuncture

- “Acupuncture appears safe to perform on patients taking warfarin for anticoagulation”

- *Sciammarella, J.; Med Acup 2002, Vol. 13(2) p.15-16*

■ Homeopathy

- “Homoeopathic remedies that are of sufficient dilutions (greater than 30x or 12c) are unlikely to interact with conventional medicines”

- *North West Drug Information Letter 2001; 118: 1*

Appear to be safe

■ Aromatherapy

- No known issues except that Wintergreen oil should be avoided
 - Salicylate content
 - *National Association of Holistic Aromatherapy (USA)*

■ Ayurvedic medicine

- No known issues except possibly with high doses of Turmeric
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Evidence of interactions

- Herbal medicines
 - Chinese herbal medicine
 - Some Natural products
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Herbal medicines

- Many reported to have Anticoagulant activity
 - Coumarin like constituents
 - Inhibitors of platelet activity
 - Hence have a theoretical potential to interact
 - Variation in constituents
 - Frequently not dealing with a standardised product
 - Will limit to only those where a report could be found in the literature
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St. Johns Wort (Hypericum)

- Used to treat mild to moderate depression
 - Probably induces cytochrome P450 enzymes
 - “Interaction of moderate clinical importance”
 - *Stockley's Drug Interactions*
 - CSM recommend that it is best avoided
 - Based upon 4 case reports, 2 showing INR increase 2 decrease
 - Personally – have successfully adjusted warfarin dose in a patient who could not tolerate other antidepressive medicines
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Ginko Biloba

- One of most popular herbal medicines
 - Reported benefits
 - on memory, Antiplatelet effects
 - Single RDBPCT involving patients on stable, long term warfarin showed no change in mean dose of warfarin
 - Isolated report of intracranial haemorrhage associated with the use of Ginko and warfarin
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Ginko Biloba

■ Conclusion

- *'Evidence is far too slim to forbid patients taking warfarin from using Ginko'*
(Stockley)

Ginseng

- Many reported benefits
 - i.e. Neuroprotective, ulcer healing
 - Conflicting information
 - Both case reports and studies in volunteers suggest that ginseng can significantly decrease INR
 - probably due to induction of cytochrome enzymes
 - Spontaneous bleeding has been reported in non-anticoagulated patients
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Ginseng

- Conclusion

- *'Information is conflicting. Be alert for both INR increases and decreases (Stockley)'*

Devil's Claw

- Has anti-inflammatory activity
 - Three papers suggested an interaction between Devil's claw and oral anticoagulants or antiplatelet agents, in particular warfarin
 - Personal experience – single patient had taken it for some weeks without our knowledge with no significant change in INR
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Melilot ‘Sweet Clover’

- Used topically for arthritic symptoms
- Single case of increased INR when used topically
 - *Chiffoleau et al Therapie (2001) 56, 321-7*

Chinese medicine

- Difficult to quantify
 - Often dealing with combinations of substances of varying constituents
 - Frequently not dealing with a standardised product
 - Labelling of contents often unclear
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Dong Quai

- Often used in Chinese medicine for menopausal and menstrual symptoms
 - In vitro studies suggest can reduce Cytochrome enzyme activity
 - Two reports a doubling of INR in a previously stable patient
 - *Page RL and Lawrence JH Pharmacotherapy (1999) 19, 870-6*
 - *Ellis GR Stephen MR BMJ (1999) 319,650*
 - Can be found in commonly available supplements
 - Personal opinion - best avoided
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Danshen

- Used in Chinese medicine for treating various cardiovascular disorders
 - Some constituents have an anti-platelet activity
 - May increase free plasma warfarin levels by reducing binding to albumin
 - Three case reports of increased INR
 - *Yu CM et al J Intern Med (1997) 241, 337-9*
 - Suggest close INR monitoring
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Quilinggao

- Popular combination product said to 'improve general health'
 - Single case report of an elevated INR, bruising and epistaxis in a patient with an otherwise stable INR
 - *Wong AL, Chan TY Ann Pharmacother. 2003 Jun;37(6):836-8*
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Boldo / Fenugreek combination

- Used for 'digestive' problems
 - Neither ingredient recognised as having anticoagulant activity
 - Single case report of modestly increased INR in patient taking a combination product
 - no reported bruising or bleeding
 - Patient's INR stabilised by a 15% reduction in warfarin dosage
 - *Lambert JP, Cormier A Pharmacotherapy (2001) 21, 509-12*
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Curbicin

- Used for problems with micturation
 - Two case reports of INR increases
 - *Yue QY Janseen K J Am Geriatr Soc (2001) 49,838*
 - Mechanism and clinical significance unclear
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Kangen-Karyu

- Combination of several plant extracts
 - Used to 'prevent ageing'
 - Does inhibit warfarin metabolism in mice, but only at doses much higher than used therapeutically
 - *Makino T J Ethnopharmacol (2002); 82(1):35-40*
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Natural products

Lycium barbarum

- Used to enhance immune system
- Isolated case of INR increase
 - *Lam AY et al Ann Pharmacother (2001) 35,1 199-1201*

Garlic

- Certain chemicals in garlic are known to inhibit platelet aggregation
 - Considered beneficial for the cardiovascular system
 - 2 case reports suggest that *high* doses of garlic extract can cause an INR increase
 - *Sunter W Pharm J (1991) 246,722*
 - Considering it's widespread use, an important interaction seems unlikely
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Cranberry juice

- Folklore use for many years
 - i.e. to prevent UTI's
 - <http://www.jr2.ox.ac.uk/bandolier/band6/b6-3.html>
 - Cranberry juice contains various flavonoids known to affect cytochrome P450 enzyme activity
 - However, a straw poll amongst patients at our clinic suggested that most did not drink pure cranberry juice itself but drinks that contained it, frequently in a low concentration
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Cranberry juice

- Until the mechanism has been better studied, the CSM recommends that patients on warfarin should be advised to limit or avoid taking cranberry juice
 - Based upon a few case reports
 - Personally if a patient feels they are benefiting from it, then it's likely to be less harmful than a UTI or antibiotics
 - Our advice keep to same amount and similar brands
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Glucosamine / Chondroitin

- Used for treating arthritic symptoms
 - Combination product widely available
 - Chondroitin may have anticoagulant activity and should be avoided by individuals taking warfarin or other anticoagulants
 - However
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What about Glucosamine on it's own?

- MHRA advice
 - Based upon 7 reports of increased INR after taking glucosamine
 - ? With Chondroitin
 - No mention of clinical significance, bleeding etc
 - “Patients on warfarin are recommended not to take glucosamine”
 - *Current Problems in Pharmacovigilance vol 31, May 2006*
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Is this advice appropriate?

- We had been advising that Glucosamine alone was safe for some years with no observed problems
 - Patients try it because we warn against NSAIDs
 - What will patients use instead?
 - OTC NSAID's, higher dose analgesics
 - Would better MHRA advice have been to suggest closer monitoring?
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Evening Primrose oil / Starflower oil

- Thought to help a variety of symptoms
 - i.e. Menstrual, Eczema, Arthritic
 - Typically contains 2 to 15% gamma-linolenic acid (GLA)
 - GLA can increase clotting times
 - Potential for an additive effect when given with anticoagulants
 - No peer reviewed references could be found
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Fish oils

- High dose use, such as with Omacor, a slight increase in bleeding time has been reported
 - Therefore the manufacturers recommend monitoring and if necessary adjustment of INR
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Fish oils

- Randomised placebo controlled trial concluded that
 - “Fish oil supplementation in doses of 3-6 grams per day does not seem to create a statistically significant effect on the anticoagulation status of patients receiving chronic warfarin therapy”
Bender NK Kraynak MA, et al. Journal of Thrombosis and Thrombolysis. 1998;5(3):257-261
 - Cold liver oil dose commonly advocated for arthritis is a fraction of Omacor dose
 - My opinion very low risk with warfarin
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Vitamin E

- Case report of increased INR
- Double blind study concluded moderate to large doses of vitamin E can be used safely in patients on warfarin
 - *Kim JM White RH Am J Cardiol (1996) 77, 545-6*

Vitamin K

- Combination herbal remedy containing vitamin K reported as reducing INR
 - Is found in commonly available multivitamin preparations
 - Green Tea
 - Single case report of significant INR reduction in a patient who consumed 2-4 litres a day
 - *Taylor JR Wilt VM Ann Pharmacother 1999 Apr;33(4);426-8*
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Ginger

- Has been reported as having the potential for an interaction with warfarin
 - *Am J Health Syst Pharm.* 2000;57(13):1221-1227
- *“No clinical evidence to support an interaction” (Stockley)*

Coenzyme Q10 (Ubidecarenone)

- Conflicting evidence
 - Small number of case reports show both INR increase and decrease
 - *Spigset O. (1994) Lancet Nov 12 Vol. 344, pp. 8933.*
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Summary

Summary

- No published evidence of interactions with some therapies
 - Acupuncture, Aromatherapy, Homeopathy, Ayurvedic medicine
 - Some evidence of clinically significant interactions
 - Herbal medicine, Chinese Herbal medicine, some natural remedies
 - Based upon a small number of reports
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Why do we hear so much about interactions with CTs?

- The media find it newsworthy!
 - Some reports about Cranberry juice were alarmist
 - The Cynic might say it suites the interest of the pharmaceutical industry for Complementary therapies to be portrayed as being unsafe
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The Way Forward

- Complementary therapies have a lot to offer
 - Beware of “Throwing the baby out with the bath water”
 - Encourage a dialog with patients who use CTs
 - Evidence would suggest they will be used by patients with or without our knowledge
 - I would rather prevent a problem than pick up the pieces!
 - Be prepared to increase INR monitoring
 - This would improve understanding of any interactions
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The Way Forward

- Report suspected reactions using the Yellow Card Scheme
 - Beware of turning theoretical problems and case reports into clinical facts
 - More research
 - Who would pay?
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Reporting suspected adverse drug reactions - Mozilla Firefox

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Reporting suspected adverse drug reactions

The Yellow Card Scheme is run by the MHRA and Committee on Safety of Medicines (CSM). The scheme is used to collect information from health professionals and patients on suspected adverse drug reactions (ADRs).

The continued success of the Yellow Card Scheme depends on the willingness of people to report suspected adverse drug reactions.

We collect Yellow Card reports from both health professionals and members of the public on:

- prescription medicines;
- herbal remedies; and
- over-the-counter (OTC) medicines.

We also collect reports on ADRs suspected to be caused by unlicensed medicines in cosmetic treatments.

To complete a Yellow Card Report on a suspected adverse drug reaction please follow one of these links:

Are you a:

- **Healthcare professional** and wish to make a report on behalf of a patient?
- **Patient, parent or carer** and wish to make a report?

Printer friendly version (new window)

Related information:

MHRA pages:

- > Committee on Safety of Medicines
- > Safety of herbal medicines: 'Herbal Safety News'
- > Yellow Card Scheme

Find: yellow Find Next Find Previous Highlight all Match case Reached end of page, continued from top

Done

Start Reporting suspected ... Microsoft PowerPoint - [...]

12:51

Any Questions?



Questions I would like to ask you

- Do you know how many of your patients use complementary therapies?
 - What is your approach when a patient asks about CTs?
 - Glucosamine - what are you recommending?
 - Where do you go for information about CTs?
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