Co-ingestion of herbal medicines and warfarin

Lindsay Smith, Edzard Ernst, Paul Ewings, Patrick Myers and Calli Smith

SUMMARY

Background: A large proportion of patients use herbal remedies with a potential to interact with prescribed drugs. Such interactions can be dangerous, particularly if the therapeutic window of the prescribed drug is small, as with warfarin.

Aims: Our aim was to estimate the prevalence of the use of herbal medicines by patients taking warfarin (co-ingestion).

Design of study: Postal questionnaire.

Setting: General practices in the South West of England.

Method: Thirty-five general practices in Devon and Somerset identified 2600 patients taking warfarin and sent postal questionnaires to them.

Results: One thousand, three hundred and sixty usable responses were received (response rate = 54.2%). One or more of the specified herbal remedies thought to interact with warfarin were taken by 8.8% of all patients. Complementary or homeopathic treatments not specified in the survey questionnaire were taken by 14.3% of responders. Overall, 19.2% of responders were taking one or more such medicines. The use of herbal medicines had not been discussed with a conventional healthcare professional by 92.2% of patients.

Twenty-eight point three per cent of responders thought that herbal medicines might or definitely could interfere with other drugs prescribed by their doctor, however, patients taking any non-prescribed medication were less likely to believe this (χ² = 20, degrees of freedom = 1, P < 0.001).

Conclusion: A substantial proportion of patients taking warfarin in southwest England self-medicate with both herbal medicines that are thought to interact with warfarin and with others of unknown effect, usually without informing their healthcare team. Patients have a responsibility to mention such non-prescribed medication to their general practitioners, and general practitioners also have a responsibility to ask whether such co-ingestion is occurring.

Keywords: alternative medicine; complementary medicine; complementary therapies; drug interactions; herb–drug interactions; self-medication; warfarin.

Introduction

COMPLEMENTARY or alternative medicine, and specifically herbal remedies, have grown in popularity. The usage of herbal medicines by the general population of the United States (US), for instance, increased by 380% between 1990 and 1997. In the United Kingdom (UK), herbal medicine is the most popular branch of complementary medicine. According to these and other survey data, medical herbalism was most commonly employed for allergies, insomnia, respiratory problems, and digestive problems.

The notion that herbal medicines are natural and therefore safe is as widespread as it is misleading. Some of these remedies have been associated with severe adverse effects caused by the toxicity of the herbal ingredients. Others may cause problems because of contamination or adulteration. The most significant risk associated with herbal medicines, however, is that of herb–drug interactions. Despite the fact that this area is still grossly under-researched, the list of herbal medicines with a potential to interact with synthetic drugs is long. Herb–drug interactions are particularly important if the therapeutic window of the synthetic medicine is small. Warfarin is an example of such an agent. As it is a commonly used drug, interactions between herbal medicines and warfarin are of particular relevance (Table 1). Given this background, we wanted to further explore the extent to which patients are taking both herbal medicines and warfarin (co-ingestion).

Method

All practices within the Somerset and North and East Devon Primary Care Research Network area were invited by letter to participate. Each participating practice was paid between £50 and £200, depending on their size, to cover their administrative costs. Approval was obtained from the Ethics Committees of West Somerset, East Somerset and Exeter.

It is normal practice in southwest England for most patients on warfarin to be monitored by their general practitioner (GP). Regular international normalised ratio (INR) tests are carried out and GPs advise on any dose change. Only a small minority of patients attend hospital anticoagulation clinics.

A questionnaire was designed to document the co-ingestion of warfarin and complementary medicines (Supplementary appendix 1). The main target was a specific group of herbal compounds that had previously been implicated for interacting with warfarin: garlic, ginseng, ginkgo biloba, feverfew, ginger, and St John’s wort (Table 1). A small pilot study was undertaken in one Somerset general practice to assess and optimise its level of patient acceptability. The pilot questionnaire was sent to 25 patients. Their responses were excluded from the main analysis and some minor modifications were made to the custom-made questionnaire.

Participating practices undertook a search of their computerised records for all patients who were taking warfarin,
and sent out the questionnaire, a covering letter, and a freepost return envelope to all such patients. Two weeks later, they sent out a short reminder letter to the same group of patients. Replies were returned to the central research office and were anonymous, unless the patient chose to write contact details on the returned questionnaire.

Useable replies were entered onto a database and SPSS was used for analysis. Data were analysed using descriptive statistics. Where appropriate, any relation between patients’ beliefs about herb–drug interactions were analysed by the length of time they had been on treatment, the reason for taking treatment, their sex, and whether they took any herbal medicines. Non-parametric comparisons were done using the Mann–Whitney statistic or Spearman’s correlation coefficient.

## Results

Out of the 159 practices in Somerset and Devon, 35 agreed to participate, and they sent out a total of 2600 questionnaire packs to patients. Of these, 84 patients contacted the research office to say they were no longer taking warfarin, and five packs to patients. Of these, 84 patients contacted the research office and were anonymous, unless the patient chose to write contact details on the returned questionnaire.

Useable replies were entered onto a database and SPSS was used for analysis. Data were analysed using descriptive statistics. Where appropriate, any relation between patients’ beliefs about herb–drug interactions were analysed by the length of time they had been on treatment, the reason for taking treatment, their sex, and whether they took any herbal medicines. Non-parametric comparisons were done using the Mann–Whitney statistic or Spearman’s correlation coefficient.

### Table 1. Data about specific herbal medicines thought to interact with warfarin.

<table>
<thead>
<tr>
<th>Name (Latin)</th>
<th>Main indication</th>
<th>Efficacy demonstrated through rigorous trials</th>
<th>Potential interaction with warfarin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Garlic (Allium sativum)</td>
<td>Hypercholesterolaemia</td>
<td>Yes(^{15})</td>
<td>Increased risk of bleeding</td>
</tr>
<tr>
<td>Ginseng (Panax ginseng)</td>
<td>Various</td>
<td>No(^{16})</td>
<td>Increased risk of bleeding</td>
</tr>
<tr>
<td>Ginkgo biloba (Ginkgo biloba)</td>
<td>Dementia</td>
<td>Yes(^{17})</td>
<td>Increased risk of bleeding</td>
</tr>
<tr>
<td>Feverfew (Tanacetum parthenium)</td>
<td>Intermittent claudication</td>
<td>Yes(^{18})</td>
<td>Increased risk of bleeding</td>
</tr>
<tr>
<td>Ginger (Kaempferia galanga)</td>
<td>Nausea/vomiting</td>
<td>Yes(^{19})</td>
<td>Increased risk of bleeding</td>
</tr>
<tr>
<td>St John’s wort (Hypericum perforatum)</td>
<td>Mild to moderate depression</td>
<td>Yes(^{20})</td>
<td>Increased risk of bleeding</td>
</tr>
</tbody>
</table>

## Discussion

Our results suggest that a considerable proportion of patients...
who take warfarin also self-medicate with herbal remedies. The vast majority do not discuss this with their doctor or other healthcare professionals. Several of the remedies that patients self-prescribe have the potential to interact with warfarin and alter their INR (Table 1). Because patients do not usually raise the subject of co-ingestion with their professional advisers, they are putting themselves at increased risk of side effects such as bleeding. Several reports have been published of incidences in which patients on warfarin have suffered serious harm through herb–warfarin interactions. In our opinion, GPs prescribing warfarin should always ask about these potential interactions because of the widespread and growing use of herbal medicines.

Our survey focused on herbal interactions with warfarin. However, the risks of herbal remedies are not confined to this particular situation. Virtually all herbal medicines are associated with some degree of toxicity owing to pharmacologically active herbal ingredients. Because the herbal medicine sector is under-regulated (herbal remedies are not normally marketed as medicines but as dietary supplements), the quality of some herbal preparations is suboptimal. In particular, there are concerns about contamination, adulteration, and misidentification. The message that seems to emerge is that both doctors and their patients have a joint responsibility to raise the issue of possible or actual herbal medicine use in general, and herb–drug interactions in particular, when warfarin is prescribed. Recently, several books that are well-suited for this purpose have become available.

Since herbal remedies are popular, and most indicators predict future growth of this sector, doctors need to reconsider their general attitude towards this subject. GPs should actively ask patients what form of complementary medicine they are using. Once it has been clarified that a patient uses herbal treatments, it is counter-productive to be dismissive about this topic. Non-judgmental and unbiased information would be more helpful for the patient and less likely to alienate patients from their GP. To give such advice would obviously require GPs to know about herbal medicines. Doctors ‘must tread a line between an apparently sympathetic stance that might be interpreted as an endorsement for unproven therapies and categorical disapproval, which would discourage patients from revealing their use of herbal remedies’. To provide informed advice, the evidence base needs improving. We would strongly suggest further primary care-based research to explore whether co-ingestion of herbal remedies and warfarin definitely causes problems with INR control and/or with side effects such as bleeding. At present it is unknown how frequently co-ingestion causes clinical problems.

Our survey has several significant limitations. It was conducted locally and yielded a suboptimal response rate. We therefore cannot be certain that the results are representative of the UK as a whole. The questionnaires were custom made for our purposes, thus their validity could be questioned. Considering these limitations, our findings should be interpreted with caution.

In conclusion, many patients in southwest England take herbal remedies in addition to warfarin without telling their healthcare team about it. Herb–warfarin interactions could put patients at risk. GPs need to be better informed and patients need to disclose more regularly about any herbal or other complementary medicine co-ingested with warfarin.

Table 2. Reasons stated by responders for taking warfarin.a

<table>
<thead>
<tr>
<th>Reason</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Irregular heartbeat</td>
<td>326 (24.5)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>162 (12.2)</td>
</tr>
<tr>
<td>Heart valve replacement</td>
<td>174 (13.1)</td>
</tr>
<tr>
<td>Deep vein thrombosis</td>
<td>174 (13.1)</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>132 (9.9)</td>
</tr>
<tr>
<td>Heart failure</td>
<td>89 (6.7)</td>
</tr>
<tr>
<td>Stroke</td>
<td>136 (10.2)</td>
</tr>
<tr>
<td>To thin the blood</td>
<td>85 (6.4)</td>
</tr>
<tr>
<td>Not sure</td>
<td>45 (3.4)</td>
</tr>
<tr>
<td>Unspecified clotting problem</td>
<td>9 (0.7)</td>
</tr>
</tbody>
</table>

*a n = 1332, missing values = 28.*

References


Supplementary information

Acknowledgements

We would like to thank all practices and patients who helped by distributing and returning questionnaires, and Mrs Karen Enright for secretarial support.