

Potential Interactions between Herbal Medicines and Conventional Drug Therapies Used by Older Adults Attending a Memory Clinic

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Abstract

Objective: Herbal medicines and conventional drug therapies are often taken in combination. The objective of our study was to identify the range of natural health products and conventional drug therapies used by older adults (aged 65 years and over) attending a memory clinic, and to specifically evaluate the frequency of potential interactions between herbal medicines and conventional drug therapies.

Design: We interviewed consecutive patients attending the Memory Disorders Clinic at the Baycrest Centre for Geriatric Care, a University of Toronto teaching hospital, between 4 July and 15 August 2000. Patients were asked to bring to their appointment all natural health products (i.e. herbal medicines, vitamins and minerals) and conventional drug therapies (i.e. prescription and over-the-counter) they were currently using. We collected information on current and previously used natural health products and current conventional drug therapies. Patients were classified as having the potential for an interaction if they were using a current herbal medicine in combination with a conventional drug therapy and the interaction had been reported previously in the medical literature.

Participants: We interviewed 195 consecutive patients attending the Memory Disorders Clinic at the Baycrest Centre for Geriatric Care, Toronto, Ontario, Canada.

Results: Of the 195 patients in our sample, 33 (17%) were 'current users', 19 (10%) were 'past users', and 143 (73%) were 'never users' of herbal medicines. Among the 52 patients who were 'current or past users', the most frequently used herbal medicines were ginkgo (*Ginkgo biloba*) [39 users], garlic (n = 10), glucosamine sulphate (n = 9) and echinacea (n = 8). Among the 33 patients who were current users, the most commonly used herbal medicines were *Ginkgo biloba* (n = 22), glucosamine sulphate (n = 8) and garlic (n = 6). Among the 33 current users, we identified 11 potential herb-drug interactions in nine patients. The 11 herb-drug interactions we identified were between ginkgo and aspirin (acetylsalicylic acid) [n = 8], ginkgo and trazodone (n = 1), ginseng and amlodipine (n = 1) and valerian and lorazepam (n = 1).

Conclusions: Herbal medicines are widely used. Almost one-third of current users of herbal medicines were at risk of a herb-drug interaction. The most common potential herb-drug interaction was between ginkgo and aspirin. This finding has important potential implications because both of these products are regularly used by older people. Physicians and other healthcare providers should be aware of potential herb-drug interactions and should monitor and inform their patients accordingly.

There is little research examining the safety of herbal medicines, particularly when taken in conjunction with conventional drug therapies (i.e. prescription and over-the-counter), despite the evidence suggesting that they are commonly used simultaneously. Eisenberg et al.^[1] found that among 677 adults who used a prescription drug therapy, almost 20% reported the concurrent use of at least one herbal medicine, a high-dose vitamin, or both. Despite reports of potentially serious adverse events due to herb-drug interactions,^[2-5] no cohort study has assessed potential interactions between herbal medicines and conventional drug therapies among older people, a population consisting of frequent users of both herbal medicines and conventional drug therapies.

We studied potential interactions between herbal medicines and conventional drug therapies among older adults (aged 65 years and over) attending a memory disorders clinic, for two reasons. First, we hypothesised that herbal medicine use may be high in this group. Older adults with cognitive impairment may use herbal medicines, since many herbal medicines target memory loss, depression and insomnia. Second, older adults often have other medical conditions for which they are

taking multiple conventional drug therapies, making them vulnerable for an interaction.

The extent to which older adults are at risk for interactions between herbal medicines and conventional drug therapies is unknown. There is concern that such interactions may be frequent and generally unrecognised.^[6,7] No standardised reporting process is in place in Canada to report interactions between herbal medicines and conventional drug therapies, and associated adverse events. The objective of our study was to identify the range of natural health products and conventional drug therapies used by older adults (aged 65 years and over) attending a memory clinic, and to specifically evaluate the frequency of potential interactions between herbal medicines and conventional drug therapies.

Methods

Population

Our sample included all consecutive patients (n = 217) attending the Memory Disorders Clinic for a follow-up appointment between 4 July and 15 August 2000, at the Baycrest Centre for Geriatric Care, a University of Toronto teaching hospital. Pa-

tients were telephoned prior to their scheduled appointment and asked to bring all natural health products (i.e. herbal medicines, vitamins and minerals) and current conventional drug therapies (i.e. prescription and over-the-counter) to their appointment. We asked about vitamins, minerals, and over-the-counter drugs, in order to determine the range of products older adults in our sample group were using.

Of the 217 patients, 195 (90%) were interviewed. A total of 22 (10%) patients were not interviewed for one of the following reasons: patient did not have time ($n = 17$); patient did not bring medications ($n = 2$); patient declined the interview ($n = 3$).

Interview

The interviews were conducted by two interviewers (JG, DL). As almost all patients were accompanied by a caregiver, the majority of interviews were conducted with the caregiver and the patient. Information was collected on herbal medicines patients were currently using or had used in the past. Current use of herbal medicines and conventional drug therapies was based on the products brought to the interview by the patient. This information was documented and confirmed by the patient and, if present, by the caregiver. The interview also provided an opportunity to obtain a herbal medicine history of past and never users. Past conventional therapies were not assessed. As this population may have had some difficulty recalling herbal medicines used in the past, a list of common herbal medicines was read to patients to serve as a memory trigger. Herbal medicines mentioned by patients that were not on our list were also recorded. From this information, we identified older adults who were 'current users' (those who were currently using herbal medicines at the time of the interview), 'past users' (those who used herbal medicines in the past but were not taking them at the time of the interview) and 'never users' (those who never used herbal medicines either currently or in the past).

Definitions

Herbal medicines, vitamins and minerals were classified as natural health products using a definition consistent with Health Canada.^[8] Natural health products were defined as a substance or combination of substances consisting of molecules and elements found in nature and homeopathic preparations sold in dosage form for the purpose of maintaining or improving health, and treating or preventing diseases/conditions. A herbal medicine is a finished product intended for self-medication that contains, as active principles, herbal ingredients that have received relatively little attention in world scientific literature, but for which traditional use is well documented in herbal references.^[8]

Identifying Potential Interactions between Herbal Medicines and Conventional Drug Therapies

Potential interactions between herbal medicines and conventional drug therapies were identified only among 'current users' of herbal medicines. We classified patients as having the potential for an interaction if they were using a herbal medicine in combination with a conventional drug therapy for which there was documentation for an interaction in both of the following: *Herbs: an everyday reference for health professionals*, published by the Canadian Pharmacists' Association and the Canadian Medical Association^[9] and in a case report or clinical investigation published in the medical literature, identified using a Medline search. We searched Medline from 1980–2000 using the subject headings for each herbal medicine and drug-interactions. The search was limited to articles in English and to those that included human subjects only. Our evaluation of interactions was limited to herbal medicines and conventional drug therapies and did not include vitamins, minerals or teas.

Results

Study Sample

Among the 195 older adults in our sample, the mean age was 73 ± 12 years, and 111 (57%) subjects were female. Patients were divided into three mutually exclusive groups based on their herbal medicine use: 'current users', 'past users' and 'never users'. Table I outlines the demographic characteristics of our sample and the mean number of products being used by each group.

Natural Health Products

Herbal Medicines

Of the 195 patients, 33 (17%) were 'current users' of one or more herbal medicines, 19 were 'past users' and 143 were 'never users' of herbal medicines. Men and women used similar numbers of herbal medicines. Among current users, use ranged from one to five herbal medicines.

Fifty-two patients (27%) were 'current or past users' of herbal medicine. Of these 52 patients, 23 (44%) had tried two or more herbal medicines and 16 (31%) had tried three or more. Among the 52 patients, ginkgo (*Ginkgo biloba*) was the most commonly used, by 39 (75%) patients. Other common herbal medicines being currently used in-

cluded garlic by 10 (19%), glucosamine sulphate by 9 (17%) and echinacea by 8 (15%) patients. In the subset of patients ($n = 33$) who were currently using herbal medicines, 14 (42%) were taking two or more herbal medicines, and 12 (36%) were using three or more. The most commonly used herbal medicines were ginkgo (22 users), glucosamine sulphate (8) and garlic (6). A complete description of the herbal medicines taken by current users and current or past users of herbal medicine is provided in table II.

Vitamins and Minerals

A total of 114 (58%) patients were found to be currently taking a vitamin. The most common were vitamin E (tocopherol) and multivitamin preparations, taken by 41% and 27% of patients, respectively. More than 50% of our sample were taking more than one vitamin (range 1–5). Only 32 people (16%) were using one or more minerals (range 1–3).

Conventional Drug Therapy

Prescription Drug Therapy

Older adults in our sample were frequent users of prescription drug therapies. Of our sample, 189 people (97%) were taking at least one prescription drug (range 1–16). Of these 189, 44% were taking more than one drug. Of the three groups, 'past us-

Table I. Descriptive information of older adults attending a memory clinic. 'Current', 'past' and 'never' users refers to the use of herbal medicines, vitamins and minerals.

	'Current users' (n = 33)	'Past users' (n = 19)	'Never users' (n = 143)
Age (years) ^a	70.2 ± 13.0	68.8 ± 14.0	74.6 ± 11.5
Male no. (%)	14 (42)	8 (42)	62 (43)
Female no. (%)	19 (58)	11 (58)	81 (57)
Current conventional drug therapy use (mean number of products used ± SD)			
Prescription drug therapies	3.5 ± 2.11	4.8 ± 3.69	3.6 ± 2.28
Over-the-counter drug therapies	1.1 ± 1.1	1.2 ± 1.71	0.97 ± 1.36
Total conventional drug therapies	4.61 ± 2.65	6.00 ± 4.9	4.56 ± 3.00
Current natural health product use (mean number of products used ± SD)			
Herbal medicines	2.1 ± 1.47	0	0
Vitamins	2.0 ± 1.17	1.3 ± 1.41	0.79 ± 0.93
Minerals	0.42 ± 0.79	0.26 ± 0.73	0.15 ± 0.37
Total natural health products	4.52 ± 2.73	1.53 ± 1.81	0.94 ± 1.08

a Mean ± SD.

SD = standard deviation.

Table II. Herbal medicine use [no. (%)] by older adults attending a memory clinic

Herbal medicine	Current user (n = 33) ^a	Current or past user (n = 52)
<i>Ginkgo biloba</i>	22 (67)	39 (75)
Garlic	6 (18)	10 (19)
Glucosamine sulphate ^b	8 (24)	9 (17)
Echinacea	0	8 (15)
St John's wort	0	7 (14)
Ginseng	3 (9)	6 (12)
Zinc ^b	4 (12)	5 (10)
Evening primrose oil	2 (6)	4 (8)
Valerian	2 (6)	4 (8)
Co-enzyme Q ^b	3 (9)	3 (6)
Kava	1 (3)	3 (6)
Phosphatidylserine ^b	2 (6)	3 (6)
Lecithin ^b	2 (6)	2 (4)
Melatonin ^b	0	2 (4)
Other (e.g. skullcap, passionflower)	16 (49)	23 (44)

a The percentages in parentheses do not total 100 because some patients were using more than one herbal medicine.

b Nonprescription items that patients reported using when asked about herbal medicine use.

ers' were taking the greatest number of prescription drug therapies (mean 4.84).

Over-the-Counter Drug Therapy

On average, each group was using one over-the-counter drug therapy. Of our sample, 109 people (56%) were taking at least one over-the-counter drug therapy (range 1–11).

Potential Interactions Identified between Herbal Medicines and Conventional Drug Therapies

We looked for potential herb-drug interactions among the 33 current users of herbal medicines. Table II describes the range of herbal medicines being used by our sample of older adults. Among the 33 current users, we identified a total of 11 potential herb-drug interactions in nine patients. Almost one-third of current users of herbal medicines were therefore at risk for a herb-drug interaction. The 11 herb-drug interactions we identified were between ginkgo and aspirin (acetylsalicylic acid) [n = 8], ginkgo and trazodone (n = 1), ginseng

and amlodipine (n = 1) and valerian and lorazepam (n = 1). The details of the potential herb-drug interactions are summarised in table III.

Discussion

Our study is among the first to identify the extent to which older adults are at risk for a potential interaction between herbal medicines and conventional drug therapies. Almost one-fifth of our sample was currently using a herbal medicine. Among current users, almost one-third was at risk for a potential interaction. Because older adults are users of herbal medicines and may be often taking multiple conventional drug therapies, they are a vulnerable population for a potential interaction. While herbal medicines may have some benefit, their concurrent use with conventional drug therapy may lead to an interaction that could result in adverse events.

The most common potential interaction was between ginkgo and aspirin. This finding has important implications for several reasons. First, both of these products are frequently used by older people.^[3] Second, both ginkgo and aspirin are over-the-counter products that can be purchased directly by the patient without the awareness of a health professional. Ginkgo is often taken by older people to improve memory; aspirin is often prescribed for cardiovascular disease. There are documented reports suggesting that this interaction could lead to a potential adverse event. When these agents are taken concurrently, ginkgo may increase the risk of bleeding associated with aspirin. Adverse effects from this interaction can be serious. For example, Rosenblatt and Mindel^[10] reported a case of spontaneous bleeding associated with the concurrent use of ginkgo and aspirin. Our results suggest that we should enquire about patients' herbal medicine use and monitor patients regularly.

Although they were less frequent, we identified the occurrence of three other interactions between herbal medicines and conventional drug therapies in our sample: ginkgo and trazodone, ginseng and amlodipine, and valerian and lorazepam. Ginkgo

may increase the risk of coma when taken in conjunction with trazodone;^[11] ginseng may interfere with blood pressure-reducing effects of agents such as amlodipine;^[12] and valerian may enhance the sedative effects of benzodiazepines such as lorazepam.^[13]

In our sample, more than one-quarter of patients were current or past users of one or more herbal medicines. Our results are consistent with previous study findings. Coleman et al.^[14] evaluated the use of unproven therapies by people with Alzheimer's disease. Among 101 caregivers of patients with Alzheimer's disease attending a support group, more than half had tried at least one alternative therapy designed to improve the patient's memory. Some 20% of these had tried three or more different therapies, including herbal medicines. Similarly, Hogan and Ebly^[15] conducted a telephone interview of 115 caregivers of older adults with cognitive impairment attending a memory clinic. Almost 40% of this group used some form of complementary therapy, which included herbal medicines.

Practical Implications

Herbal medicine use has gained popularity partly because these products are considered 'natural' and are, therefore, generally assumed to be safe.^[16] However, this acceptance of herbal medicines as safe may have serious consequences. Herbal medicines are marketed as dietary supplements and are not subject to the rigorous standards established for conventional drug therapies. As a result, their quality and content are largely unregulated.^[17] Furthermore, in a study by Klepser et

al.^[18] more than 60% of those who used herbal medicines did not disclose this information to their healthcare provider. Similarly, physicians may not routinely ask patients about their herbal medicine use.^[18] Many herbal medicines should not be taken with certain conventional drug therapies, or the patient should be monitored regularly while concurrently using herbal medicines and conventional drug therapies. However, this information is not always communicated between the patient and the healthcare provider. Healthcare professionals must be aware that patients are using these substances. They should discuss this use with patients, and monitor for potential herb-drug interactions, in order to prevent adverse events. This is especially important among older people who are at high risk for an interaction between a herbal medicine and conventional drug therapy.

Interactions between herbal medicines and conventional drug therapies can lead to adverse events, some of which can be serious. The World Health Organization has received more than 5 000 reports of adverse events thought to be related to herbal medicines.^[6] This number is thought to represent substantial under-reporting because patients taking herbal medicines may be less likely to report adverse events when they are associated with a herbal medicine, compared with a similar event associated with a conventional drug therapy. Barnes et al.^[19] found that among 515 herbal medicine users in the UK, approximately one-quarter would consult their physician for a serious adverse event as a result of a conventional drug therapy, but this was not true when the event was associated with a herbal medicine. Herbal medicine users should be

Table III. Potential herb-drug interactions identified among older adults using herbal medicines

No. of current herbal medicine users (n = 33)	No. of potential interactions (n = 11) ^a	Interaction between the herbal medicine and conventional drug therapy	Potential adverse event from the interaction
<i>Ginkgo biloba</i> : 22	8	Aspirin ^[9,10]	Increases risk of bleeding
	1	Trazodone ^[9,11]	Increases risk of coma
Ginseng: 3	1	Amlodipine ^[9,12]	Interferes with blood pressure medication
Valerian: 2	1	Lorazepam ^[9,13]	Enhances sedative effects of benzodiazepines

a We identified 11 potential interactions among nine current herbal medicine users.

aware of possible interactions between herbal medicines and conventional drug therapies and better communicate their herbal medicine use to their physicians.

Limitations

There are limitations in this study. First, our sample is not representative of all older adults. Our study population may be more likely to use herbal medicines and conventional drug therapies because they attend a memory clinic. As well, having additional characteristics about the sample would be helpful. However, this is a group at risk for a potential herb-drug interaction and it provided an opportunity to determine the extent to which potential herb-drug interactions may occur. Second, we have not explored the extent to which physicians and patients are discussing herbal medicine use. It is likely that communication about herbal medicine use is limited. Our research may heighten physician awareness of the potential for herb-drug interactions and the need for patients to discuss their herbal medicine use with their physician. Third, our results may underestimate potential herb-drug interactions. Examining other factors such as frequency of use and dose would also have been important to consider. We did not evaluate interactions with vitamins or minerals. Most people were using vitamins; therefore we may have underestimated the number of natural health products being used. Furthermore, using other sources of information may have identified more interactions between herbal medicines and conventional drug therapies. However, we chose two high-quality sources. In addition, past and never users may have had a problem recalling all of the information correctly, despite the assistance of a caregiver.

Conclusion

Herbal medicines are widely used. Almost one-third of current users of herbal medicines were at risk for a herb-drug interaction. The most common potential herb-drug interaction was between ginkgo and aspirin. This finding has important po-

tential implications because both products are regularly used by older people. Physicians and other healthcare providers should be aware of potential herb-drug interactions and should monitor and inform their patients accordingly.

Acknowledgements

Dr Paula Rochon was supported by a Career Investigator Award, Canadian Institutes of Health Research. Dr Morris Freedman was supported by the Saul A. Silverman Family Foundation, Toronto, Canada, as part of a Canada International Scientific Exchange. Jennifer Gold and Dara Laxer were supported by the Kunin-Lunenfeld Applied Research Unit and a Summer Research Studentship at the Baycrest Centre for Geriatric Care. Julie Dergal, Monica Lee, Malcolm Binns and Krista Lancôt were supported by the Kunin-Lunenfeld Applied Research Unit. The authors have no conflicts of interest directly relevant to the content of this study.

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