ADVERSE EFFECTS OF UNCONVENTIONAL THERAPIES IN THE ELDERLY: A SYSTEMATIC REVIEW OF THE RECENT LITERATURE

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ABSTRACT

Unconventional therapies are increasingly popular, not least in populations of elderly individuals. This review summarizes the evidence regarding the risk unconventional therapies may entail for the elderly. Computerized literature searches were performed to locate all reports with original data on this topic. Most of the evidence found was anecdotal by nature and thus has obvious limitations. The results show that elderly patients can suffer harm from unconventional therapies. Herbal treatments are associated most frequently with adverse events. They can cause both direct toxicity and unwanted herb-drug interactions. Acupuncture, spinal manipulation and even massage therapy have also been implicated. Indirect risks exist if unconventional therapies are employed as a substitute for conventional treatments. It is concluded that unconventional therapies are not risk-free for elderly patients. All parties involved ought to be educated with a view of minimizing this risk, and more research is needed to increase our understanding of this area.

INTRODUCTION

Unconventional treatments have become increasingly popular in the US and elsewhere. Between 1990 and 1997, usage within the US general population increased from 33 to 42% [1]. Similarly, sales figures for herbal medicines have increased almost exponentially and, in 1997, have exceeded \$US 350 million [2]. Elderly individuals have not been excluded from this wave of popularity. A recent survey of US women aged 65 years and over suggested that herbal products were used by 45% of these individuals within the last 12 months; the average number of herbal products used per person was 2.5 [3]. Another survey with US and Japanese geriatric outpatients showed that 74% of older Japanese, 61% of older white Americans and 47% of older African American individuals used at least one 'alternative' medical therapy [4].

While some of these treatments offer some hope for the elderly [5], there may also be risks involved [6]. This article is aimed at reviewing some of the potential dangers of unconventional therapies for the elderly.

METHODS

Computerized literature searches were carried out without language restrictions in the following databases: Medline (via Pubmed), Embase, The Cochrane Library, Amed, CISCOR. The search terms were: acupuncture, adverse effects (events), alternative, Chinese medicine, chiropractic, elderly, geriatrics, herbal medicine (or therapies), massage, phytomedicine, risk, safety, side-effects (events), unconventional (therapies, medicine). The bibliographies of all articles thus found were hand-searched for further relevant publications. All articles reporting original data on adverse events (e.g. case reports, case series, epidemiological studies, clinical trials) in elderly individuals were considered. To be included in this review, the adverse event(s) had to be recent (publications from 1990 onwards) and of a potentially serious nature. The articles thus obtained were read by the present author and are described in narrative form below.

RESULTS

Toxic reactions to herbal medicines

Asian herbal mixtures

Chinese herbal mixtures are often prescribed as individualized mixtures of several plants. Such mixtures have repeatedly been associated with liver toxicity. A 63-year old Chinese woman living in California developed fulminant hepatitis and encephalopathy two months after taking such a mixture containing 12 different plants prescribed by a herbalist [7]. Her life was fortunately saved through a liver transplant. The explant liver showed massive centrilobular necrosis with peripheral bile ductular proliferation and inflammation. The plant implicated from this mixture was *paeonia* sp.

Heavy metal contamination is a problem repeatedly associated with Chinese herbal mixtures. A report from Taiwan [8] describes the case of a 72-year old Chinese woman who took a Chinese herbal remedy for 12 months. She developed loss of appetite, general malaise and other symptoms indicative of lead poisoning. Her blood lead level was tested and found to be elevated at 130 mg/dL. The Chinese herbal remedy was also analyzed and contained 20,000 µg lead/g. The patient was treated with chelation therapy. The eventual outcome was not reported.

Sho-saiko-to is the Japanese name of a Chinese herbal mixture (Xiao-chai-hutang) which is also sometimes called Tj-9. It is composed of skullcap, licorice, bupleurum, Asian ginseng, banxia, jujube and ginger.

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The remedy has been reported to have caused severe pneumonia in two patients [9]. A 61-year old man had taken sho-saiko-to for about 50 days for his liver cirrhosis when he developed fever, diarrhea and dyspnea. CT scan showed fine granular opacities in the upper lung fields. Despite aggressive treatment including corticosteroids and mechanical ventilation, the patient unfortunately died on the 45th day in hospital. Postmortem examination revealed alveolar septal thickening and marked hyperplasia of type 2 pneumocytes in the lungs. The second patient was a 68-year old man who developed pneumonia 8 days after starting sho-saiko-to. He had irregular infiltrates in both lower lungs, bronchoalveolar lavage showed an abnormally high presence of lymphocytes, and biopsy revealed exudates of fibrin and neutrophils in the alveolar spaces with patchy intraluminal organisation. The patient responded to prednisolone and was discharged in his 40th day on hospital. In both cases, drug lymphocyte stimulation tests of peripheral blood were positive to sho-saiko-to.

Chelidonium majus (Greater celandine)

Two elderly patients (aged 65 and 66 years) suffered from acute hepatitis after self-medicating supplements of greater celandine [10]. There were no obvious causes for the condition and liver biopsies revealed signs of moderate drug-induced hepatitis. In both cases, the signs and symptoms normalized within 2-3 months after discontinuation of the herbal remedy.

European herbal mixtures

A 64-year old Belgian woman who had opted to be treated exclusively with "alternative" medicines was admitted to hospital in a confused state [11]. During the subsequent days, her condition deteriorated and she became comatose. The problem was eventually found to be due to bromate intoxication. Amongst her bottles of "alternative" medicines, a product called "Nerventonicum" was found. It contained, amongst other ingredients, 30 g natrium bromatum. The investigators were confident that bromate poisoning was the cause of the patient's condition.

A 69-year old Dutch woman was admitted to hospital with signs and symptoms of hepatitis [12]. She had self-medicated 6 – 15 tablets per day of a herbal mixture (Venencapsan®) containing horse chestnut leaf, milfoil, celandine, sweet clover, milk thistle and dandelion root. She also took levothyroxin and ibuprofen. The usual causes of hepatitis were excluded, the herbal remedy discontinued, and her liver function subsequently normalized. About two months later, her symptoms reappeared shortly after she had restarted the herbal treatment. A liver biopsy showed mild portal inflammation, focal areas of mild steatosis, ballooning and Kupfer cell hyperplasia. The herbal treatment was discontinued for good, and the patient made an uneventful recovery. The investigators were confident that the herbal remedy was the cause of the toxic hepatitis and considered horse chestnut leaf and sweet clover as possible toxic agents.

A 69-year old US man was taking 14 tablets of a herbal mixture when he started experiencing anorexia, weight loss and jaundice [13]. He was admitted to hospital and diagnosed to suffer from toxic hepatitis. All obvious reasons for this condition were excluded and the most likely cause was determined to be the herbal mixture. It contained 21 single plants of which at least two (chaparral and comfrey) had been implicated as hepatotoxic. The herbal remedy was discontinued whereupon the patient fully recovered within 8 weeks.

Ginkgo biloba (Ginkgo)

A 61-year old, previously healthy man presented with a 5-day history of headache, back pain, nausea and sleepiness [14]. He was diagnosed to suffer from subarachnoid hemorrhage. As no plausible reason was found he was questioned about intake of OTC medications and admitted to having taken 40 mg ginkgo tablets 3-4/day for about 6 months. In view of the fact that ginkgo is a known inhibitor of platelet-activating factor, the investigators thought it possible that ginkgo had contributed to the hemorrhage.

Hypericum perforatum (St John's wort)

A 76-year old woman who had an unremarkable medical history and did not take prescribed or OTC medications decided to self-medicate a St John's wort extract at a dose of 75 mg/day [15]. Three weeks later she developed delirium and psychosis and had to be admitted to hospital. She was diagnosed as suffering from Alzheimer's dementia and acute delirium with psychotic features. She was put on risperidone and donepezil. St. John's wort was discontinued. Her condition improved over the course of several days. At follow-up one month later, she had no recollection of the events preceding the hospitalization and her functional level had returned to its pre-hospitalization status. The authors consider St John's wort as the likely cause of the delirium with psychotic features.

Larrea tridentata (Chaparral)

A 60-year old US woman had taken chaparral, a herb recommended for its antioxidant properties, for about 10 months [16]. When she developed flu-like symptoms, she trebled her daily dose to 6 capsules per day. Two weeks later she developed jaundice. On admission to hospital she was confused and later developed sepsis, hypotension, seizures and renal failure. She received orthotopic liver and cadaveric renal transplants. Her explant liver showed large areas of lobular necrosis and collapse, nodular regeneration, marked portal inflammation and bile ductular proliferation. Her post-operative course was complicated by infections and acute rejection of the liver transplant but, eventually, she made a satisfactory recovery. Chaparral has previously been associated with toxic liver damage, and the investigators believe that, in this case, a causal relationship is likely.

Lupinus (Lupin)

A 72-year old Portuguese woman presented to an emergency department with classic anticholinergic

signs: sudden onset of nausea and vomiting, blurred vision, generalized weakness and tachycardia [17]. She had taken a herbal product containing lupin seeds in the belief that it would cure her recently diagnosed type II diabetes mellitus. Analysis of the product identified the preponderant compound as oxosparteine which has powerful anticholinergic effects. Lupin seeds are commonly taken as an appetizer in Southern Europe and the Middle East.

Lycopodium serratum (Jin Bu Huan)

Jin Bu Huan has been used for 1000 years in Chinese medicine mainly as a sedative and an analgesic drug. A 66-year old woman had taken this remedy for about three months for back pain [18]. Subsequently she had developed fever, nausea, fatigue and elevated liver enzymes. The herbal treatment was discontinued and her liver function subsequently normalized. Unbeknown to her physicians, she then resumed her Jin Bu Huan treatment whereupon her liver enzymes again became pathological. The herb was again discontinued. This time the patient did not restart this therapy, and at follow-up her liver function tests were normal.

Mexican herbal mixture

A case of adulteration of a traditional Mexican remedy was reported from the US [19]. A 69-year old man had an 8-month history of painless muscular weakness, particularly of the lower extremities. The patient was concomitantly taking several prescribed drugs for paroxysmal supraventricular tachycardia and chronic obstructive pulmonary disease. He was also diagnosed to have compression fractures suggestive of steroid etiology, and there was a suggestion of moon facies. Urine analysis detected triamcinolone, a drug that he had not been prescribed. Further enquiries revealed that the patient had also taken herbal remedies obtained in Mexico. These tablets were analyzed and found to contain 5.4 mg triamcinolone per dose. Thus the patient's muscle weakness, compression fractures and Cushing-like face were most likely the result of glucocorticoid excess caused by adulteration of the Mexican herbal remedy.

Ophiopogon japonicus (Mai-Meue-Dong-Tang)

This herbal medicine has apparently been used in traditional Chinese medicine for bronchitis, pharyngitis and coughs for the past 2000 years. A 66-year old Japanese woman had self-medicated this remedy and subsequently fell acutely ill [20]. She developed Stevens-Johnson syndrome, a severe type of erythema exsudativum, with bullous and eroded skin lesions over her entire body as well as liver dysfunction. She was treated with corticosteroids and made a full recovery over about one week. A re-challenge with one hundredth of the original dose confirmed a causal relationship between *ophiopogon japonicus* and these adverse events.

Scutellaria (Skullcap)

Skullcap has been repeatedly associated with hepatotoxic reactions. Western skullcap formulations should

originate from *Scutellaria lateriflora*. Yet in the UK, the American germander (*Teucrium canadense*) has been widely used to replace *Scutellaria lateriflora* in commercial skullcap products. A 74-year old woman presented with influenza-like symptoms and jaundice and was found to have abnormal liver function tests [21]. She had been taking several herbs, including skullcap. The authors thought that the herbal medicine was the most plausible cause for her hepatitis.

Teucrium chamaedrys (Germander)

Even though the hepatotoxicity of germander has long been recognized, it is still widely available as a herbal remedy. A 68-year old French woman was admitted to hospital with a 4-week history of jaundice and fatigue [22]. She had self-medicated a herbal slimming aid (Tealine®) which contained germander and *Camellia thea*. She was also on prescribed dexfenfluramine. Her liver tests were abnormal and a diagnosis of toxic liver damage was made after all other causes had been excluded. The patient's condition deteriorated over the next two weeks, a liver transplant was considered but not performed because of her age. Tragically, the patient died of progressive liver failure.

Viscum album (Mistletoe)

A 73-year old man with a 5 year history of centrocytic non-Hodgkin's lymphoma presented with subcutaneous nodules in the abdominal wall at the sites where he had previously received subcutaneous injections of mistletoe, a widely used 'alternative' treatment for cancer [23]. The nodules turned out to be infiltrations by the centrocytic lymphoma. The patient died 6 weeks later of bilateral pneumonia. The authors hypothesized that mistletoe has a growth-promoting action on lymphoma cells, mediated by high local concentrations of interleukin-6 liberated from the skin by mistletoe lectins.

Herb-drug interactions

Based on pharmacological actions, numerous herb-drug interactions can be expected [24]. Because herbal medicines are complex mixtures of pharmacologically active ingredients, the likelihood of herb-drug interactions is considerable. This issue seems particularly relevant for elderly patients who are likely to take one or more prescribed drugs concomitantly. A recent survey showed that older Canadian adults were prescribed 3.6 prescription drugs on average, used 2.3 OTC products (including vitamins and minerals) and 0.6 herbal medicines [25].

Five cases of interactions of St. John's wort (*Hypericum perforatum*) with sertraline have been reported by the same group [26]. A 78-year old woman with a recent history of depression was treated successfully with sertraline 50 mg/day. Her other medications included calcium carbonate and conjugated oestrogens for osteoporosis. She self-prescribed St. John's wort 300 mg three times daily. Four days later, she developed dizziness, nausea, vomiting, and headache. She was advised to stop all medications, and her symptoms resolved over two to three days. She later resumed her

prior prescription medications, including sertraline, with no adverse effects.

A 64-year old man was taking sertraline 75 mg/day for depression [26]. He began taking St. John's wort 300 mg twice daily. He developed nausea, epigastric pain, and anxiety after three days of therapy. His symptoms resumed after stopping all of his medications for one week. He later resumed sertraline in doses up to 100 mg/day with overall improvement in his depressive symptoms.

An 82-year old man, with minimal residual deficits after a stroke, was taking sertraline 50 mg/day for major depression [26]. Overall, he displayed improvement in his mood symptoms. Other medications included aspirin and a multivitamin supplement. Two days after starting St. John's wort 300 mg/twice daily he developed nausea, vomiting, anxiety, and confusion. A CT scan of the brain revealed an old left middle cerebral artery infarction. He was advised to stop both the sertraline and St. John's wort and given oral cyproheptadine for presumed serotonin syndrome. His symptoms improved within five days and he later resumed the sertraline without problems.

A 79-year old man with well-controlled insulin-dependent diabetes was treated with sertraline 50 mg/day for depression [26]. Two days after taking St. John's wort 300 mg three times daily, he developed nausea, anxiety, and feelings of restlessness and irritability. He stopped both antidepressants and cyproheptadine was prescribed for seven days. His symptoms improved within one week, and he later resumed the sertraline.

An 84-year old woman with a long history of depression and anxiety was taking nefazodone [26]. When she developed increasing anxiety she began taking St. John's wort 300 mg three times daily. She developed nausea, vomiting, and restlessness within three days. She was instructed to stop both medications but chose to continue the St. John's wort. Over a one week period, her symptoms gradually improved. At follow-up she continued to display some mild to moderate symptoms of depression and anxiety but refused prescription medications.

A 63-year old patient with a liver allograft developed severe acute rejection 14 months after the transplantation [27]. Two weeks previously he had self-medicated St. John's wort which significantly lowered his cyclosporine levels. His cyclosporine dose had to be doubled at the expense of adverse effects. The patient made a full recovery after the problem was recognized and St. John's wort had been stopped.

Ginkgo biloba taken on its own has been suspected to have caused brain hemorrhage in several instances [28, 29]. There is also reason to suspect that it interacts with warfarin. A 78-year old woman had been maintained on warfarin following a coronary artery bypass five years earlier [30]. Following a two-day history of inability to feed herself, severe apraxia and a change in cognitive deficits, a CT scan of the brain showed a left parietal hemorrhage. Her PT was 16.9 and her PTT was 35.5. An echocardiogram showed no source of embolus,

and the anticoagulation was allowed to reverse. It was later determined that the patient had been taking a Ginkgo preparation (dosage not stated) for two months before the onset of the hemorrhage.

A 70-year old man had been receiving aspirin (325 mg/day) for three years following coronary artery bypass surgery [31]. He was admitted to hospital complaining of blurred vision one week after he had self-medicated with Ginkgo. A fine stream of blood was oozing down from the 12 o'clock position of the margin of the iris into the inferior angle. There was no history of eye trauma, ischemia, or vascular occlusion and bleeding stopped spontaneously after five minutes. The terpenoid ginkgolide B, a component of Ginkgo biloba, is a potent inhibitor of platelet-activating factor [32], and the antithrombotic effects of Ginkgo were demonstrated in an animal study [33].

A 66-year old man had been stable on warfarin for atrial fibrillation when he decided to self-medicate with danshen (*Salvia miltiorrhiza*), a Chinese herbal remedy recommended for a variety of conditions including cardiovascular disease [34]. His other medications included digoxin and propranolol. After experiencing chest pain and melena he was admitted to hospital with overt bleeding from the gastrointestinal tract which turned out to originate from a previously undiagnosed gastric carcinoma. On admission, his INR was >5.5 and his hemoglobin was 7.6 g/dl. Warfarin and danshen were discontinued and the patient was treated with fresh frozen plasma and packed red cells. Danshen has been shown in various test systems to influence blood coagulation through its inhibition of platelet functions [35] and warfarin elimination [36].

A 62-year old man with a history of mitral valve replacement was prescribed digoxin, captopril, furosemide and warfarin [37]. His INR was stable at around 3.0. Two weeks after self-prescribing danshen, the patient presented with non-specific chest pain, increasing dyspnea, and decreased exercise tolerance. He had an increased cardiac silhouette and a massive right pleural effusion. The patient's hemoglobin and platelet counts were 7.6 g/dl and 333x10⁹/L, respectively. His INR was 8.4 and his activated partial thromboplastin time (APTT) was above 120 seconds. The patient's warfarin and danshen were discontinued, and he received fresh frozen plasma and packed red blood cells where upon his INR decreased to 2.0. Over the next two weeks, warfarin was re-introduced and the patient was stabilized on his previous dose of 5 mg/day.

A 74-year old man was noted to have increased serum digoxin concentrations (without signs of toxicity) while taking Siberian ginseng [38]. Common causes of increased serum digoxin were ruled out, and the association with ginseng use was confirmed by dechallenge and rechallenge. It remained, however, unclear whether ginseng was interfering with digoxin elimination or causing a false serum assay result. It was argued that the patient's rise in serum digoxin concentration could have been due to cardiac glycosides contained in *Periploca sepium*, a common substitute for *E. senticosus* [39].

A 64-year old woman experienced insomnia, headache, and tremulousness after adding Panax ginseng to her phenelzine (60 mg/day) therapy [40, 41]. She also consumed ginseng tea and subsequently experienced the same symptoms. She had used ginseng tea prior to her phenelzine therapy with no adverse effects. After stopping ginseng for three years she inadvertently conducted a re-challenge with the same ginseng-containing product taken in addition to her phenelzine. She again became sleepless and tremulous, but also significantly more depressed. Ginsenosides (saponin glycosides in ginseng) inhibit cyclic adenosine monophosphate (AMP) phosphodiesterase; the effects of various ginsenosides on cortical steroid secretion and cyclic AMP phosphodiesterase activity appear to be parallel [42]. These effects of ginsenosides could account for their psychoactive effects.

A 70-year old woman was admitted to hospital with a flaccid quadriplegia which proved to be due to severe hypokalemia [43]. The problem turned out to be the result of relatively small amounts of liquorice (*Glycyrrhiza glabra*) taken in combination with antihypertensive treatment. Liquorice has mineral corticoid effects which may cause potassium and water retention when taken concomitantly with antihypertensive agents.

A 46-year old woman with a history of rheumatic heart disease, stroke, and atrial fibrillation took warfarin, digoxin, and furosemide for atrial fibrillation [44]. Her INR had been stable for two years. Then her INR dropped slightly below the therapeutic goal of 2.0. She denied having missed any warfarin doses or beginning new drugs; however, she had consumed two to three servings of collard greens the previous week. No dosage adjustment was made in her warfarin regimen. A month later her PT was 23.5 seconds and her INR 4.05. No identifiable cause was found. The warfarin dose was held for one day, the dosage of 5 mg/day was resumed, and a one-week follow-up appointment was made but she did not return to the clinic for a month. At that time, an increased PT of 27.0 seconds and an INR of 4.9 was measured. Again, no cause was found. Eventually the patient admitted that, for 4 weeks, she had been taking dong quai for perimenopausal symptoms as recommended by an herbalist. The patient was instructed to miss one day of warfarin, then resume with 5 mg/day, and to discontinue dong quai. Two weeks later, her PT was 21.6 and her INR was 3.41. The patient had discontinued dong quai and required no changes in warfarin therapy. Two weeks later (4 weeks after stopping dong quai), her PT and INR were at therapeutic levels.

A 68-year old Vietnamese-born Australian woman was admitted to hospital following a two-week history of weight loss, anorexia, malaise, leg pain, as well as urinary and fecal incontinence [45]. She was diagnosed to suffer from a recurrence of sarcoma with metastases. During her stay in hospital she experienced a perforated duodenal ulcer, a pulmonary embolus and a urinary tract infection. She was put on warfarin but it proved impossible to stabilize her INR. Her daughter

was observed massaging her legs with an Asian herbal ointment (no further details as to its herbal ingredients provided). The product was analyzed and shown to contain 50% methylsalicylate. The remedy was discontinued whereupon the INR stabilized. The authors think that the herbal topical treatment had potentiated the anticoagulant effect of warfarin.

Acupuncture

Contrary to what many advocates believe, acupuncture is not entirely free of adverse effects and serious complications [46]. Tissue trauma and infection are amongst the most important of these events. A Norwegian survey disclosed a total of 403 adverse events of acupuncture, and 11 of these instances related to patients of 60 years or older [47]. A review of the Japanese literature uncovered 21 cases of infection after Japanese-style acupuncture. Two patients were 80 years or older [48]. Table 1 summarizes recent case reports of adverse events of acupuncture experienced by elderly individuals [49-65]. A 67-year old man was admitted to hospital with a one-month history of intractable back pain and high fever (39.2°C). His white cell count (11900/mm³) and CRP level (20.6 md/dL) were elevated (Origuchi 2000). He reported to have received an unusual type of acupuncture twice, 6 and 7 months prior to admission. This therapy termed 'depot gut' involves the implantation of a plain sheep's gut thread into the meridian point through a spinal anesthesia needle. CT investigation revealed a low density mass in the left psoas muscle and the left ventral portion of the distal aorta. The former turned out to be an abscess and the latter was a false aneurysm. Both were treated surgically and the aorta had to be replaced with a graft. Several foreign-body-type giant cells were scattered in the aortic wall. The patient made a full recovery which was sustained at two-year follow-up. The authors think that this case of infectious aneurysm and psoas abscess was caused by acupuncture.

Spinal manipulation

Spinal manipulation as performed by chiropractors and other healthcare providers has been repeatedly associated with serious adverse events, particularly when performed on the upper spine [66]. A recent review of the published literature (1925-1997) located 177 case reports of serious complications after manipulations of the cervical spine [67]. The age range of the patients thus affected was 4 months to 87 years. Osteoporosis should be regarded as a contra-indication to spinal manipulation. In addition to these probably rare events, spinal manipulation is associated with frequent (~50%) transient mild adverse effects [68]. Table 2 lists recent cases of adverse effects experienced by elderly individuals [69-72].

Massage therapy

Even a treatment as seemingly safe as massage is not entirely risk-free for the elderly. A 61-year old man received a shiatsu massage from a shiatsu therapist at the base of his palm and thenar muscle [73]. Subse-

Table 1: Adverse events of acupuncture in elderly patients.

First author (Year) [Ref number]	Patient	Indication	Therapist (therapy)	Adverse event	Outcome	Causality
Blackard (1991) [49]	64-year old woman	pain	acupuncturist (needle acupuncture)	deep vein thrombophlebitis	full recovery	likely
Keane (1993) [50]	65-year old woman	neck pain	acupuncturist (needle acupuncture)	spinal epidural hematoma	full recovery	likely
Spelman (1993) [51]	61-year old woman	rheumatoid arthritis	acupuncturist (needle acupuncture)	endocarditis	death	likely
Abumi (1996) [52]	60-year old woman	neck pain	acupuncturist (embedded needle)	one needle had penetrated into medulla oblongata and one the dura mater, progressive motor and sensory disturbances	surgical removal of needles, full recovery	certain
Apaloo (1996) [53]	71-year old man with pacemaker	paresthesia in left leg	medical acupuncturist (electro-acupuncture)	interference of electric current with patient's pacemaker; patient fainted	experience was reproduced and subsequently electroacupuncture was abandoned	possible
White (1996) [54]	70-year old woman with pacemaker	neck pain	acupuncturist (needle acupuncture)	cardiac arrhythmias (for 24 hours after acupuncture)	full recovery	possible
Kataoka (1997) [55]	69-year old woman	low back pain	acupuncturist (embedded needles)	cardiac tamponade	cardiac surgery for needle removal, followed by full recovery	certain
Kirschenbaum (1997) [56]	76-year old Chinese man	shoulder pain	acupuncturist (needle acupuncture)	pyarthrosis of the left shoulder joint	arthrotomy with subsequent full recovery	likely
Vilke (1997) [57]	69-year old woman	low back pain	acupuncturist (embedded needles)	cardiac tamponade	cardiac surgery for needle removal, followed by full recovery	certain
Fulde (1998) [58]	74-year old man	arthritis	acupuncturist (needle acupuncture)	large pneumothorax	chest drainage, full recovery	certain
Matusuyama (1998) [59]	72-year old Japanese woman	back pain	physician (needle + electro acupuncture)	pseudoaneurysm of renal artery with rupture	surgery followed by full recovery	
Yazawa (1998) [60]	67-year old Japanese woman	chronic shoulder stiffness	acupuncturist (needle acupuncture)	high cervical epidural abscess with vertebral osteomyelitis	full recovery after antibiotic therapy	likely
Chang-du (1998) [61]	70-year old Chinese man	not mentioned	acupuncturist (electric scalp acupuncture)	episode of angina pectoris	full recovery	possible
	66-year old Chinese woman	not mentioned	acupuncturist (electric scalp acupuncture)	episode of angina pectoris	full recovery	possible
Halvorsen (1999) [62]	60-year old woman	chronic pain	qualified acupuncturist (needle acupuncture)	pneumothorax	full recovery	very likely
Origuchi (2000) [63]	67-year old man	intractable pain	acupuncturist (‘depot gut’)	psoas-abscess, false aortic aneurysm	major surgery, followed by full recovery	likely
Kirchgatterer (2000) [64]	83-year old woman	pain	acupuncturist (needle acupuncture)	perforation of the heart, patient experienced syncope	patient survived	certain
Woo (2001) [65]	79-year old woman	osteoarthritis	not mentioned (needle acupuncture)	hyco bacteriosis	full recovery	likely

Table 2: Adverse events of spinal manipulation in elderly patients

First author (year)	Patient	Indication	Therapist (therapy)	Adverse event	Outcome	Causality
Haldeman (1992) [69]	82-year old woman	knee osteoarthritis	chiropractor and orthopedic surgeon (manipulation)	bone fracture	not mentioned	uncertain
	72-year old woman	pain	chiropractor (23 treatment sessions within 6 weeks)	multiple spinal compression fractures	not mentioned	possible
McParland (1996) [70]	67-year old woman	back pain	massage therapist (craniosacral intraoral)	pain and swelling in temporo-mandibular joint for 1 month	full recovery	likely
Ruelle (1999) [71]	64-year old woman	back pain	chiropractor (manipulation of lumbar spine)	thoracic epidural hematoma	surgical evacuation of hematoma, full recovery	likely
Stevinson (2001) [72]	70-year old man			bilateral vertebral artery dissections, brainstem stroke	full recovery	likely
	'woman in her 60's'			myelopathy, paresthesias in all extremities	permanent neurological deficit	likely

quently he noted a painless weakness of the left thumb without sensory symptoms. The investigators are certain that the forceful approach of shiatsu caused peripheral nerve damage in this case.

A potentially more serious case related to a 72-year old woman who received a vigorous massage of her calf muscles for 10 minutes [74]. Subsequently she developed a pulmonary embolism, and the investigators believed it likely that this complication was caused by a venous thrombosis dislodged through the mechanical action over the peripheral leg veins. The outcome of the patient has not been reported.

Indirect risks

Whenever unconventional treatments are used as a substitute for effective conventional therapy even seemingly harmless treatments may turn dangerous. The case of a 64-year old woman with a metastatic malignant melanoma is a harsh reminder of this type of scenario [75]. Her diagnosis was delayed because of her husband's advocacy of 'alternative' medicine. She finally discharged herself against the advice of her medical team and died 20 days later.

DISCUSSION

These data clearly show that unconventional therapies do carry risks for elderly individuals. The evidence available to date is based almost exclusively on case reports; systematic investigations informing us about the incidence of adverse events in the elderly are so far missing. There are some indications, however, that the problem is not negligibly small: a recent report from the

World Health Organization (WHO) Monitoring Center included 8,985 case reports of adverse events associated with herbal medicines reported between 1968 and 1997. About 650 of the patients concerned were 60 years and older [76].

Elderly people may be at a particular risk to experience adverse effects of herbal treatments. Firstly, their metabolism and elimination of pharmacologically active ingredients may be reduced. Secondly, they are more likely than younger individuals to be multimorbid and thus more likely to take prescribed medicines in parallel with unconventional treatments. This, in turn, increases the risk of herb-drug interactions. The relatively large number of such events mentioned above seem to confirm this notion.

The existing evidence and hence this review have several limitations. Many of the case reports are inconclusive in terms of cause-effect relationship and many lack detailed description of the clinical situation. Often, the assumption that a given problem was caused by an unconventional therapy is based simply on the fact that no other plausible cause could be identified. This review (even though systematic) is most likely incomplete. Many case reports are published as 'Letters to the Editor' often in journals that are not listed in electronic databases. Moreover, under-reporting is likely to be (even) higher than with conventional drugs: patients assume that natural therapies are inherently safe; thus an association between a symptom and an unconventional treatment will often not be made by the patient. And even if it is, many patients do not report to their doctor the fact that they employ unconventional treat-

ments. Even if they do, the doctor is not likely to report such an event in any formal fashion. In a recent case series about serious adverse events of chiropractic, we determined underreporting to amount to exactly 100% [72]. Most countries have no post-marketing surveillance schemes for herbal medicines or other unorthodox treatments. Unconventional therapies (and therapists) remain uncontrolled and unregulated in most parts of the world.

How can the safety for elderly patients be increased? Healthcare professionals should be familiar with all treatments their patients use regardless whether these are conventional or unconventional [77]. Given the present popularity of unconventional therapies they should familiarize themselves with this subject with a view of being in a position to advise their patients responsibly. Rigorously evidence-based texts to inform themselves have recently become available [78]. Regulators should re-consider their position in respect to some of the treatments involved, particularly herbal medicine. To give this sector a "free ride" does not seem to be an option that is in the interest of the patient. Last but not least, the patient should be educated and needs to learn that 'natural' does not always mean 'safe'.

CONCLUSION

In conclusion, unconventional therapies can cause harm to elderly patients. At present our understanding of this is incomplete. More research and educational efforts are therefore needed.

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Abbreviations:

AMP = Adenosine Monophosphate Rate

APTT = Activated Partial Thromboplastic Time

INR = International Normalized Ratio

PTT = Partial Thrombine Time

WHO = World Health Organization

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