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Herbs, health and hazards; a nephrology viewpoint on current concepts and new trends

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Abstract

Existence of effective component such as scent, flavor and therapeutic properties in herbs make them suitable as dietary supplement and remedies. Many people believe that products labeled "natural" are always safe and good for them. This is not necessarily true. Herbal medicines do not have to go through the testing that drugs do, but a nephrology view point on one hand may indicate lots of renal injury caused by herbal drugs and on the other hand some beneficial medicinal plant in order to treatment of kidney chronic diseases. Hence, this study has been tried to give some significant information about herbal supplement you are taking.

Introduction

Using of herbal medicines has been increased universally in recent years, and dietary supplements to treat various chronic diseases and to promote health. It is predicted that, world population will be more than 7.5 billion in the next years (1). A vast percentage of people have confidence in traditional practitioners of medicinal plants for their medical needs in developing countries (2). The historical usage of herbal medicines has helped in preparation of existing drugs from medical plants. Use of medicinal plants is as old as human civilization and continuous efforts are being made towards its perfection. About 200 000 biologic products are known from plant origin. Some plants with drug base have been used for centuries. Hence, medicinal plants and their bioactive molecules are in demand forever and also a central point of research (3). Traditional use of herbal medicines implies substantial historical use, and this is certainly true for many products that are available as 'traditional herbal medicines.' In many developing countries, a large proportion of the population relies on traditional practitioners and their armamentarium of medicinal plants in order to meet health care needs (4). The pharmacological treatment of disease began long ago with the use of herbs methods of folk healing throughout the world commonly used herbs as part of their tradition. Properties of medicinal plant are due to the presence of various complex chemical ingredients classified as flavonoids, alkaloids, glycosides, saponins, tanins, carbohydrate and essential oils (5). Many medication currently used in conventional medicine are obtained from natural plants. For instance, metformin which is common remedy for administration of type 2 diabetes with hypoglycemic activity is derived from *Galega officinalis* (6).

Core tip

Existence of effective component such as scent, flavor and therapeutic properties in herbs make them suitable as dietary supplement and remedies. Many people believe that products labeled "natural" are always safe and good for them. This is not necessarily true. Herbal medicines do not have to go through the testing that drugs do, but a nephrology view point on one hand may indicate lots of renal injury caused by herbal drugs and on the other hand some beneficial medicinal plant in order to treatment of kidney chronic diseases.

Materials and Methods

This review article discusses the administration, antioxidant and toxic properties, safety of herbal drugs and also has a nephrology viewpoint of consumption of natural medicine. For this review, we used a variety of sources by searching through Web of Science, PubMed, EMBASE, Scopus and directory of open access journals (DOAJ). The search was performed using combinations of the following key words and or their equiva-

lents such as medicinal plant, antioxidant activity, toxicity, safety, kidney and herbal drugs.

Administration of herbal drugs

The consumption of medicinal herbs without studies of efficacy and safety can result in several side effects that may affect various parts of the body. Studies using medicinal plants for the treatment of various disorders must be aware of the possibility of renal toxicity.

Herbal remedies are drugs, plain and simple. They contain chemical compounds that are consumed on a systematic basis for their pharmacological effects (7). The fact that they derive from plants is irrelevant. The point that specific chemicals are not refined and given is precise amounts does not mean they are not pharmacologically active biochemical but means that when taking medicinal herbs you are getting a mixture of many chemicals in unknown doses (8). The use of alternative drugs separated from plants and animals is increasing all over the world. But they are not tested for efficacy and safety; their ingredients are unidentified and the amount and route of administration are not regular. Potentially toxic chemicals are added to them to increase their effectiveness and erroneous identity has led to the use of toxic plants instead of the originally anticipated herb. Public awareness and regulation of the use of these medicines are required to eradicate illness from the community (9).

Antioxidant activity

There is an increasing interest in natural antioxidants, such as polyphenols, present in medicinal and dietary plants, which might help preventing oxidative damages caused by free radicals. It has been determined that the antioxidant effect of plant products is mainly attributed to phenolic compounds such as flavonoids and phenolic acids. Herbal medicines have been focused as a new resource of antioxidants elements with limited obstacles. Natural antioxidants can protect the human body from free radicals and delay the growth of many chronic diseases such as retarding the lipid oxidative rancidity in foods (10). Current studies have evaluated the capacity of plant products as antioxidants against various diseases induced by free radicals. Total antioxidant capacity of plant mostly depends on not only the content and composition of phenolic compound, but also on the contents of other antioxidants, for example ascorbic acid. Besides that there could be synergism or antagonism between the active combinations. Thus, the assessment of antioxidant activity in real materials is very difficult and the total antioxidant effects must be defined experimentally. Because seasonal changes affect the contents of plants too, it is difficult to compare the activities of different plants (11).

Toxicity

On one hand herbal medicines are extensively used in the developing world, where in many places they suggest a more widely available and reasonably priced alternative to pharmaceutical drugs. Many people believe that herbal medications are more natural than pharmaceuticals and it can be a strong reason for the growing popularity of medicinal plants.

But on the other hand herbal remedies, can cause different illnesses, from allergy to liver or kidney malfunction, to cancer, and even death (12).

While some of people who use complementary and alternative medicines (CAMs) have been increased, there are rising clinical reports on the organ toxicities associated with consumption of herbal drugs in recent years due to an enhancing proportion of the populations that have been using CAMs. This matter and the potential toxicities of herbal remedies may suggest the probable renal toxicity caused by medicinal plants. Toxicity testing can reveal some of the risks that may be associated with use of herbs (13). In addition to, many plants produce toxic secondary metabolites as natural protection from adverse conditions. In some toxicologic and medicinal relevant plant species like *Digitalis purpurea*, *Podophyllum peltatum* and *Solanum nigrum*, these contaminated substances are not separated from therapeutically active elements. Being stationary autotrophs, plants have evolved different means of alteration to tackle with environments and co-existence with herbivores and pathogenic microorganisms. Thus, they make a range of metabolites named 'phytoanticipins' or as general 'phytoprotectants' that are stored in specialized cellular sections and released after specific environmental stimuli like damage due to herbivores, pathogens or nutrient depletion (14).

Some of the phytochemicals produced by plants against herbivorous insects also end up being dangerous to humans, due to vastly conserved biological resemblances are shared between both taxa as seen in most pathways involving carbohydrate, nucleic acid, protein, and lipid metabolism. Human neurochemicals, often with similar biological functions are also reportedly present in insects. These include signaling molecules, neuropeptides, hormones and neurotransmitters; whose functions can be mimicked or antagonized by phytochemicals like alkaloids, flavonoids, terpenoids and also saponins (15).

A large amount of alkaloids provide feeding deterrents via agonistic or antagonistic activity on neurotransmitter systems. Similarly, some lipid soluble terpenes have shown inhibitory properties against mammalian cholinesterase, whilst some interact with the GABAergic system in vertebrates. In addition to these, saponins are strong surfactants that can interrupt lipid-rich cellular membranes of human erythrocytes and microorganisms which describes the potent antimicrobial features of this group of phytochemicals. Aristolochic acid, a nitrophenanthrene carboxylic acid in *Aristolochia* species and available in other botanicals has also been identified as a toxic phytochemical implicated in the occurrence of nephropathy and carcinogenesis (16).

Another implication in the toxicity of individual herbs is the existence of toxic minerals and heavy metals like mercury, arsenic, lead and cadmium. Lead and mercury can intimate severe neurological injury. Toxicity and also safety of some herbal ingredients has been called into question

recently, due to the detection of adverse events associated with their use and, increasingly, because of the illustration of clinically relevant interactions between herbs and prescription drugs (17).

Safety issues of herbal medicines

Traditional herbal products are heterogeneous in nature. They need various tests for quality control and the regulatory process. Most herbal products on the sell have not been for safety and effectiveness. They may possess arsenic, lead, mercury and corticosteroids as well as toxic organic substances in harmful amount (18). Hepatic failure, renal failure and death after consumption of medicinal plants have been reported. Side effects of some medicinal plants are currently reviewed. Sometimes patients use traditional and conventional remedies instantaneously. The relation of these two drugs may be dangerous and have raised serious alarm among experts about the care of the patients. Plant materials are used through developing and developed countries, over-the-counter drug products and raw materials for the pharmaceutical industries, and symbolize a fundamental section of universal medication market. It is therefore essential to establish internationally recognized guidelines for assessing their quality. The safety of drugs that are derivate from herbal resources and supplement use is of particular concern in patients with renal disease, and reliable evidence is not always available. Because dialysis patients believe that CAM can help prevent the progression of their renal disease may be drawn to use of this therapeutic system (19).

A nephrology viewpoint

Kidneys are the main victim because they are involved in the degradation and excretion of a myriad of chemical materials. It is suggested that renal injury has been accompanying with the use of the medicinal plants in the treatment of different disorders. Traditional herbal treatment is one of CAM, which is broadly used by many people to treat a range of different diseases, including diabetes**.** Kidneys play the main role in excretion of these substances and acute kidney injury is a regular and significant sign of their poisonous properties (20).

The most usual renal lesions include interstitial nephritis, acute tubular necrosis and cortical necrosis. Patients often present late to hospitals with multi-organ involvement. The diagnosis might be ignored without having the history. These factors culminate in high mortality rates. Research about this entity is hard due to the remoteness of the areas, unfamiliarity with local cultures, and secrecy (21). The use of herbal remedies is common in large parts of the developing world, especially amongst the rural population. The use of complementary and alternative herbal medicines increased in the treatment of various diseases. Some herbal treatments can be a reason for potential toxicity that may be renal toxicity caused by the ingestion of herbs. Since kidneys play a vital role in the metabolism and excretion of these substances and acute kidney injury is a common and important manifestation of their toxicity. Also the most usual renal lesions include acute tubular necrosis, cortical necrosis, and interstitial nephritis (22). Several factors, such as active uptake by tubular cells and high concentration in the medullary interstitial, make specifically the kidneys vulnerable to toxic insults. Therefore, herbal medicine may be the source of kidney injury. Renal involvement associated with the use of traditional medicinal products can take several forms including acute kidney injury, tubular function defects, renal papillary necrosis, dyselectrolytaemias, systemic hypertension, chronic kidney disease (CKD), urolithiasis and urothelial cancer. Patients with pre-existing CKD can extend difficulties due to medicinal plant use; some cases are *Ginkgo biloba*-induced hemorrhagic complications, AAN became identified to western physicians in early 1992 when Vanherweghem et al discovered two similar cases of rapidly progressive fibrosing interstitial nephritis in young women. It was later found that one herb in a weight-reducing formula (*Stephania tetrandra*) was inadvertently replaced by *Aristolochia fangchi* by through the suppliers. Also *A. fangchi* contains AA, a nephrotoxic and carcinogenic alkaloid (23).

Herbs and kidney disease

Some medicinal plants for example *Berberis vulgaris*, *Nigella sativa*, *Phyllanthus niruri* and *Oenothera biennis* are consisted of two common flavonoids such as catechin and epicatechin, strongly decrease calcium deposition in kidney stone, so these herbs are useful in treatment of urinary calculi that is one of the most painful disorder known to men, because the antioxidant activity of these substances inhibited peroxidative damage to the renal tubular membrane surface (18,21). The other common kidney disorder is glomerulonephritis that have an underlying autoimmune pathogenesis and are routinely treated with corticosteriods and various cytotoxic drugs. Some of the most common forms of chronic glomerulonephritis like immunoglobulin A-nephropathy and membranous nephropathy actually loss effective treatment concepts. The response towards cytotoxic drugs is highly variable and not reliably predictable. Recently, reported remissions of membranous nephropathy following using of an herbal remedy obtained from *Astragalus membranaceus* refreshed prospects and curiosity among patients and nephrologists. So nephrologists have a generally enhanced awareness into complementary and alternative therapies and a change of their traditionally reluctant attitude towards herbal drugs appear to be the consequence. *Astragalus* has been studied in animal models of renal disease for its effect on reactive oxygen species (ROS) and cytokines, reperfusion injury, and mechanisms of renal fibrosis. Quite different kidney disorders give out the pathologic mechanisms that initiate renal fibrosis in their final stage. *Astragalus* can lead to decrease proteinuria and adriamycin-induced nephrotic syndrome in animal models of immune complex nephritis (24).

On the other hand, use of herbal supplements may be unsafe for CKD patients, since your body is not able to clarify left-over outcomes similar to a healthy human. Firstly,

CKD patients should know some significant facts about herbs since use of few plants have been examined in CKD patients. Also not only safe herbal drug for healthy persons may not be safe for someone but also can be hazardous for patient with chronic kidney disorder so they need to be very cautious about their use of these products. Secondly, the exact content, purity, safety and effectiveness of these products are unknown and there are lots of complicated requirement for testing. Thirdly, all CKD patients should consider possible impurity in herbal preparation because they can be contain toxic heavy metals such as lead or mercury and to tell the truth these herbal remedies may contain harmful mineral for CKD patients like potassium (19,23). Furthermore some herbs that may serve as diuretics may also lead to "kidney damage or irritation, like bucha leaves and juniper berries, moreover Uva Ursi and parsley capsules also can have destructive effects too. Some herbs such as Echinacea, ginkgo, garlic, ginseng, ginger, and blue cohosh can interfere with prescription drugs. Transplant patients are especially at risk, as any interaction among herbs and their drugs which could possibly put them at rejection or losing the kidney risk. In this situation consultation with an expert pharmacist is vital about any medicines or herbs you want to take to avoid potential problems (25).

Conclusion

Some herbal medicine may exert renal toxicity through their inherent properties. If we want to found some degree of toxicity, the risks can be weighed against the benefits and decisions can be made regarding their continued availability, in a manner similar to that which is presently performed for nephrotoxic pharmaceutical agents. Importantly, the inherent properties of the herb are not the only source of herb-associated renal disorders, as herb-drug interactions, mistakes in dosage and identification, and contaminants within the mixture are all issues of concern. Strict controls on the presence of adulterants within herbal medicines, labeling of dosages and contraindications, and manufacturing techniques must be maintained to ensure the safety of those consuming herbal medicines. Medicinal plants may be used as crude extracts or standard, enriched fractions in pharmaceutical preparations. Some plants have also other properties such as antihypertensive, reno-protective and retino-protective activities which help better control of complication. Perhaps the biggest problems with herbal medicines are a lack of standardization and of safety regulations. Standardization of herbal medicine that may contain hundreds of chemical constituents, with little or no evidence indicating which might be responsible for the presumed or proven therapeutic effect, is a particularly thorny issue. Using alternative medicine is growing at a notable speed. Herbal drugs and nutritious supplements are CAM therapies that have grown quicker than any other CAM treatments. Little information is available about herbs and dietary supplement use in the CKD population. These products contain a myriad of pharmacologically hazardous active potent components used by people with kidney disease.

Authors' contribution

Search and primary draft by SK; Final edition by MRK.

Conflicts of interest

The authors declared no competing interests.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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