Hazards of Herbal Prescriptions: A Case Report and a Review

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Abstract Introduction: Herbal products are increasingly gaining popularity for treatment of common diseases, despite their limited utility. Public people are not aware of the many hazards resulting from unsupervised use of herbal products. Moreover, many physicians are not aware of this risk of alternative medicine. All of these factors make true challenges for clinical practitioners because of the hazards of herbal prescriptions that may lead to many health effects, organ damage and even death. Case presentation: A 16-years old Egyptian male was presented to the Toxicology Unit of the Emergency Hospital in Mansoura University in a bad condition, one dayafter ingestion of a substance, which they use for treatment of parasitic infestation. After ingestion, he experienced vomiting, diarrhea and abdominal cramps. There was no past history of medical diseases, surgical operations or drug therapy. Also, there was family history of diseases relevant to this current condition. Examination and bedside investigations showed a confused patient with tachycardia and hypertension not responsive to treatment. The patient was admitted to ICU and gastric lavage, after air way protection, was done. Laboratory investigations were completed that showed striking elevations of serum ALT, AST, serum creatinine, serum creatine kinase and potassium levels, that remained risingdespite daily renal dialysis and supportive care by a team of nephrologist, medical internist, ICU care and a chest care with the toxicologist. The patient condition, despite this, remained very bad and developed bleeding from orifices and DIC, pleural effusion, lung collapse and respiratory depression supervenes despite ventilator care in monitored ICU setting. Finally, the patient was arrested and continuous resuscitation efforts failed and he died. Conclusion: Unsupervised herbal products use may carry extreme hazards upon health, up to death of the individual. Orientation of this hazard is essential for both the public and physicians. Herbal products use should be inquired upon in case of sudden deterioration of individual's health. Unsupervised traditional medicine practice may lead to many health problems that can be faced during clinical practice and should be considered by physicians.

Keywords: herbal, prescriptions, hazards, renal failure, liver damage, awareness

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1. Introduction

Herbal medicine has its origins in ancient cultures including those of the Egyptians, American Indians and Chinese. It involves the medicinal use of plants to treat disease and enhance general health and wellbeing (Leung and Siu, 2013).

Herbal preparations are increasingly used despite limited evidence for their therapeutic efficacy and increasing warning of their hazards. Herbal preparations are increasingly gaining popularity despite their many adverse effects that may end in tragic events and death. This provides many new clinical challenges (Teschke et al., 2014).

Herbal preparations are used by the public commonly for treatment of anxiety, arthritis, depression, high blood pressure, insomnia, hormonal imbalances such as premenstrual tension, migraines, obesity, skin problems such as eczema, chest problems, gastrointestinal and other disorders (Chen et al., 2014). Herbal products are commonly used also by the public for special population as children and pregnant females for their belief that these products are safer and more effective than prescription drugs, and that they have fewer adverse effects (Park et al., 2010).

Also, the use of herbal supplements is prevalent among patients who are taking prescription medications and elderly people who have other comorbidities, exposing them for potential herb-drug-disease interactions (Cherniack et al., 2001).

Tachjian et al. (2010) stated that the number of visits to providers of complementary and alternative medicine exceeds those to primary care physicians, for annual outof-pocket costs of 30 billion dollars in the USA.

The investigators believed that multiple factors contribute to the increased use of complementary alternative medicine (CAM), including the obesity epidemic, the prevalence of chronic disorders and pain syndromes, anxiety, depression, the general desire for good health and wellness, disease prevention, the increasing cost of conventional medicines, and the traditional belief that CAM is safer and more effective than prescription drugs that commonly have adverse effects.

Because herbs are regarded as food products, they are not subject to the same scrutiny and regulation as traditional medications. As a result, manufacturers are exempt from pre-market safety and efficacy testing before the release of an herbal product and from any postmarketing surveillance. Although herbal remedies are perceived as being natural and therefore safe, many have adverse effects that can sometimes produce lifethreatening consequences (Liwa et al., 2014).

Despite the paucity of scientific evidence about the safety or efficacy of herbal products, widespread promotion of CAM products in the popular media and unsubstantiated health care claims seem to be driving their demand and forcing even conventional medical practitioners to incorporate CAM therapies into their practice. This resulted in an increased number of visits to CAM providers, whereas the number of visits to primary physicians remained, in essence, unchanged, according to study performed by Eisenberg and colleagues (1998). Millions of people are therefore exposed to the risk of these potential adverse interactions, especially with products that contain several herbs.

There is paucity of research about health hazards of herbal products use (Tachjian et al., 2010). Here we report a case of health hazards of unsupervised use of a herbal preparation.

2. Case Presentation

A 16-years old Egyptian male was presented on 27th of December 2011 to the Toxicology Unit of the Emergency Hospital in Mansoura University in a bad condition. The patient was a student, from rural area and had no special habits of medical importance (e.g. smoking). The relatives gave history of ingestion of a substance since one day, which they commonly brought from the 'spice dealer' for the intent of treatment of parasitic infestation. It was given to the patient orally for one time at one table spoon (about 10 grams) dissolved in water. Few hours after the ingestion, the patient is said by attendants to have experienced attacks of vomiting, diarrhea and abdominal cramps.

The patient relatives deny any past history of medical diseases, surgical operations or drug therapy. Also, they denied any family history of diseases relevant to the current condition.

Examination showed that the patient was confused (GCS: 13 -14), there was tachycardia (pulse 120 beat/minute and was regular, Blood pressure showed hypertension (180/100 mmHg). There was tachypnea (Respiratory Rate 32-36/ minute, and there was mild chest crepitation. Temperature was 37 \mathbb{C} ., and the pupil was regular, reactive, rounded, equal and central.

Chest X-ray showed no abnormalities. Chest specialist was consulted further and detects nothing abnormal also at that time. There were present corrosions about the lips, tongue and the oral cavity. The patient complained of severe burning sensation extending from the mouth to the stomach. The patient showed dryness of his mouth, hoarseness of voice and urine retention (anticholinergic manifestations). The patient relatives denied presence of any intervention outside the hospital. Arterial blood gases showed compensated metabolic acidosis (PH 7.2, PCO₂ 27 mmHg, HCO₃ 18 mmol/L, Na 133 mEq/L, K 3.5 mEq/L).

The patient was admitted to the ICU. Urinary catheterization was done and the patient received fluids, sodium bicarbonate and 2 ml. of furosemide diuretic. There was output of very dark-colored urine.

Gastric lavage was done after airway protection and single dose of activated charcoal was given. The patient received fluid therapy in the form of Glucose 10%, saline 0.9% and Ringer Lactate solutions, oxygen inhalation, antacid and symptomatic treatment in the form of antiemetic if there is vomiting, anti-colic for abdominal cramps, intestinal anti-septic for diarrhea.

It was suspected that this patient had received a harmful material in mistake for the herbal product intended to treat his parasitic infestation.

Benzodiazepine injection was used for tachycardia with no response. A cardiology consultation was done and used beta-blocker for control of the increasing heart rate with no response. Also, the increased blood pressure failed to decrease on diuretic treatment.

The ABG continued to show compensated metabolic acidosis.

Organ function testing showed ALT 2341U/L (reference range 20-45 U/L), AST 2844 U/L (reference range 25-40 U/L), serum bilirubin 0.4 mg/dl, serum Albumin 3.2 and serum creatinine 1.3 mg/dl. Serum uric acid was 7.2 mg/dl, random blood sugar was 130 mg/dl.

Urine analysis showed frank Haematuria ++++, Bilirubinuria ++++, Proteinuria +++, Myoglobinuria ++, Urate crystals +++ and Epithelial cells +++.

Based on the above mentioned data, a diagnosis of acute fulminant hepatitis with hemolysis and rhabdomyolysis was done.

A work-up that involved appropriate imaging and laboratory investigations began. Abdominal ultrasound was ordered that revealed unremarkable appearance of liver and kidneys. Consultation of internal medicine and nephrology for the sharp rise of organ function tests, together with proceeding in completion of investigations and continuation of symptomatic treatment. Hemostatic agents were administered (Ethamsylate, Tranexamic acid and vitamin K). Renal dialysis began but serum was rising to 4 mg/dl and 6 mg/dl. Also, serum K continued to raise until reached 6.9 mEq/L, despite taking all measures to control hyperkalaemia in the form of administration of NaHCO3, glucose and insulin and renal dialysis.

The patient was still anuric.

Two days after, CT chest was done that revealed extensive pneumonia, lung collapse with minimal pleural effusion. The patient was on mechanical ventilation.

Daily renal dialysis was continued and renal biopsy revealed presence of immune nephritis and antiglomerular basement membrane (GBM) antibody at 1/10 titer.

So, immune nephritis was suspected.

Serum CK was 41351 U/L (reference range 32-294 U/L) and LDH level was 4211U/L. (reference range120-249 U/L). Immunologic studies revealed Anti DNA antibodies to be negative and Anti-neutrophil cytoplasmic antibodies (cANCA and pANCA) to be negative. Complete blood count showed White blood cells count of 21000/cc, platelet count of 193/cc, Haemoglobin content of 8.8 g/dl.

INR 1.2, serum potassium level was 7.7 mEq/L and serum creatinine 6.9 mg/dl.

Despite whole blood and platelet transfusion, the patient showed bleeding from the mouth, bloody stool in enema (melena and hematochasia) and bleeding from nose. Disseminated intravascular coagulation (DIC) was suspected to set in with the deterioration of respiratory parameters despite ventilator care, continuously rising serum creatinine despite daily dialysis.

The sudden onset, short duration of patient's symptoms suggests chemical or toxin exposure and the multi-organ damage and continuous deterioration of the patient condition despite all supportive care done for him suggests exposure to a stain used for hair dying instead of the myrrh that he intend to use.

Fifteen days after admission of the patient and continuous care of the medical team of toxicologist, nephrologist, internal medicine and ICU specialists, respiratory distress with spastic respiratory muscles set in, dormicum and pancuronium were used without improvement. CT chest still showed pleural effusion and lung collapse.

Consultation to cardiothoracic specialist was done. He inserted a chest tube to the patient that drains bloody fluid (haemothorax). The patient arrested and continuous resuscitation for 1.5 hours failed and death occurred.

3. Discussion

The use of herbal remedies is widespread and increasing dramatically, yet current laws allow them to be marketed as dietary supplements not subject to the same regulations required for prescription drugs. Thus, the purity, efficacy, and safety of herbal products are often unknown.

In this case, an herbal product was purchased from a person who is not specifically an herbal therapist, but is generally a 'spice-dealer'. The product was intended to be 'myrrh' which has many uses amongst them is the treatment of parasitic infestation. Good types of 'myrrh' are clear yellow or light-brown in color, while bad types are opaque and dark- colored or black. In this case, the patient purchased black preparation that might be a hairdying chemical sold in mistake for myrrh.

This chemical is very toxic to kidneys and liver, producing organ damage and ultimately leads to death (Madnani and Khan, 2013). This is similar to the scenario of this case. The patient is considered a victim for unsupervised herbal products use that is prescribed from non-specialist, giving unknown compounds from non-labeled containers, with unknown concentration and unsupervised use; the factors that end in loss of life of the user of this prescription.

Myrrh (Tonkal and Morsy, 2008)

Myrrh is a red-brown resinous material, derived from the dried sap of the tree *Commiphoramyrrha*, its name is derived from the Hebrew '*murr*' or '*maror*', meaning "bitter" in arabic.

The plant 'Commiphoramyrrha' (= Commiphoramolmol, Commiphoraabbysinica) is a shrub-like tree. This tree has a thick, light grey trunk with sharp spines protruding from its main branches.

It is Native to Ethiopia, Somalia, north-eastern Africa, the Middle East, and Yemeni and in desert regions.

Myrrh is obtained by wounding the trees repeatedly to bleed them of the gum. Myrrh gum is waxy, and coagulates quickly. After the harvest, the gum becomes hard and glossy. The gum is yellowish, and may be either clear or opaque. It darkens deeply as it ages, and white streaks emerge.

Myrrh was used medicinally over 3,700 years ago. It has many properties and used as anti-microbial (bacterial, viral), anti-fungal, astringent, aids in wound healing, general tonic &stimulant, carminative, stomachic, anticatarrhal, expectorant, diaphoretic, vulnerary, locally antiseptic, immune stimulant, circulatory stimulant, antiinflammatory and antispasmodic.

Mirazid, an Egyptian drug made from myrrh, is used as an oral treatment of parasitic infestation, including fascioliasis and schistosomiasis (Yakoot, 2010).

Sheir et al., 2001 stated that side effects of myrrh were transient and mild and occurred in only 11.8% of the treated cases and in none of the healthy volunteers. The most frequently reported side effects were giddiness, somnolence, mild fatigue, and abdominal pain or discomfort. The four patients who were intolerant to praziquantel tolerated myrrh with no side effects. Myrrh had no significant effects on liver functions, serum creatinine, or electrocardiographic findings, nor did it have any significant effects on liver and kidney functions in healthy volunteers. In conclusion, myrrh has been shown to be a safe and effective anti-parasitic drug at the recommended dose of 10 mg/kg/day for six days.

Hair dying chemicals

Despite considerable research, the issue of health effects of hair dyes is still open to discussion. Many observational studies have investigated the association between personal use of hair dyes and many health hazards such as allergic reactions, asthma, andon long term use of hair dying chemicals, it be a risk factor of cancer incidence. Moreover, these chemicals create a state of oxidative stress in the body that can lead to organ dysfunction (Madnani and Khan, 2013).

The above case study teaches us that the public should not use herbal products without medical supervision. The product may have impurities. It may be mixed with fatal compounds.

Moreover, it may be expired or may be used in noneffective dose or in otherwise, a fatal dose. There may accumulation of heavy metals in medicinal plants not subjected to quality standards before marketing to the public. Some herbs, also, have potent ingredients and should be treated with great care. For example, the heart drug digitalis is derived from the herb foxglove (Sarma et al., 2011).

Also, it is very important that people do not selfdiagnose any health conditions. Any medication (herbal or otherwise) should be taken under the supervision of a knowledgeable practitioner (Colsonand De Broe., 2005).

Problems Related to the Use of Herbal Products (Neergheen-Bhujun, 2013)

The use of herbal products is complicated by numerous problems as summarized below:

- Lack of Scientific Evidence of Safety and Efficacy
- Lack of Regulatory Oversight
- Lack of Quality Control
- Public Misinformation
- Lack of Knowledge about Herb-Drug Interactions by Patients and Health Care Providers

Prevention (Institue of Medicine, USA, 2005)

There is increasing need for orientation of both the public and the physicians about the CAM and the guidelines to use it.

Manufacturers of herbal products should be required to register with the FDA and to provide evidence of good manufacturing practices (i.e. standardization, storage, preparation techniques, labeling, and manufacturing sites). Evidence of the safety and efficacy of the herbal product should be obtained by well-designed clinical trials, premarketing approval regarding safety, and strict postmarketing surveillance.

There is need forhealth education for both the public and the physiciansabout the use of herbal products and their risk, early detection and management of herbal toxicities, scientific scrutiny of their benefits, and research on their safety and effectiveness. Regulatory policies are also needed to protect persons from untoward effects on their health and finances. The principles and standards of evidence for safety and efficacy of drugs used in conventional medicine should also apply to herbal and other CAM products, with decisions about their use based on the results of scientific inquiry rather than on long-held but untested beliefs or traditions.

4. Conclusion

Herbal medicine is gaining popularity and people are increasingly using it more than the primary care physicians. So, increasing numbers of exposure to the risks of this type of medical practice should be considered by the clinicians.

It is more needed now than the previous times that regulatory laws exist for practice of CAM. Herbal products should be labeled with active ingredients and concentration listed clearly on the label. In addition, manufacturers should report adverse events to the FDA. Moreover, there should be present a supervision upon both the herbalist and the consumer.

Abbreviations

C, Degree Centigrade; ALT, Alanine transaminase; AST, Aspartate transaminase; CAM, Complemetary and Alternative Medicine; GCS, Glasgow Coma Scale; CK, Creatine kinase; CT, computerized tomography; ED, Emergency Department; ICU, Intensive Care Unit; mEq/L, milliequivalent per liter; mmol/L, millimol per liter.

Conflicts of Interest

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