A systemic review of vegetable poisoning and challenges in management

Sukhdeep Singh[1], Mahesh Kumar[2,*], Arvind Kumar[3], Rishabh Kumar Singh[4]

[1,3]Professor, [2]Assistant Professor, [4]Senior Resident, Dept. of Forensic medicine and Toxicology, [1,3,4]Lady Hardinge Medical College, Connaught Place, Delhi, [3]Indira Gandhi Medical College, Shimla, Himachal Pradesh, India

***Corresponding Author: Mahesh Kumar**
Email: mahesh25881@gmail.com

Abstract
Plants have been friends and foes to the humanity. The plant products as a remedy to many ailments have been used since the advent of human civilisation. On the darker side many plants on the planet are hazardous to human health. The accidental or intentional consumption can be deleterious to the physical as well as mental well being of the individual. The aim of this review was to highlight common plant poisons along with signs, symptoms, differential diagnosis and management Search of the literature was done from PubMed, EMBASE, MEDLINE, EBook, done to elaborate upon this vast topic. The Role of Poison Information centres is vital in establishing epidemiology and management of poisoning. Identifying new plant poisons and developing their treatment protocols along with spreading awareness is of great significance to the society.

Keywords: Plant poisons, Vegetable poison, Alkaloids, Toxin, Antidote, Poison information centre.

Introduction
The knowledge of poisons is existing since ancient time and supposed to be as old as human civilization. It may be defined as any substance which when ingested, inhaled or absorbed or when applied to, injected into, developed within the body by its chemical action, may cause damage to structure or disturbance of function". Poisons are of vegetable, animal, or mineral depending upon source of origin.

Aims and Objectives
The objective was to conduct systemic review of literature to characterize manifestation of different plant poisons, diagnosis and management along with the role of regional poison information centers in cases of poisonings

Materials and Methods
PubMed, EMBASE, MEDLINE, EBook, search of the literature were done to evaluate the vegetable poisoning & challenges in management.

Review of Literature
The history of poison originated before 4500 BC.[1] Early poisons were exclusively extracted from plant and animal toxins and some minerals. Plants are beneficial as foodstuffs and many have medicinal properties. However, some plants also have the potential to produce toxicity.[2] Socrates (470–390 BC) was sentenced to death by hemlock. Pedanius Dioscorides was a Greek army physician, classified poisons according to their origin (animal, vegetable, or mineral) and his book *De Materia Medica* is one of the most influential herbal books and is a precursor to all modern pharmacopeias.[3] Indian surgeon Sushruta defined the stages of slow poisoning, antidotes and traditional substance for treatment of poisoning.[4]

A large number of plants can cause adverse effects when ingested by animals or people. Plant toxicity is due to a wide diversity of chemical toxins that include alkaloids, glycosides, proteins and amino acids however there are toxic plants for which a specific chemical responsible for toxicity has not been yet determined.

Fortunately, adverse effects often do not occur or are generally mild following most toxic plant ingestions and no therapeutic intervention is necessary. However, some plants are extremely toxic and ingestion of small amounts can cause rapid death. The diagnosis of plant intoxication can be challenging. Analytical tests are available to detect some plant toxins but diagnostic utility is often limited by test availability and timeliness of results. With a few notable exceptions, antidotes are available only for some plant toxins. General supportive and symptomatic care often is sufficient to successfully treat a symptomatic patient.[5]

Though this topic is utterly vast and vivid, here some very important and frequently encountered poisons are discussed in terms of their mechanism of action, signs and symptoms, diagnostic and therapeutic challenges in managing their toxicities.

Abrus precatorius
The plant seeds of abrus are used as beads and in percussion instruments, are highly toxic because of the presence of abrin. It prevents protein synthesis by inactivating the 26S subunit of the ribosome. Symptoms of poisoning include nausea, vomiting, convulsions, liver failure, and death, usually after several days of ingestion. The differential diagnosis of abrin poisoning include sister poison Ricin, and viperine bite along others.

L-abrin biomarker is useful in suspicious abrin poisoning.[6] Supportive and symptomatic management of abrin poisoning is mainstay of treatment including adequate hydration and correction of electrolyte abnormalities. Life-threatening complications such as liver failure, renal failure, and cerebral edema warrant the testing of renal and liver function.[7]

Ricin is a toxic, naturally occurring lectin produced in the seeds of the castor oil plant, Ricinus communis. Ricin's widespread availability makes it a viable biological weapon. Ricin is very toxic if inhaled, injected, or ingested. It acts as a toxin by inhibiting protein synthesis.[8] Ingestion of ricin causes pain, inflammation, and hemorrhage in the mucous membranes of the gastrointestinal system lead to nausea, vomiting, diarrhea, difficulty in swallowing, melena and hematemesis. Hypovolemia caused by gastrointestinal fluid loss can lead to organ failure in the pancreas, kidney, liver, and GI tract and progress to shock. Symptoms of ricin inhalation are different from those caused by ingestion. It include a cough, fever, asthma dry, sore throat, congestion while skin exposure of ricin can cause an allergy. This is indicated by edema of the eyes and lips, erythema, skin blisters. It can be differentially diagnosed from abrin poisoning, toxin inhalation (such as staphylococcal enterotoxin B or trichothecene mycotoxins), and chemical warfare agents such as phosgene. Aerosolized ricin is distinguished from routine infections by progressive respiratory symptoms in spite of antibiotics.[9] Symptomatic and supportive treatments include intravenous fluids or electrolytes, airway management, assisted ventilation, or giving medications to remedy seizures and low blood pressure are mainstay of treating ricin poisoning. Possible treatments if the ricin has been ingested recently is ingesting activated charcoal or by performing gastric lavage.[10]

Marking nut (Semecarpus anacardium, oriental cashew nut)

It is a product of deciduous tree found in the outer Himalayas is believed to contain therapeutic properties and has been used extensively in Ayurvedic medicine since ancient times. This blackish nut leaves an indelible ink and is recognized to have caused washerman's dermatitis among British soldiers in the 1940s.[11] Several case reports of contact dermatitis caused by the marking nut have been described from sub continental India, related to its use as hair dye, voodoo treatment, remedy for eczema or tattoo removal. The contact allergen is thought to be urushiol.[12,13] Anaphylaxis to the marking nut subsequent to oral ingestion is mediated by specific IgE to one or more allergenic protein.[14] It has to be distinguished from other types of allergic contact dermatitis.

Calotropis (Madar, Akdo)

Calotropis is a wild plant found throughout India. Their active principles toxins are Calactin, Calotropin, Calotoxin, and Uscharidin.[15] The flowers, leaves, root bark, and milky juice of calotropis are extensively used in the form of poultice, tincture, powder, and snuff, by practioners of indigenous medicine and also by quacks and laymen. The juice is used as a vesicant, as a depilatory, as a remedy for skin affections, and as a counter irritant and rubifacient for relief of pain. From the medico-legal point of view the juice is used for procuring criminal abortion, for purposes of suicide, infanticide, and homicide, and cattle and arrow poison when administered internally, calotropis acts as a gastro-intestinal irritant and cerebrospinal poison. When dropped in the eye it produces severe irritation and chemosis of conjunctiva and anesthesia, and the inflammatory reaction may involve the eyesight.[16] Management is supportive.

Croton tiglium (Jamālgoṭa)

It is an important medicinal plant, which is used for the treatment of constipation, dyspepsia, dysenteries, gastrointestinal disorders, intestinal inflammation, rheumatism, peptic ulcer, visceral pain, and headache.[17,18] The toxicity of *C. tiglium* seeds is due to the presence of phorbol esters and crotonic acid along with other constituents. Poisoning by ingestion leads to injury of, the digestive tract manifesting as abdominal cramps burning sensation in the whole abdomen along with bloody diarrhea, congestion, serious edema of GI tract. Mainstay of treatment is supportive. Antispasmodic and Oral Rehydration Therapy (ORT) is of great help

Argemone Mexicana

Epidemic dropsy is a clinical state resulting from use of edible oils adulterated with *Argemone Mexicana* oil. Sanguinarine and dehydrosanguinarine are two major toxic alkaloids of *Argemone* oil, which cause widespread capillary dilatation, proliferation and increased capillary permeability. Leakage of the protein-rich plasma component into the extracellular compartment leads to the formation of oedema. The haemodynamic consequences of this vascular dilatation and permeability lead to a state of relative hypovolemia with a constant stimulus for fluid and salt conservation by the kidneys. Illness begins with gastroenteric symptoms followed by cutaneous erythema and pigmentation. Respiratory symptoms such as cough, shortness of breath and orthopnoea progressing to frank right-sided congestive cardiac failure are seen. Mild to moderate anaemia, hypoproteinaemia, mild to moderate renal azotemia, retinal haemorrhages, and glaucoma are common manifestations. The largest epidemic of the disease in India affected Delhi and its neighboring states during the months of August-September 1998. Over 3000 persons fell ill, and more than 65 died in the state of Delhi alone.[19]

There is no specific therapy. Removal of the adulterated oil and symptomatic treatment of congestive cardiac failure and respiratory symptoms, along with administration of antioxidants and multivitamins, remains the mainstay of treatment. Selective cultivation of yellow mustard, strict enforcement of the Indian Food Adulteration Act, and exemplary punishment to unscrupulous traders are the main preventive measures.[20]

Epidemic dropsy must be distinguished from hypoproteinaemic states, filariasis, venous insufficiency, and Beri-Beri, hypothyroidism and nephrotic syndrome. Mortality is usually due to heart failure, pneumonia, respiratory distress syndrome or renal failure and is around 5%.[21]

Ergots

The causative agents of most ergot poisonings are the ergot alkaloid class of fungal metabolites. Ergot alkaloids also have had medical applications for centuries, first in obstetrics to promote labor and reduce uterine hemorrhaging, and most recently in treatment of migraines The adrenergic blockage by ergopeptines (e.g., ergovaline or ergotamine) leads to potent and long-term vasoconstriction, and can result in reduced blood flow resulting in intense burning pain (St. Anthony's fire), edema, cyanosis, dry gangrene and even loss of hooves in cattle or limbs in humans.[22] It is used for conducting criminal abortions. Management is largely supportive in absence of antidotes

Digitalis

It is a genus of herbaceous perennials, contain cardiac glycosides, particularly one called digoxin, extracted from various plants of this genus. It is used to increase cardiac contractility and as an antiarrhythmic agent to control the heart rate, particularly in the irregular atrial fibrillation.

Digitalis toxicity results from an overdose of digitalis and causes nausea, vomiting and diarrhea, the appearance of blurred outlines (halos), drooling, abnormal heart rate, cardiac arrhythmias, weakness, collapse, dilated pupils, tremors, seizures, and even death. Bradycardia also occurs.. More serious toxicity occurs with intentional ingestions.Conditions to consider in the differential diagnosis of digitalis toxicity includes organophosphate toxicity, Arrhythmias, First, Second and Third-degree heart block. Electric cardioversion is generally not indicated in ventricular fibrillation in digitalis toxicity, as it can increase the dysrhythmia. Also, the classic drug of choice for ventricular fibrillation in emergency setting, amiodarone, can worsen the dysrhythmia caused by digitalis, therefore, the second-choice drug lidocaine is more commonly used.[23]

Aconitum

also known as aconite, wolf's bane, queen of poisons[24,25] Aconitine alkaloid derived from root, flowers, leaves, stems of various aconite species is highly and fast actin toxin.[26] Accidental consumption of aconite as little as 2 mg of pure aconite or 1 gm. of plant may cause death due to cardiopulmonary arrest.[27] The initial signs and symptoms nausea, vomiting, and diarrhea but characteristic features of aconite poison are burning, tingling, and numbness sensation of the lips, tongue, mouth, and throat. Aconitine poisoning mainly affects CNS, heart, and muscle tissues, aconitine-induced ventricular tachycardia, arrhythmias asystole, or paralysis of the heart or respiratory center lead to death, have been reported in many case reports.[28] Management is supportive. The only *post mortem* signs are those of asphyxia.[29]

Nerium oleander

Nerium is a plant toxic in all its parts. Oleander is one of the most poisonous commonly grown garden plants. Among these compounds are oleandrin and oleandrigenin, known as cardiac glycosides, which are known to have a narrow therapeutic index and can be toxic when ingested. Oleander is a common cause of poisoning and death in tropical and subtropical countries, with 170 cases seen at a single hospital in Sri Lanka.[30,31]

Ingestion of this plant can affect the gastrointestinal system, the heart, and the central nervous system. Cardiac reactions consist of irregular heart rate, sometimes characterized by a racing heart at first that then slows to below normal further along in the reaction. Extremities may become pale and cold due to poor or irregular circulation. The effect on the central nervous system may show itself in symptoms such as drowsiness, tremors or shaking of the muscles, seizures, collapse, and even coma that can lead to death.

Poisoning and reactions to oleander plants are evident quickly, requiring immediate medical care in suspected or known poisonings of both humans and animals.[32] Induced vomiting and gastric lavage are protective measures to reduce absorption of the toxic compounds. Charcoal may also be administered to help adsorb any remaining toxins.[33]

The treatment of oleander poisoning is empirically based on the treatment of digitalis-glycoside toxicity and consists of supporting the patient hemodynamically. This may include administering atropine for severe bradycardia, lidocaine hydrochloride to control dysrhythmias, placing a temporary venous pacemaker; or electrical counter shock and administering digoxin-specific Fab antibody fragments (Digibind).[34]

Conium maculatum, poison hemlock

Hemlock is highly poisonous plant, native to Europe and North Africa. It contains the alkaloids coniine, N-methylconiine, conhydrine, pseudoconhydrine, and gamma-coniceine. Coniine disrupts the workings of the central nervous system through inhibitory action on nicotinic acetylcholine receptors.[35] Due to high potency, the ingestion of seemingly small doses can easily result in respiratory collapse and death. Coniine causes death by blocking the neuromuscular junction in a manner similar to curare; this results in an ascending muscular paralysis with eventual paralysis of the respiratory muscles which results in death due to lack of oxygen to the heart and brain. For an adult, the ingestion of more than 100 mg of coniine (about six to eight fresh leaves, or a smaller dose of the seeds or root) may be fatal.[36]

Coniine also has significant toxic effects on the kidneys. The presence of rhabdomyolysis and acute tubular necrosis was shown in patients who had died from hemlock poisoning. Differential diagnosis of hemlock poisoning includes Botulism, Nicotine, Encephalopathy. Death can be prevented by artificial ventilation until the effects have worn off 48–72 hours later.

Curare

Is a common name for various plant alkaloid arrow poisons originating from Central and South America. They function by competitively and reversibly inhibiting

the nicotinic acetylcholine receptor (nAChR. This leads to weakness of the skeletal muscles and can eventually cause death by asphyxiation due to paralysis of the diaphragm. Curare poisoning can be diagnosed by signs of neuromuscular junction blockade such as paralysis including respiration but not directly affecting the heart. Curare poisoning mimics the total locked-in syndrome in that there is paralysis of every voluntarily controlled muscle in the body (including the eyes), making it practically impossible for the victim to confirm consciousness while paralyzed.[37] Spontaneous breathing is resumed after the end of the duration of action of curare, which is generally between 30 minutes to 8 hours, depending on the variant of the toxin and dosage. Cardiac muscle is not directly affected by curare, but if more than four to six minutes has passed since respiratory cessation the cardiac muscle may stop functioning by oxygen-deprivation, making cardiopulmonary resuscitation including chest compressions necessary.[38] Muscle paralysis can be reversed by administration of a cholinesterase inhibitor such as pyridostigmine.[39] Curare poisoning can be managed by mechanical ventilation

Strychnine

It is a highly toxic, crystalline alkaloid used as a pesticide, particularly for killing small vertebrates such as birds and rodents. Strychnine results in muscular convulsions and eventually death through asphyxia, when inhaled, swallowed, or absorbed through the eyes or mouth.[40] Strychnine is a neurotoxin which acts as an antagonist of glycine and acetylcholine receptors affecting the motor nerves in the spinal cord which control muscle contraction. *S. nux-vomica* seeds are generally effective as a poison only when they are crushed or chewed before swallowing as the pericarp is quite hard and indigestible; poisoning symptoms may ztherefore not appear if the seeds are ingested whole. The spasms,which start 10-20 minutes after the exposure spread to every muscle in the body, with nearly continuous convulsions, and get worse at the slightest stimulus. The convulsions progress, increasing in intensity and frequency until the backbone arches continually. Convulsions lead to lactic acidosis, hyperthermia and rhabdomyolysis. These are followed by postictal depression. Death comes from asphyxiation caused by paralysis of the neural pathways that control breathing, or by exhaustion from the convulsions. The subject usually dies within 2–3 hours after exposure. The principles of management of strychnine intoxication are similar to those of any acute poisoning.[41]

There is no specific antidote for strychnine. "The convulsions are often triggered by stimuli so patients are generally kept in quiet, dark rooms." Treatment of strychnine poisoning involves an oral application of an activated charcoal infusion which serves to absorb any unabsorbed poison Anticonvulsants such as phenobarbital or diazepam are administered to control convulsions, along with muscle relaxants such as dantrolene to combat muscle rigidity. If the patient survives past 24 hours, recovery is probable. Tannic acid can be administered which precipitates the strychnine as an insoluble tannate salt, and then to anaesthetise the patient with chloroform until the effects of the strychnine had worn off. The condition must be differentiated from epilepsy, tetanus, meningitis, hysteria and phenothiazine intoxication. Strychnine is absorbed very rapidly from the gastrointestinal system.[42] The 20% of an ingested dose is excreted unchanged in the urine, 70% in the first 6 hours. So strychnine poisoning can be reliably identified from study of the urine, particularly in those first 6 hours.[43]

Dhatura

Dhatura is a genus of nine species of flowering plants. All species of Datura are poisonous, especially their seeds and flowers. In ancient times it was used in Ayurveda as a medicine All Dhatura plants contain alkaloids such as scopolamine, hyoscyamine, and atropine, primarily in their seeds and flowers. Because of the presence of these substances, Datura has been used for centuries in some cultures as a poison for suicide and murder. From 1950 to 1965, the State Chemical Laboratories in Agra, India, investigated 2,778 deaths caused by Dhatura ingestion[44] Due to the potent combination of these anticholinergic substances, it typically produces effects similar to that of an anticholinergic delirium, hyperthermia; tachycardia; bizarre, and aggressive behavior. There is severe mydriasis with resultant painful photophobia that can last several days. Pronounced amnesia is another commonly reported effect. Due to their agitated behavior and confused mental state, victims of Datura poisoning are typically hospitalized. Gastric lavage and the administration of activated charcoal can be used to reduce the stomach's absorption of the ingested material. physostigmine is usedas an antidote. Benzodiazepines can be given to curb the patient's agitation, and supportive care with oxygen, hydration, and symptomatic treatment is often provided.

Cannabis

The plant is native to central Asia and the Indian subcontinent.[45] Cannabis has long been used for hemp fibre, oils, medicinal purposes, and as a recreational drug. The active principle of THC (cannabinoids), which is obtained by curing the flowers. Various compounds, including hashish and hash oil, are extracted from the plant. The psychoactive effects include a state of relaxation, and to a lesser degree, euphoria from its main psychoactive compound, tetrahydrocannabinol. Philosophical thinking, introspection and metacognition have been reported among cases along with anxiety and paranoia. Cannabis, can include an increase in heart rate and hunger. Normal cognition[46] is restored after approximately three hours for larger doses via a smoking pipe, bong or vaporizer. However, if a large amount is taken orally the effects may last much longer. After 24 hours to a

few days, minuscule psychoactive effects may be felt, depending on dosage, frequency and tolerance to the drug.

The term "marijuana" typically refers to tobacco-like preparations of the leaves and flowers. The cannabinoid δ-9-tetrahydrocannabinol (THC) is the major psychoactive constituent. "Hashish" is the resin extracted from the tops of flowering plants and generally has a much higher THC concentration. Marijuana is the most commonly used illicit drug in the United States

Differential diagnoses of THC toxicosis include human pharmaceuticals with central nervous system stimulatory effects, drugs with central nervous system depressant effects and hallucinogenic mushrooms.[47] Most common clinical symptoms are tachycardia, palpitations, confusion and headache. The symptoms typically appears in 1.5 to 3hrs after the ingestion. Conjunctival hyperemia, mydriasis and hypothermia can also be found. The diagnosis can be confirmed by the search of cannabinoids in the urine.

Opium

Opium is the dried latex obtained from the opium poppy (scientific name: *Papaver somniferum*). Approximately 12 percent of the opium latex is made up of the analgesic alkaloid morphine, which is processed chemically to produce heroin and other synthetic opioids for medicinal use and for illegal drug trade. The latex also contains the closely related opiates codeine and thebaine.

Opium poisoning which is rarely seen nowadays. Its main symptoms are a cold, clammy skin, a slow respiration rate, and pin-point pupils. In all cases of suspected poisoning, gastric lavage should be performed and the gastric contents kept for analysis.

The toxic effects of opium, including potentially fatal depression of the respiratory centre, are generally due to the morphine.Gastric lavage supported when necessary by nalorphine and Mechanical ventilation was effective treatment in the majority of cases because of the slow absorption of opium.[48]

Role of Poison information centers

The Poisons Information Centre (PIC) is a specialized unit of toxicology providing information on prevention, early diagnosis and treatment of poisoning and hazard management. Most of the developed and many developing countries have well established poison control centres with poisons information service, patient management facility and analytical laboratory. In India, the National Poisons Information Centre (NPIC) was established in February 1995 in the Department of Pharmacology at the All India Institute of Medical Sciences, New Delhi. The centre provides toxicological information and advice on the management of poisoned patients adopted to the level of the enquirer. The basis of this service is the databases on poisoning, drug reactions and also the continuous and systematic collection of data from the library.

Well equipped laboratory service is an essential component of a poisons control programme, providing analytical services on emergency basis to help in diagnosis and management. Toxicovigilance and prevention of accidental poisoning is another major function of PIC. Thus a poison centre provides a service with considerable health benefits, reducing morbidity and mortality from poisoning and gives significant financial savings to the community.

A poison centre affiliated to tertiary care centre has to be equipped to provide informationwhether a particular exposure is hazardous, and the kind of treatment that should be administered. Poisons centers aim to promote the evidence-based, cost-effective management of poisoning and to ensure that unnecessary or ineffective treatment is avoided.[49]

Conclusion

Vegetable or plant poisons have been known for poisoning since ancient times,however identifying newer plant poisons, their scientific classification,mechanism of action,elaboration of their signs and symptoms along with differential diagnosis and newer modalities of treatment have been of great help to the society. The establishment of poison information centres has been crucial for coordination of effective diagnosis and treatment of cases of poisoning.There is a very important role of community physicians,health workers in spreading the awareness about the various plant poisons and saving the society from a number of accidental mortality and morbidity.

Conflict of interest: None

Acknowledgement

I acknowledge the support of Deptt. of Forensic Medicine, LHMC Dept. of Forensic Science, Galgotia University, Greater Noida completion of this article.I also acknowledge Dr Garima Singh for providing her valuable time and support.

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How to cite this article: Singh S, Kumar M, Kumar A, Singh RK, A systemic review of vegetable poisoning and challenges in management. *Int J Forensic Med Toxicol Sci* 2019;4(1):4-9