



## Review

# Medical management of ricin poisoning

Rashmi Aggarwal<sup>1</sup>, Hemant Aggarwal<sup>2</sup>, Pradeep Kumar Chugh<sup>3</sup>

<sup>1</sup>Department of Thyroid and Endocrine Research, Chemical Biological Radiological and Nuclear (CBRN) Defence Institute of Nuclear Medicine and Allied Sciences (INAMS), Brig. S. K. Mazumdar Road, Delhi-110054, India.

<sup>2</sup>Badshah Khan Hospital, New Industrial Township, Faridabad-121001, Haryana, India.

<sup>3</sup>Department of Cardiology, Institute of Nuclear Medicine and Allied Sciences (INAMS), Brig. S. K. Mazumdar Road, Delhi-110054, India.

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### Corresponding author

#### Rashmi Aggarwal

Department of Thyroid and Endocrine Research,  
Chemical Biological Radiological and Nuclear (CBRN) Defence Institute of Nuclear Medicine and Allied Sciences (INAMS),  
Brig. S. K. Mazumdar Road,  
Delhi-110054, India.  
Phone: +91-11- 23905239  
Email: drarashmi@yahoo.co.in

### Abstract

Ricin is a biological toxin which can be extracted from the castor bean plant. The scientific name of this plant is *Ricinus communis*. The Centre for Disease Control and Prevention (CDC) has categorized ricin to be a category B agent. Exposure to ricin can occur by oral ingestion, inhalation or parenteral administration. The severity of symptoms of ricin toxicity is dependent on the route of exposure and the dose of ricin. Diagnosis is based on epidemiological and clinical parameters. Currently no antidote, vaccine or specific therapy is available for ricin poisoning. Treatment of ricin toxicity is largely symptomatic and supportive in nature. The treatment should be prompt and meticulous to limit mortality.

**Key words:** Biological toxin, Castor beans, Ricin poisoning

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Ricin is a potentially lethal biological toxin which can be extracted from the beans of castor plant (*Ricinus communis*). After castor oil is extracted from the castor beans, the toxin ricin remains in the residual mesh, from which it can be easily extracted and used for notorious purposes. Owing to the ease of availability of the native plant and the hassle free extraction of the ricin toxin from it, it has made ricin a potent biological toxin. Ricin has been categorized as a category B bio-terror agent by the Centre for Disease Control and Prevention (CDC)<sup>1</sup>.

*Ricinus communis* is the name given by the famous naturalist Dr. Carolus Linnaeus. Ricin is a Latin word which actually means tick and Linnaeus named it so because castor bean looked like a tick, Communis means common in Latin. Castor plants were commonly naturalized in many parts of the

world. Castor oil is a strong and effective cathartic or laxative. It is also used topically to treat warts or corns. Castor oil is also used in oils, paints, varnishes and industrial machines. During both the world wars – first and second this lubricating oil was used in aircrafts but during the Second World War when there was an acute shortage of this lubricating oil, the US government subsidized the cultivation of castor beans in San Joaquin valley of California. The ricin toxin which remains in the castor meal after the oil has been extracted can be easily removed by a simple procedure. Castor oil itself never contains any ricin. During the preparation of castor oil, the ricin-containing resin portion of the plant is separated from the non-ricin-containing oil portion. Ricin is also thought to be activated during oil extraction especially if extraction is done under heated conditions. Ricin can be

prepared in three different forms: liquid, crystalline or dry powder. Ricin is water soluble, odorless and tasteless. The chemical and physical properties of ricin make it a potential agent for use as a terrorist weapon through contamination of food, beverages, or other consumer products.



Fig 1. *Ricinus communis* plant

### Historical use of ricin

Although ricin has never been used for mass casualty so far there have been isolated incidents of ricin being used for homicide. The classical example is the assassination of Georgi Markov, a prominent Bulgarian journalist who was assassinated in London on September 10, 1978, allegedly from a ricin injection in the thigh<sup>2</sup>. Mr. Georgi Markov was stabbed on the right thigh by the penetrating tip of an umbrella while he was waiting at the bus stop. The man holding the umbrella left hurriedly in a taxi but before leaving he did say sorry to Mr. Markov in a sort of foreign accent. He experienced severe pain at the site of injury but ignored it and went home. After six hours he was feeling extremely weak and was admitted next day to the hospital in a serious condition and died four days later. The medical sequence of events following this injection and the possible cause of his death will be discussed a little later in this article.



Fig 2. Umbrella gun with which Mr. Georgi Markov was attacked

### Clinical manifestations of ricin toxicity

There are five different routes by which exposure to ricin can occur both in humans and animals and they are as under:

1. Inhalation route of exposure
2. Oral administration
3. Injection or parenteral administration
4. Dermal contact
5. Ocular contact

The clinical signs, symptoms and pathological manifestations of ricin poisoning usually depends on two things

1. Route of exposure
2. Dose of the toxin

#### Modes of exposure

1. Inhalation exposure may occur through an aerosol, powder or dust<sup>3</sup>
2. Ingestion can occur through contamination of food, water, or consumer products
3. Parenteral exposure can occur by direct injection (as happened in case of Mr. Georgi Markov)

#### Clinical manifestations on inhalation

Experimental animal studies looking at aerosol toxicity in monkey have shown a clinical picture characterized by acute onset of nasal congestion, urticaria, wheezing along with ocular irritation. It is thought that air borne ricin exposure may cause an allergic response. Post mortem finding in these monkeys showed features of severe pneumonia along with inflammation of the airways<sup>4</sup>. This inflammation and necrosis was more marked in distal airways and alveoli.

#### Clinical manifestation on ingestion

Symptoms usually appear 4-6 hours after ingestion. Patients usually complain of colicky abdominal pain, vomiting, diarrhea, severe heart burn<sup>5</sup>. Hematemesis and melena may also occur. Excessive loss of fluid from the body can cause hypotension and electrolyte imbalance. Hypotension, dehydration and circulatory collapse may lead to shock during this time<sup>6</sup>. Patient may complain of thirst, sore throat, fever and cramps. Death may occur by the third day. Post mortem finding after oral ingestion includes wide spread and multi focal ulceration and hemorrhage in both gastric and intestinal mucosa.

#### Clinical manifestations on injection

Parenteral administration of ricin leads to the development of flu like symptoms with fever, nausea,

vomiting, anorexia, fatigue, hypotension and circulatory shock. Laboratory finding in such patients include elevated liver transaminases, creatinine kinase, hyperbilirubinemia.

Post mortem finding in these cases include focal necrosis and edema in brain, intestine, myocardium and kidneys.

**Clinical finding in case of Mr. Markov**

Ricin was used in the assassination of Georgi Markov, a Bulgarian journalist who was residing in Britain. He was 49-years-old and was a famous Bulgarian novelist and play writer. At the time of his assassination he was working for the BBC. On September 7, 1978 while he was standing on a bus stop in London, he was stabbed on his right thigh with the tip of an umbrella. He immediately experienced pain at the local site of stab on the right thigh. Five hours later he felt generalized weakness and the next day, he was admitted to the hospital with high grade fever, nausea, vomiting, and tachycardia. On physical examination, he had very high fever and the doctors looking after him noticed a 6-cm diameter region of inflammation and induration in his right thigh. His further medical findings are depicted in table 1.

Mr. Markov died three days after the attack probably due to multiple organ failure. At the time of his death his white cell count rose to 32,000/mm<sup>3</sup> from 26,300/mm<sup>3</sup>. His ECG showed complete atrio-ventricular conduction block.

His autopsy revealed severe pulmonary edema, hemorrhage and necrosis involving multiple organs of the body including small bowel, lymph nodes in the right groin area that was close to the injection site, myocardium, testicles, spleen, adrenals and pancreas.

**Structure of ricin and pathogenesis of ricin toxicity**

Ricin is the member of the type 2 RIPs (ribosome-inactivating proteins). There are three types of Ri-

bosome Inactivating Proteins<sup>7</sup>. RIPs have been identified in plants, fungi, algae and bacteria.

1. Type I Ribosome Inactivating Proteins: They are single chain proteins and have a molecular weight of approximately 30 KDa
2. Type II Ribosome Inactivating Proteins: They are heterodimer and consist of two chains—Chain A and Chain B.
3. Type III Ribosome Inactivating Proteins: They are synthesized in an inactive precursor form called Pro RIPs. These inactive precursor or Pro RIPs will require proteolytic action to form active RIPs.

Ricin is a type II Ribosome Inactivating Protein which has two chains which are bound by a disulphide bond.

*Chain A:* It is approximately 32 KDa in molecular weight and it inactivates ribosomal RNA by depurinating a specific adenosine residue (A4324) near the 3' end of 28S ribosomal RNA. This halts the binding of elongation factor-2, which ultimately results in the inhibition of protein synthesis<sup>8</sup>.

*Chain B:* It is approximately 34 KDa in molecular weight. It binds to the glycoprotein present on the surface of epithelial cells and helps the chain A to enter the cell.

**Management**

Treatment is mainly symptomatic as there is no specific antidote for ricin. The management of ricin toxicity is largely supportive. The initial assessment of ricin poisoned patient begins with assessment of patient's airway, breathing and circulation.

*Management for oral poisoning*

For management of oral exposure supportive treatment is in form of maintaining fluid and electrolyte balance as oral administration of ricin leads to gastrointestinal fluid losses and hypotension. Intravenous fluids and vasopressor agents can be administered to such patients<sup>9</sup>.

**Table 1:** Clinical features of ricin poisoning in Mr. Georgi Markov

Immediate	Local Pain	
Within 5 hours	Weakness	
15-24 hours	High grade fever, nausea, vomiting	
36 hours	Critically ill with fever, tachycardia, swollen and sore inguinal lymph nodes	
2 days after attack	Hypotension, vascular collapse and shock, WBC – 26,300/mm <sup>3</sup>	

When the route of exposure of ricin is through ingestion, gastrointestinal decontamination should ideally be performed. If patient presents within one hour of ingestion and the general condition of the patient is stable, gastric lavage can be done. Some authors feel that a single dose of activated charcoal can be administered to patients who are not vomiting even though the adsorption of ricin by charcoal is unknown.

#### **Treatment goals for ricin poisoning via oral route**

Immediate replacement of body fluids  
Aggressive therapy with vasopressor agents if patient is hypotensive  
To correct electrolyte imbalance

Ricin poisoning through inhalational and parenteral routes are of much greater severity and lethality than oral poisoning. This is because the absorption of ricin through oral and dermal routes is minimal.

#### *Management for inhalational exposure*

When the route of exposure of ricin is through inhalation, general supportive and symptomatic treatment to reduce acute pulmonary edema and respiratory distress is indicated. Symptomatic treatment in such cases includes administration of oxygen, bronchodilator drugs, endotracheal intubation and positive end expiratory pressure.

#### **Diagnosis**

Diagnosis of ricin poisoning can be made depending on following two features

1. Clinical parameters
2. Epidemiological information

The epidemiological information includes history of ingestion of seeds of castor bean plant or occurrence of multiple cases with similar illness happening during a short period of time.

#### *Laboratory diagnosis*

Laboratory diagnosis of ricin poisoning will depend on identification of ricin in the following two types of samples

1. Biological fluids
2. The environmental samples from the area where the given patient was exposed<sup>10-12</sup>. Confirmation of ricin can be done by immunologically based methods<sup>13</sup>.

For detection of ricin in biological samples, the selected body fluid or any other specimen can be assessed for identification of ricinine. Ricinine is thought to be a marker of ricin toxicity and can be

detected by high performance liquid chromatography.

Ricin can be detected in environmental cases qualitatively by time-resolved fluorescence immunoassay (TRFIA) and polymerase chain reaction (PCR) in the given specimens. There is, however no commercially available assay currently available for detection of ricin in biological samples.

#### **Vaccination**

Prophylaxis against ricin poisoning can be tried through vaccination. There is currently no vaccine available for human use. However, development of ricin vaccine has focused on following two things.

1. Formalin inactivated toxoid
2. Deglycosylated A chain of ricin

Both the above mentioned vaccine preparations give protection only against aerosolized ricin. A recombinant protein vaccine named RiVax has been developed by BioPharma and is undergoing clinical trials<sup>14</sup>.

#### **Conclusion**

Ricin is one of the most potent plant toxin known to the mankind. It is obtained from the bean of castor plant (*Ricinus communis*). It is a byproduct of castor oil production. Owing to its high toxicity, stability, wide spread availability and ease of production, ricin can be used as a potential bio weapon. The ricin has been categorized as a Category B agent (second –highest priority) by the CDC. Clinical manifestations of ricin poisoning will depend on the route of administration of ricin. Although it is toxic by several routes but the toxicity is maximal when the route of administration is through inhalation. After a lethal dose of ricin aerosol, death may occur in 36 to 48 hours. The cause of death is hypoxemia due to massive pulmonary edema and alveolar flooding. Clinicians and health care providers should have a high index of suspicion whenever they come across an outbreak of severe respiratory or gastrointestinal illness. There is neither an antidote nor a vaccine to treat ricin toxicity and so the treatment is symptomatic and supportive.

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**Conflict of interest:** None

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