Clinical and pathological studies on intoxication in horses from freshly cut Jimson weed (Datura stramonium)-contaminated maize intended for ensiling

R Binev*, I Valchev and J Nikolov

ABSTRACT
Spontaneous intoxication in 34 horses after ingesting freshly harvested maize that was to be used for ensiling and heavily contaminated with young Datura stramonium plants, is described. The clinical status of all horses was monitored for 7 days, and included body (rectal) temperature, respiratory and heart rates, colour and moistness of visible mucosae, changes in pupil size, appetite, thirst, general behaviour, locomotion, sensory perceptions, urination and defaecation. The intoxication was accompanied by altered clinical status, namely mild hyperthermia, tachycardia, polypnoea, dyspnoea and shallow breathing, mydriasis, dry oral, rectal, vaginal and nasal mucosae, acute gastric dilatation and severe intestinal gas accumulation, anorexia to complete refusal of feed, decreased or absent thirst, absence of defaecation and urination. As a result of the treatment, the clinical parameters normalised between days 2 and 5. Necropsies and pathological studies were performed on two horses that died, revealing toxic liver dystrophy, cardiac lesions and substantial dystrophic and necrotic processes in the kidneys. The observed clinical signs, the pathomorphological changes and the applied therapy could be used in the diagnosis, differential diagnosis, prognosis and treatment of Jimson weed intoxication.

Key words: atropine, horses, intoxication, Jimson weed (Datura stramonium), scopolamine, tropine alkaloids.

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INTRODUCTION
Jimson weed (Datura stramonium) is an annual plant in the family Solanaceae. The toxic principles are tropane benzodona alkaloids which possess strong anticholinergic properties. They include hyoscyamine (stems, leaves, roots, seeds), hyoscine (roots), atropine (d,l-hyoscyamine) and scopolamine (l-hyoscyine). All parts of the plant are toxic, but the greatest amount of alkaloids are contained in ripe seeds, young, dried leaves and stems and leaves of young plants. They act as competitive antagonists to acetylcholine at peripheral and central muscarinic receptors at a common binding site. Poisoning results in widespread inhibition of parasympathetic innervated organs. The wide distribution, high toxicity and the potential for occurrence in foodstuffs are responsible for the numerous incidents in humans.

Cases of Jimson weed intoxication are considerably less frequent in animals such as cattle, swine, dogs and goats and poultry. In horses, poisoning has occurred after ingestion of Jimson weed seeds and dried tef hay contaminated with young Datura plants (Datura stramonium and D. ferox).

There are no published reports of cases of intoxication in horses from freshly cut Jimson weed (Datura stramonium)-contaminated maize intended for ensiling. The objective of this study was to evaluate the usefulness of clinical and morphological parameters of horses after Jimson weed intoxication for rapid and correct diagnosis, differential diagnosis, prognosis and effective treatment of this intoxication.

MATERIALS AND METHODS
In October 1999, 3 stallions were referred to the Clinic of Internal Diseases and Clinical Toxicology at the Faculty of Veterinary Medicine, Stara Zagora Bulgaria. The history revealed that 18 hours previously, 34 horses, owned by the Horse Station of the Faculty of Agriculture of the Trakia University, were fed ad libitum with freshly harvested and chopped maize that was to be used for ensiling and heavily contaminated with young D. stramonium plants. All animals that ingested the forage manifested signs of intoxication to varying degrees. The animals with the most evident clinical signs were referred to the clinic.

The examination in situ showed that the horses were 3–14 years old, with a live body weight of 400–600 kg, of various breeds (Trakehner, Hanoverian, Danube, East-Bulgarian, Arabian etc.) and type. The animals were of both sexes: 18 mares, 12 stallions and 4 geldings.

Depending on the severity of clinical signs, the animals were divided into 3 groups:

Group 1 (n = 18) – horses with typical clinical signs: 9 stallions, 1 gelding, 8 mares, 3 of them pregnant.

Group 2 (n = 16) – horses with less obvious signs of intoxication: 3 stallions, 3 geldings, 2 pregnant mares, 8 lactating dams (the suckling foals were not included in the group).

Group 3 (n = 18) – horses owned by the Mounted Police, housed on the same premises under similar conditions, but fed another forage, served as controls.

The complete clinical status of all groups of horses was assessed on post-intoxication days 1, 2, 3, 4, 5, 6 and 7, and comprised body (rectal) temperature via an electronic thermometer (GT 2038 Geratherm Medical, Germany), respiratory and heart rates, colour and moistness of visible mucosae, changes in pupil size, appetite, thirst, general behaviour, locomotion, sensory perceptions, urination, and defaecation using routine clinical diagnostic methods.

Two horses that died were necropsied and specimens for histological examination were fixed in 10 % neutral formalin and processed using routine histological techniques. The specimens were embedded in paraffin blocks, sectioned on a microtome (cross-section thickness of 5 µm) and stained with haematoxylin and eosin.

Data were statistically processed using ANOVA (Statistica, Statsoft Inc., http://
Results

Clinical studies

Clinical findings observed on the animals in group 1 included:

1. Colic symptoms: These were pronounced, especially on post-intoxication days 1–2. The colic symptoms were more severe in the group with Jimson weed intoxication (50 %) compared to the control group (25 %).

2. Rectal examination: This revealed greenish-black intestinal contents with numerous small erosions and superficial necroses on the bowel mucosa.

3. Gross examination: The stomach was not dilated, and in some areas, the enlarged and blood-filled central veins of lobules were observed.

4. Morphological studies: The pathoanatomical study evidenced a strong intestinal and gastric gas accumulation. In 1 horse, the stomach was ruptured, and in the other one, the diaphragm. The wound edges were irregular and impregnated with clotted blood, thus showing that the rupture took place before death. The mesenterial blood vessels were highly hyperaemic, and on the mesenterium and intestinal serosa, petechial haemorrhages were present. The gastric, intestinal and bowel mucosa were diffusely reddened. In the stomach and intestinal content, seeds and seed pods of Jimson weed were found. In the animal with the ruptured stomach, similar contents were found in the abdominal cavity as well. Multiple small erosions and superficial necroses on the bowel mucosa were observed. Mesenterial lymph nodes were oedematous, with a moist rose-red cross-section and single haemorrhages. The liver had a clay-yellow colour and in some areas, the enlarged and blood-filled central veins of lobules were observed.

Gross examination revealed a bilateral enlargement of the abdomen (in most cases more evident on the left side). Rectal examination of all animals revealed strong intestinal gas accumulation, especially in colon \textit{paramum ventrale et dorsale sinistrum}. In three-quarters of the animals, this was accompanied by an increase in caecal and gastric volume. Within 3–5 days most of the clinical signs had normalised, the last ones to do so being moistness of the mucosae, appetite and normal colour of conjunctivae (by post-intoxication days 3–6).

By day 3, polydipsia, frequent urination and defaecation were observed in 12 horses (66.6 %). The faeces were soft to aqueous, with a very unpleasant odour and greenish in colour. These changes receded after the 5th to 6th day.

In spite of therapy (see below), 2 horses died on the 2nd day.

In group 2, statistically significant changes in body temperature were not detected. Gross examination revealed bilateral enlargement of the abdomen and the rectal examination showed all horses to have a weak intestinal gas accumulation in colon \textit{paramum ventrale et dorsale sinistrum} and the caecum. The stomach was not dilated.

The sucking foals (n = 8) of dams from this group did not show signs of intoxication. Only 2 of them (25 %) had diarrhoeic faeces, and more frequent defaecation was evident on days 2 and 3.

Morphological studies

Several hours (3–5) before two of the horses in group 1 died, they were recumbent with stretched forelegs, often followed by lateral recumbency accompanied by kicking in the direction of the abdomen and looking in the same direction. Sweating, grinding of teeth, flared nostrils, clonic seizures, hypothermia (35–35.5 °C), accelerated, weak, soft and hardly perceptible heart rate (100–120/min), elevated respiratory rate (50–60/min) and shallow respiration were also observed.

The pathoanatomical study evidenced a strong intestinal and gastric gas accumulation. In 1 horse, the stomach was ruptured and in the other one, the diaphragm. The wound edges were irregular and impregnated with clotted blood, thus showing that the rupture took place before death. The mesenterial blood vessels were highly hyperaemic, and on the mesenterium and intestinal serosa, petechial haemorrhages were present. The gastric, intestinal and bowel mucosa were diffusely reddened. In the stomach and intestinal content, seeds and seed pods of Jimson weed were found. In the animal with the ruptured stomach, similar contents were found in the abdominal cavity as well. Multiple small erosions and superficial necroses on the bowel mucosa were observed. Mesenterial lymph nodes were oedematous, with a moist rose-red cross-section and single haemorrhages. The liver had a clay-yellow colour and in some areas, the enlarged and blood-filled central veins of lobules were observed.

Table 1: Change in clinical parameters in horses after intoxication with Jimson weed (\textit{Datura stramonium}) (groups 1 and 2) and in the control group (group 3).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group</th>
<th>Day after the intoxication</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Body temperature (°C)</td>
<td>38.8 ± 0.3°C</td>
<td>38.6 ± 0.2°C</td>
</tr>
<tr>
<td></td>
<td>37.8 ± 0.2°C</td>
<td>37.4 ± 0.1°C</td>
</tr>
<tr>
<td></td>
<td>37.5 ± 0.2°C</td>
<td>37.2 ± 0.1°C</td>
</tr>
<tr>
<td>Heart rate (per min)</td>
<td>98.8 ± 8.3°C</td>
<td>72.4 ± 5.4°C</td>
</tr>
<tr>
<td></td>
<td>65.4 ± 7.1°C</td>
<td>58.3 ± 6.7°C</td>
</tr>
<tr>
<td></td>
<td>37.8 ± 5.8°C</td>
<td>39.1 ± 4.8°C</td>
</tr>
<tr>
<td>Respiratory rate (per min)</td>
<td>64.5 ± 7.3°C</td>
<td>34.2 ± 5.8°C</td>
</tr>
<tr>
<td></td>
<td>30.2 ± 5.6°C</td>
<td>16.2 ± 2.8°C</td>
</tr>
<tr>
<td></td>
<td>16.2 ± 2.3°C</td>
<td>14.3 ± 2.4°C</td>
</tr>
</tbody>
</table>

*aP < 0.05; bP < 0.01; cP < 0.001.*
clearly distinguishable. The mucosae of the spleen, kidneys, epicardium and the endocardium of both atria exhibited petechial and more extensive haemorrhages. The lungs were strongly reduced in size, hyperaemic with an increased density. The meninges were strongly hyperaemic.

The mucosae of intestines and the colon manifested various degrees of dystrophic necrotic processes, often resulting in complete desquamation of the lining and glandular epithelium.

Massive hyperaemia of vessels and mucosal oedema, more apparent in the large intestines, was present. The sinuses of mesenterial lymph nodes were filled with erythrocytes and in the parenchyma, single haemorrhages were present. In the lungs, strong congestive hyperaemia and infiltration of the interstitium with erythrocytes was noticed. The cardiac musculature revealed granular dystrophy, cloudy swelling, hyalinisation of the myocardium, hyperaemia and haemorrhages with interstitial oedema (Fig. 1).

In the liver, varying degrees of granular and fatty dystrophy, karyolysis and pyknosis of hepatocytic nuclei was observed (Fig. 2). The central veins and their capillaries were highly distended and overfilled with blood. In the renal parenchyma, extensive, strong and general dystrophic and necrotic changes and disintegration were present, with epithelial desquamation of the renal tubules.

The lethal histopathological changes were similar in both animals.

**Treatment**

In horses in group 1, a single gastric lavage with suspension of activated charcoal was performed via naso-oesophageal intubation. Half an hour later, a solution of 300 g MgSO₄ (Biovet, Pestera, Bulgaria) and 500 g activated charcoal in 5 l water was administered via naso-oesophageal intubation.

The inflated intestines were perforated via the rectum by means of a long needle covered by the hand. The procedure was performed after identifying the site with the strongest intestinal gas accumulation. For controlling the exiting gas, the needle was connected to a rubber tube, the distal end of which was inserted into a container with water.

A single bloodletting was done in all horses. The amount of blood was calculated according to body weight, on average 10 ml/kg. For 4 consecutive days intravenous administration of 3 l Ringer solution (Balkanpharma, Troian, Bulgaria), 10 g ascorbic acid (Vitamin C, Biovet, Pestera, Bulgaria), 1 g thiamine (Vitamin B₁, Biovet, Pestera, Bulgaria), 100 ml sodium N-acetyl methionine (5 % Metionin, Sinaps, Veliko Tarnovo, Bulgaria) and 20 ml 20 % caffeine sodium benzoate (Biovet, Pestera, Bulgaria) was continued. Medication therapy was extended to intramuscular administration of benzylpenicillin procaine and dihydrostreptomycin (Intramicin, Ceva Sante Animale, France) at a dose of 5 ml/100 kg body weight, every 24 hours. As an antidote, pilocarpine hydrochloride (5 % Pilocarpin, Biovet, Pestera, Bulgaria) was administered subcutaneously: on post-intoxication day 1, 100 mg 6 times at 2-hour intervals; on post-intoxication day 2, 100 mg 4 times at 4-hour intervals, and on post-intoxication days 3 and 4, 100 mg 3 times at 6-hour intervals.

During the application of pilocarpine hydrochloride, the clinical status of animals was monitored with regard to the restoration of the moisture levels of visible mucosae, the pupils, heart and respiratory rates, defaecation and urination. After 3–5 administrations of pilocarpine hydrochloride, it was noticed that mucosal moistness was restored, although for a very short time in the beginning (from 30–60 minutes). After 2–3 days, this interval increased to several hours (3–5), but a complete restoration of moistness was only observed by days 5–6. The other clinical parameters normalised between the 3rd and 5th days. The diluted pupils were not influenced during the first 3 days of pilocarpine hydrochloride application, but returned to normal between days 4 and 5.

In horses from group 2, venesection was done on post-intoxication day 1 and 100 mg pilocarpine hydrochloride was administered thrice at 4 hourly intervals.

**DISCUSSION**

The toxic effect of Jimson weed results from the antimuscarinic action of the alkaloids it contains. The increased heart rate observed by us and by other authors is due to removal of the parasympathetic component of vagal block and correlated with...
observed histopathological alterations (granular dystrophy, cloudy swelling, hyalineisation of the myocardium, hyperaemia, haemorrhages with interstitial oedema). The observed polyneuropathy with dyspnoea is in accordance with data from literature\textsuperscript{1,2,14,17,28,44} and is probably a consequence of the colic syndrome and corresponds to morphological changes in lung parenchyma — the strong congestive hyperaemia and infiltration of the interstitium with erythrocytes. The dilatation of the pupils is a clinical sign of this intoxication\textsuperscript{1,6,22,28,32,37,39} and was a further manifestation of parasympathetic changes in the colon and caecum) and lack of urination and defaecation. An anticholinergic sign is the constriction of urinary bladder sphincter, hyperaesthesia, impaired thermoregulation, correlating with observed anuria and instead its synthetic analogue physostigmine has been discontinued but it is for internal use cannot be used in horses with intoxication. We therefore used pilocarpine hydrochloride as an antidote — a cholinomimetic with a direct effect (an antagonist of cholinoreceptors). There are no data on the relative efficacy of these preparations and whether phystostigmine or pilocarpine hydrochloride is more or less effective in Jimson weed (\textit{Datura stramonium}) intoxication remains to be determined.

**CONCLUSIONS**

The clinical signs manifested after intoxication with Jimson weed were hyperthermia, tachycardia, polyneuropathy with dyspnoea, acute gastric dilatation, secondary intestinal gas accumulation, myodystrophy, dry mucousae, complete refusal of feed, lack of thirst, defaecation and urination. In lactating mares, the course of Jimson weed intoxication was more rapid, without the typical signs. The succumbing foals did not manifest signs of intoxication. The prognosis is more favourable if polydipsia, polyuria and frequent defaecation are observed during the recovery from intoxication. The pathomorphological studies showed a toxic liver dystrophy and extensive dystrophic and necrotic changes in the kidneys and myocardium. The applied schedule of treatment is effective in the initial stage of the intoxication. The clinical signs, morphological alterations and the effect of the treatment in Jimson weed intoxication are directly related to the stage of intoxication.

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