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Original Contribution

CLINICAL AND PATHOLOGICAL STUDIES OF JIMSON WEED (DATURA STRAMONIUM) POISONING IN HORSES

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ABSTRACT

A spontaneous intoxication in 34 horses after intake of freshly harvested ensiled maize, accidentally contaminated with young *Datura stramonium* plants was followed. In a 7-day study, the full clinical status was monitored and this included among others the following: body (rectal) temperature, respiratory and heart rates, colour and humidity of visible mucosae, changes in pupil size, appetite, thirst, general behaviour, locomotion, sensory perceptions, urination, defecation. Results manifesting in these clinical parameters were a generalised intoxication associated with 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 defecation and urination. On treatment, the clinical indices were normalized between days 2 and 5. In dead horses (n=2), necropsies and pathological studies were performed. They revealed a toxic liver dystrophy, cardiac lesions and substantial dystrophic and necrotic processes in 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: horses, intoxication, Jimson weed (*Datura stramonium*), tropane alkaloids, atropine, scopolamine

INTRODUCTION

Jimson weed (*Datura stramonium*) is an annual plant from the *Solanaceae* The toxic principles are tropane belladonna alkaloids which possess strong anticholinergic properties (1 – 4). These alkaloids include, hyoscyamine (stems, leaves, roots, seeds) (5), hyoscine (roots); atropine (*d,l*-hyoscyamine) and scopolamine (*l*-hyoscine) (5 – 10). All parts of the plant are toxic, but the greatest amount of alkaloids is contained in ripe seeds (4, 7, 11, 12), young, dried leaves (13) and stems and leaves of young plants (5). They act as competitive antagonists to acetylcholine at peripheral and central muscarinic receptors at a common binding site (4, 8, 11). Poisoning results in widespread inhibition of parasympathetic innervated organs (8, 11, 14 - 16).

The wide distribution, the strong toxicity and the potential for occurrence in foodstuffs are responsible for the numerous incidents in humans (3, 6, 7, 10, 11, 14, 15, 17 – 33).

The cases of Jimson weed intoxication in animals are considerably less frequent – cattle (34), swine (9, 35 - 37), dogs (38, 39), sheep and goats (40) and poultry (12, 41). In horses, poisoning has occurred after ingestion of Jimson weed seeds (42 - 44) and dried tef hay contaminated with young *Datura* plants (*Datura stramonium* and *Datura ferox*) (13).

Datura stramonium contamination in ensiled maize and the subsequent intoxication in horses fed on it is an event whose reports have not been vigorously pursued. Hence this formed the motive for carrying out studies on the clinical and morphological investigations in horses so exposed. The strategic importance is to fashion out ways of diagnoses, the prognosis and effective treatment of the condition.

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MATERIALS AND METHODS

In October 1999, three stallions had been referred to the Clinic of Internal Diseases and Clinical Toxicology of the Faculty of Veterinary Medicine, Stara Zagora in Bulgaria. The history revealed that 18 hours before, 34 horses, owned by the *Horse Station* of the Faculty of Agriculture in the Trakia University, were fed *ad libitum* with freshly harvested and chopped maize meant for ensiling but found to be heavily contaminated with young *Datura stramonium* plants. All animals that ingested the forage manifested signs of intoxication to varying degrees, the animals referred to the clinic being those with the most evident clinical signs.

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

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

- Group one (n=18) – horses with typical clinical signs: 9 stallions, 1 gelding, 8 mares, 3 of them pregnant.
- Group two (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 three (n=18) – horses (owned by the Mounted Police), housed in the same premise under similar conditions, but fed another forage, served as controls.

The complete clinical status of all groups of horses was followed up in dynamics by post intoxication days 1, 2, 3, 4, 5, 6 and 7 with respect to body (rectal) temperature via an electronic thermometer (GT 2038 Geratherm Medical, Germany), respiratory and heart rates, colour and moisture of visible mucosae, changes in pupil size, appetite, thirst, general behaviour, locomotion, sensory perceptions, urination, defecation, etc. using routine clinical diagnostic methods.

The 2 horses that died were necropsied and specimens for histological examination were obtained. They were fixed in 10% neutral formalin and processed using the routine histological technique. The specimens were embedded in paraffin blocks, cut on a microtome (cross section thickness of 5 μm) and stained with haematoxylin-eosin (H/E).

All results were statistically processed using the ANOVA test (Statistica software). The significance of differences was evaluated against the control group for each time interval. The results were determined as significant at the $p<0.05$ level.

RESULTS

I. Clinical studies

The changes in the clinical parameters (body temperature, heart and respiratory rates) are presented on **Table 1**. In horses from the first group, significant changes in studied parameters occurred by post intoxication days 1 and 2. The rectal temperature was elevated on days 1 and 2 respectively – 38.8 ± 0.2^0C ($p<0.01$) and 38.6 ± 0.2^0C ($p<0.01$) vs the respective control measurements – 37.5 ± 0.2^0C and 37.2 ± 0.1^0C.

Table 1. *Change in clinical indices in horses after intoxication with Jimson Weed (Datura stramonium) (I and II group) and controls (III group).*

		Days after the intoxication						
Indices	Groups	1st	2nd	3rd	4th	5th	6th	7th
Body temperature (C°)	I	38.8±0.3[c]	38.6±0.2[c]	37.9±0.1	38.0±0.2	37.6±0.3	37.9±0.3	37.5±0.2
	II	37.8±0.2[b]	37.4±0.1	37.4±0.1	37.6±0.2	37.8±0.2	37.2±0.2	37.4±0.3
	III	37.5±0.2	37.2±0.1	37.9±0.2	37.7±0.3	37.3±0.2	37.5±0.2	37.4±0.2
Heart rate (min^{-1})	I	98.8±8.3[c]	72.4±5.4[c]	54.5±6.3	41.3±5.8	50.2±6.3	43.0±5.0	38.7±4.2
	II	65.4±7.1[b]	58.3±6.7[a]	48.3±6.2	38.8±6.3	48.4±4.2	46.6±5.8	42.3±3.3
	III	37.8±5.8	39.1±4.8	40.2±7.1	38.8±5.5	42.4±4.8	37.8±5.2	35.0±5.0
Respiratory rate (min^{-1})	I	64.5±7.3[c]	34.2±5.8[b]	15.8±2.6	14.5±2.6	12.7±1.8	14.4±2.9	13.2±2.6
	II	30.2±5.6	16.2±2.8	18.2±2.1	13.7±1.4	14.4±2.3	12.7±1.8	13.4±1.1
	III	16.2±2.3	14.3±2.4	16.8±1.4	15.6±2.3	14.8±1.8	13.8±2.1	15.2±2.7

[a]$p<0.05$; [b]$p<0.01$; [c]$p<0.001$.

Heart rates were accelerated on days 1 and 2 respectively – 98.8±8.3 min^{-1} ($p<0.01$) and 72.4±5.4 min^{-1} ($p<0.01$) respectively, compared to the control values (37.8±5.8 min^{-1} and 39.1±4.8 min^{-1} respectively). A weak, soft and rhythmic pulse and a visible cardiac shocks in cardiac region were registered.

The respiratory movements were also accelerated on days 1 and 2 respectively – 64.5±7.3 min^{-1} ($p<0.01$) and 34.2±5.8 min^{-1} ($p<0.01$), vs the respective controls – 16.2±2.3 min^{-1} and 14.3±2.4 min^{-1}. They were shallow and associated with widely open nostrils. By post intoxication day 3, the studied parameters were normalized.

The clinical signs in this group were the most visible – mydriasis, complete refusal of food, lack of thirst, defecation and urination, dry mucosae (oral, nasal, vaginal and rectal), diffusely reddened conjunctivae, disturbances in locomotion, hyperesthesia, muscle cramps and hyperreflexia.

The colic symptoms in horses from this group were moderately severe and continuous. The animals hit the ground with their forelimbs, turned their head to the abdomen (mostly on the left side) and stood with legs wide apart (urinating posture).

The inspection revealed a bilateral enlargement of the abdomen, in most cases more visible on the left. The rectal examination in all animals showed the presence of a strong intestinal gas accumulation, especially in *colon primum ventrale et dorsale sinistrum.* Increase in 75 % of cases was accompanied by caecal and gastric volume.

Within days 3–5, the majority of altered clinical signs were overcome. The signs that were the last to normalized were the humidity of mucosae, the appetite and the normal colour of conjunctivae (by post intoxication days 5–6).

By day 3, polydipsia, frequent urination and defecation were observed in 12 horses (66.6 %). The faeces were softened to aqueous form, with a very unpleasant odour and greenish colour. The registered changes faded away after the 5^{th} – 6^{th} day.

Despite the therapy (see below), two horses died on the 2^{nd} day.

In animals from group II, significant changes in body temperature were not detected. The heart rate was accelerated by days 1 and 2 – 65.4±7.1 min^{-1} ($p<0.01$) and 58.3±6.7 min^{-1} ($p<0.05$), respectively, vs the control values of 37.8±5.8 min^{-1} and 39.1±4.8 min^{-1}. The pulse was weak and soft. The respiratory rate was accelerated for only by the first day– 30.2±5.6 min^{-1} ($p<0.05$) versus controls (16.2±2.3 min^{-1}).

In animals from group II, the colic symptoms were alternating with short painless episodes. The other clinical signs were less obvious and transient. Only by post intoxication day 1, the following clinical signs were observed – mydriasis in 9 horses (56.2 %), complete refusal of feed (n=4) (25 %), anorexia (n=12) (75 %), lack of thirst (n=4) (25 %) and lack of defecation (n=8) (50 %), dry mucosae (n=5) (31.2 %), diffusely reddened conjunctivae (n=2) (12.5 %) and nervous signs (n=3) (18.8 %). The frequency of urination was unchanged.

The inspection did not show enlargement of the abdomen and the rectal examination in all horses showed a weak intestinal gas accumulation in *colon primum ventrale et dorsale sinistrum* and the caecum. The stomach was not dilated.

The suckling foals (n=8) of dams from this group did not show signs of intoxication. Only in two of them (25 %), diarrhoeic faeces and more frequent defecation occurred between days 2 and 3

II. Morphological studies

Several hours (3-5 h) prior to the lethal issue in both horses, the animals were recumbent with stretched forelegs and this position was frequently changed to lateral recumbency accompanied by kicking in the direction of the abdomen and looking in that same direction. Sweating, grinding of the teeth, widely open nostrils, clonic seizures, hypothermia (35-35.5^{0}C), accelerated, weak, soft and hardly perceptible heart rate (100-120 min^{-1}), enhanced respiratory rate (50-60 min^{-1}) and shallow respiration were also observed.

The pathoanatomical study evidenced a strong intestinal and gastric gas accumulation. In one horse, the stomach was ruptured and the other one – the diaphragm, the wound edges being irregular and impregnated with clotted blood, thus showing that the rupture took place before the death. The mesenterial blood vessels were highly hyperaemic, and on the mesenterium and intestinal serosa, petechial haemorrhages were present. The gastric, intestinal and bowel mucosae were diffusely reddened. In the stomach and intestinal content, seeds and seedpods of Jimson weed were found. In the animal with the ruptured stomach, similar content was 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-reddish cross section and single haemorrhages. The liver was of a clay-yellow colour and in some areas enlarged and blood-filled central veins of lobules were 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 and with increased density. The meninges were strongly hyperaemic.

During the histopathological study, the mucosae of intestines and the colon manifested various degrees of dystrophic-necrotic processes, often resulting in a complete desquamation of the lining and glandular epithelium.

A massive hyperaemia of vessels and mucosal oedema, more visible in large intestines, were present. The sinuses of mesenterial lymph nodes were filled with erythrocytes and among the parenchyma, single haemorrhages were observed. In the lungs, a strong congestive hyperaemia and infiltration of the interstitium with erythrocytes were noticed. The cardiac musculature revealed granular dystrophy, cloudy swelling, hyalinization of the myocardium, hyperaemia, haemorrhages with interstitial oedema (**Figure 1**).

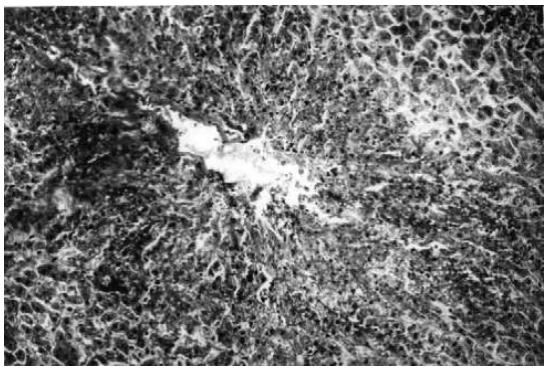

Figure 1. *Morphological changes in horses after intoxication with Jimson Weed (Datura stramonium). Toxic liver dystrophy in the region of the central vein, bar = 2.5 μm.*

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

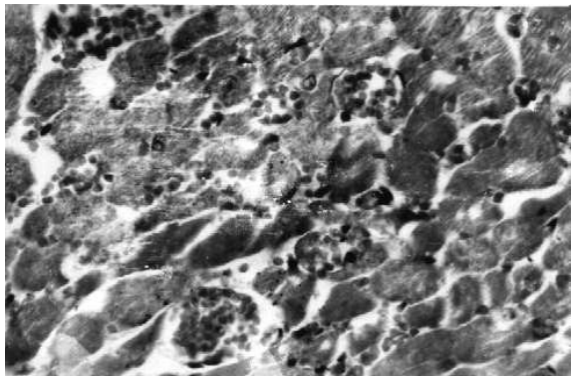

Figure 2. *Morphological changes in horses after intoxication with Jimson Weed (Datura stramonium). Granular dystrophy and hyalinization of the cytoplasm of myocardiac fibres. Strong blood vessel hyperaemia, bar = 3 μm.*

The histopathological changes in horses with lethal issue were similar in both animals.

III. Treatment

In the horses in the first group, a single gastric lavage with suspension of activated charcoal was performed via a naso-oesophageal intubation. Half an hour later, a solution of 300 g $MgSO_4$ (Biovet, Pestera, Bulgaria) and 500 g activated charcoal, in 5 l water was administered via a naso-oesophageal intubation.

The inflated intestines were perforated via the rectum. The rectum was penetrated by means of a long needle hidden in the hand. The puncture 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 whose distant end was put into a container with water.

A single bloodletting was done in all horses. The amount of blood was calculated according to the body weight – on the 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 B_1, Biovet, Pestera, Bulgaria), 100 ml sodium N-acethyl methionine (5 % Methionine, Sinaps, Veliko Tarnovo, Bulgaria) and 20 ml 20% caffeine sodium benzoate (Biovet, Pestera, Bulgaria) were applied. Medication therapy was extended by intramuscular administration of benzylpenicilline procaine and dihydrostreptomycin (Intramicin, Ceva Sante Animale, France) in dose 5 ml/100 kg body weight, every 24 hours. As an antidote, pilocarpine hydrochloride (5% Pilocarpin,

Biovet, Pestera, Bulgaria) was s.c. applied: by post intoxication day 1: 100 mg 6 times at 2 hour intervals; by post intoxication day 2: 100 mg 4 times at 4 hour intervals and by 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 humidity of visible mucosae, the pupils, heart and respiratory rates, defecation and urination. After 3-5-fold administration of pilocarpine hydrochloride, we noticed that initially, the humidity of mucosae was restored, although for a very short time in the beginning (from ½ to 1 h). After 2-3 days, this interval increased to several hours (3-5), but a complete restoration of humidity was observed by day 5-6. The other clinical parameters normalized between the 3rd and 5th days. The dilated 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 II, venesection was done by by post intoxication days 1 and 100 mg pilocarpine hydrochloride was administered thrice at 4 hour intervals hour intervals.

DISCUSSION

The toxic effect of Jimson weed results from the antimuscarinic action of the alkaloids it contains (1, 4, 7 - 9, 11, 15, 19, 42, 45 - 50). The increased heart rate observed by us and by other authors (6, 14, 18, 22, 24, 29, 40, 42, 44) is due to removal of the parasympathetic component of vagal block and correlated with observed histopathological alterations (granular dystrophy, cloudy swelling, hyalinization of the myocardium, hyperaemia, haemorrhages with interstitial oedema). The observed polypnoea with dyspnoea in accordance with data from literature (6, 14, 22, 24, 29, 40, 42, 44), are probably a consequence of the colic seizure and correspond 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 (3, 4, 13, 17, 20, 24, 34, 38, 43, 51, 52) and was a further manifestation of parasympathetic block (6, 14, 20, 22, 24, 29, 33, 48, 49, 53 - 56). The observed hyperthermia is very interesting for discussion, taking into consideration that the peripheral vasoconstriction in man could not be a cause for elevation of body temperature (45). On the other side however, due to the rapid development of the intoxication, we did not notice histopathological data for inflammatory processes in horses with lethal issue. We assume that hyperthermia was resulting from impaired thermoregulation, correlating with strongly hyperaemic meninges. Alkaloids of Jimson week inhibit the secretion of cholinergic innervated glands and this is an explanation for the dry mucosae (oral, nasal, rectal, vaginal) (4, 6, 7, 14, 18, 20, 22 - 24, 26, 29, 40, 43, 48, 51, 52, 55). Subsequent to the inhibition of parasympathetically innervated organs (7, 8, 15, 48, 50 - 52, 55, 57) a paralytic ileus occurs (43, 44, 47, 50, 51, 54), followed by a secondary intestinal gas accumulation, clinically manifested by acute gastric dilatation, increased volume of bowels (especially the colon and caecum) and lack of defecation. An anticholinergic sign is the constriction of urinary bladder sphincter resulting in accumulation of urine, correlating with observed anuria (6, 7, 18, 24, 34, 48, 52, 55). Our observations about the lack of thirst, urination and defecation are in accordance with literature (6, 12 - 15, 24, 37, 40, 42, 52, 55) but differ from cited cases of intoxication (44), accompanied with polyuria, polydipsia, and defecation. In our opinion, these are characteristic features for counteracting the intoxication. With regard to the clinical picture, the reported nervous signs (disturbances in locomotion, hyperaesthesia, hyperreflexia and tremor, correlating with meningeal hyperaemia) observed by both us and other investigators (6, 31, 32, 34, 40, 52) are in accordance with the well-known CNS signs due to these alkaloids.

Most investigators (18, 23, 24, 26, 30, 45, 52) consider physostigmine therapy as the most effective in anticholinergic toxicity. It could be however stated, that in critical cases the preparation has no effect (30) and that it can produce complications such as seizures and cardiac arrhythmia (3, 46). In Bulgaria, the use of physostigmine is discontinued and instead, its synthetic analogue rivastigmine is employed, but it is for internal use and thus, could not be used in horses with intoxication. That is why, pilocarpine hydrochloride was used as an antidote – a cholinomimetic with a direct effect (antagonist of cholinoreceptors). We have no data about the efficacy of both preparations for comparative purposes and could not therefore recommend definitely physostigmine or pilocarpine hydrochloride as more or less effective in Jimson weed (*Datura stramonium*) intoxication.

CONCLUSIONS

The clinical signs manifested after intoxication with Jimson weed were: hyperthermia, tachycardia, polypnoea with dyspnoea, acute gastric dilatation, secondary intestinal gas accumulation, mydriasis, dry mucosae, complete refusal of feed, lack of thirst, defecation and urination.

In lactating mares, the course of Jimson weed intoxication was more rapid, without the typical signs.

The suckling foals did not manifest signs of intoxication.

The prognosis is more favourable, if during the recovery from intoxication polydipsia, polyuria and frequent defecation are observed.

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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