

Hepatogenous Photosensitization Neonatal Calf Raised on *Brachiaria decumbens* Pasture

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ABSTRACT

Background: Hepatogenous photosensitization occurs when there is a liver injury that prevents the excretion of phylloerythrin, which absorbs solar radiation, leading to the release of free radicals, which result in cellular damage. Lithogenic saponins present in grasses of the genus *Brachiaria* spp. are capable of inducing the formation of bile crystals, leading to hepatogenic photosensitization. Lactating animals can develop the condition when ingesting breast milk containing saponins. This study aims to report the diagnosis, clinical evolution and treatment of a case of hepatogenic photosensitization in a 22-day-old lactating Tabapuã calf.

Case: The animal was raised with its mother on pasture composed exclusively of *Brachiaria decumbens*. Physical examination revealed skin erythema, yellowish diarrhea, corneal opacity and corneal ulcers in both eyes. The animal presented alopecic and reddish areas on the back, flanks, rump, limbs and face. Upon manipulation, the fur and skin came off, revealing a reddish subcutaneous layer. Among the laboratory tests requested, the blood count showed leukocytosis due to lymphocytosis and hyperfibrinogenemia. The results of the egg and oocyst count per gram of feces, the hematozoan test and the skin scraping were negative. The presumptive diagnosis of hepatogenic photosensitization was based on the anamnesis and clinical signs and later confirmed by the response to the established treatment measures. Treatment consisted primarily of removing the mother and calf from the *Brachiaria decumbens* pasture and from exposure to sunlight. Vitamin and amino acid complexes, anti-inflammatory drugs and antibiotics were also used. To treat the corneal ulcers, it was necessary to use several ophthalmic drugs, the dosages of which had to be adjusted during treatment. In addition, 2 subconjunctival injections of 0.2% meloxicam were performed in both eyes, and a grid keratotomy procedure was performed. After complete healing of the ulcers, dexamethasone ophthalmic ointment was used to reduce scarring. After 54 days of treatment, the calf showed complete remission of clinical signs, with re-epithelialization and significant hair growth in the affected areas.

Discussion: The study reports a case of a lactating calf, so the ingestion of toxins occurred via breast milk. The mother was raised on *Brachiaria decumbens* pasture, a species with high concentrations of lithogenic saponins. Clinical signs included corneal ulcers, a condition rarely reported in cases of hepatogenic photosensitization. The calf is a Tabapuã breed, with more pigmented skin, showing that even dark-skinned animals can develop severe forms of the disease. The main treatment measures are changing the animal's diet and removing it from direct sunlight. In this case, since it is a lactating animal, the mother needed to change its diet in order to stop the transfer of toxins via milk. Prevention and control measures should be considered in cattle affected by the disease. Strategies such as gradual adaptation to pasture and nutritional supplementation can reduce the risk of poisoning. In addition, reproduction of the affected animal and the use of *Brachiaria* spp. species with lower concentrations of saponins can be avoided. It is important to consider the occurrence of the disease in lactating animals when considering possible diagnoses. Clinical and epidemiological knowledge, early diagnosis and rapid intervention are crucial for a good prognosis of the disease.

Keywords: beef cattle, intoxication, tabapuã, neonate.

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INTRODUCTION

The sensitivity of the skin to light, due to the action of certain drugs, plants or other substances, is called photosensitization [29]. Many outbreaks of hepatogenous photosensitization have been observed in animals grazing *Brachiaria* spp. In Brazil, it is known that steroidal lithogenic saponins from *B. decumbens* and *B. brizantha* are primarily responsible for causing the disease [24]. The metabolism of saponins, mainly protodioscin, in the case of *Brachiaria decumbens*, results in the formation and deposition of insoluble crystals, which cause biliary obstruction, inflammation and necrosis of hepatocytes and photosensitization, due to the impossibility of excreting phylloerythrin [25].

Depigmented skin is most affected by lesions, but in severe cases dark skin is also affected. Initially, the skin becomes red and later, exudation and crusting occur [2]. Necrosis and dry gangrene then occur, leaving the damaged skin with the appearance of tree bark, which later comes off. There may be ulcerations on the ventral part of the tongue, keratitis, corneal opacity and blindness [6].

Diagnosis is based on anamnesis, clinical signs and laboratory tests [15]. Treatment includes removing animals from pasture and sun exposure and applying topical ointment to wounds [2].

Given the scarcity of case reports of hepatogenous photosensitization in suckling calves, this study focuses on describing the diagnosis, clinical evolution and treatment of a case of the condition in a neonatal calf.

CASE

Assistance was requested from the UFLA Large Animal Veterinary Hospital for a 22-day-old female bovine, Tabapuã breed, in the municipality of Lavras-MG complaining of hair loss. According to the history, she was kept in an exclusive pasture of *Brachiaria decumbens* with her mother and another cow with a calf, which did not present symptoms. In recent years, there have been no similar cases on the property. Previously, the property had been managed to place an earring on the 17th day of life and the animal did not show any changes. After 5 days, when it was handled again, they observed hairless and reddish areas on the animal's back, which is when they requested assistance.

On physical examination, the animal had a heart rate of 130 beats per minute, a respiratory rate of

40 movements per minute, pink mucous membranes, a rectal temperature of 40°C and liquid, yellowish feces. On inspection, the corneas were observed to be opaque and edematous. Staining with 1% fluorescein ophthalmic solution revealed a corneal ulcer, occupying a significant part of the eyeball in both eyes (Figure 1).

There were alopecic and reddish areas on the back, flanks, rump, limbs and face and, in some of these areas, there was thickening of the skin and cuts (Figure 2A). Upon manipulation, the hair and skin came off in a block revealing a reddish subcutaneous layer (Figure 2B).

The hemogram showed leukocytosis (16600 mm³; Ref.: 4000-12000 mm³), lymphocytosis (11122 mm³; Ref.: 1800-9000 mm³) and there was also hyperfibrinogenemia (1400 mg/dL; Ref.: 300-700 mg/dL). The result of the egg count per gram of feces (OPG) and oocyst count per gram of feces (OOPG) was negative, as was the search for hematozoa in the peripheral blood smear. Skin scrapings were collected from several regions to investigate scabies, fungi and bacteria, but

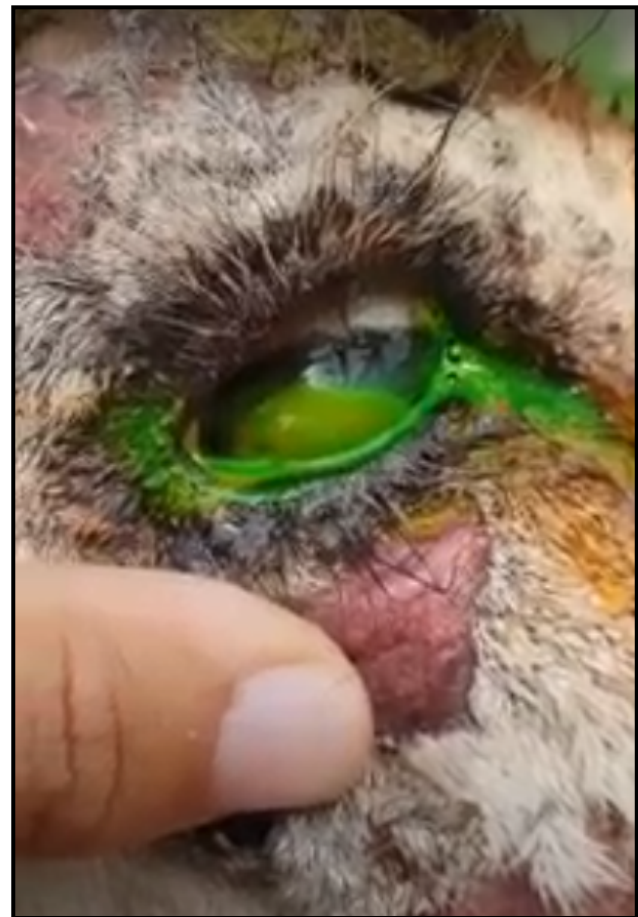


Figure 1. Fluorescein test 1% sodium, showing corneal ulcer in a Tabapuã calf, treated by the team at the UFLA Large Animal Veterinary Hospital, with hepatogenous photosensitization.

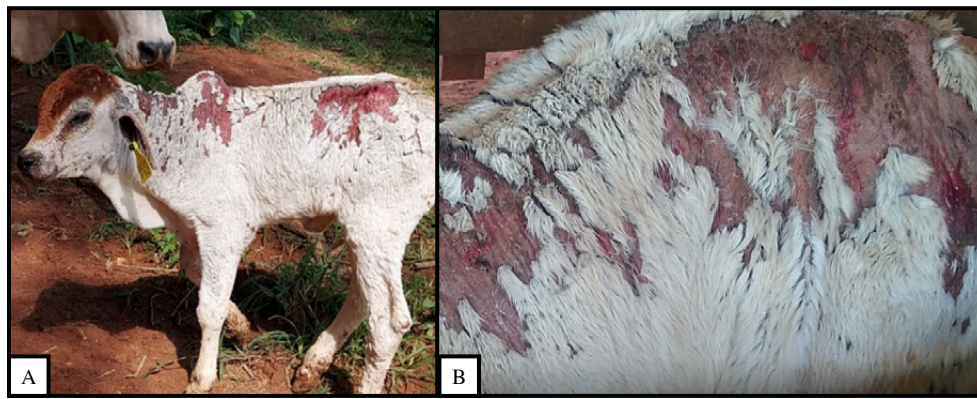


Figure 2. Tabapuã calf, with hepatogenic photosensitization, treated at the UFLA Large Animal Veterinary Hospital. A- Alopecic, erythematous and irregular areas in the face, back, rump and limbs. B- Areas with skin detachment in the dorsal region at the 1st visit.

none of these were found. Based on the anamnesis and physical examination findings, a presumptive diagnosis of hepatogenous photosensitization was made.

The following treatments were administered: vitamin and amino acid complex¹ [Mercepton® - 5 mL, IM, SID, for 5 days], vitamin B12¹ [Monovin B12® - 1 mL, IM, q 48h, totaling 3 applications]; flunixin meglumine² [Desflan® - 1.1 mg/kg, IM, SID, for 3 days]; sulfamethoxazole+trimethoprim² [Trissulfon® - 30 mg/kg, IM, SID, for 7 days]; zinc oxide ointment³ [Unguento® - topical application to alopecic areas, BID, until the condition resolved]. It was recommended that

the mother and calf be immediately removed from the *Brachiaria decumbens* pasture and from exposure to the sun.

The treatment of corneal ulcers lasted 41 days. It was necessary to use several topical ophthalmic drugs until the corneal ulcers were completely resolved and the corneal scar was reduced. The drugs used were changed and their dosages adjusted during this period, according to the evolution of the lesions. The dosage of drugs and immunobiologicals used to treat corneal ulcers are described in Table 1. In addition, 2 subconjunctival injections of meloxicam² [Maxicam

Table 1. Dosage of drugs and immunobiologicals used to treat corneal ulcers in a Tabapuã calf diagnosed with hepatogenous photosensitization, treated at the UFLA Large Animal Veterinary Hospital.

Drug/ Immunobiological	Frequency of application	Duration of treatment	Volume/ Quantity	Days of treatment
Equine heterologous serum	4 times a day	41 days	0.1 mL	1st to 41st
Diclofenac sodium eye drops 0.1%	4 times a day	12 days + 20 days	0.1 mL	1st to 12nd 21st to 41st
Ciprofloxacin hydrochloride eye drops	4 times a day	12 days	0.1 mL	1st to 12nd
EDTA 0,35%	4 times a day	5 days	0.1 mL	13rd to 18th
Carboxymethylcellulose eye drops	3 times a day	17 days	0.1 mL	13rd to 30th
Ofloxacin eye drops 0.3%	5 times a day	8 days	0.1 mL	14th to 22nd
Vitamin A ophthalmic ointment 5,000 IU/Kg	3 times a day	25 days	250 mg	17th to 41st
Chondroitin sulfate eye drops 3%	3 times a day	12 days	0.1 mL	17th to 29th
Moxifloxacin eye drops 0.5%	5 times a day	20 days	0.1 mL	21st to 41st
Dexamethasone ophthalmic ointment	Twice a day	10 days	250 mg	31st to 41st

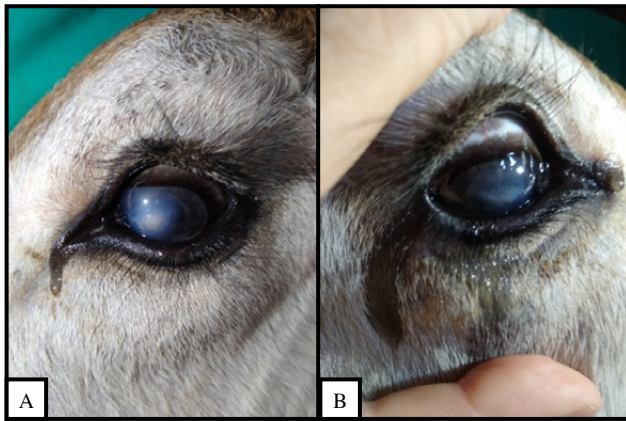


Figure 3. Tabapuã calf with hepatogenous photosensitization, treated at the UFLA Large Animal Veterinary Hospital. Scars from corneal ulcers in the left (A) and right (B) eyes.

0.2%® - diluted in NaCl to a concentration of 0.02%] were performed in both eyes, one application being performed on the 20th day of treatment and the other on the 41st. A grid keratotomy procedure was performed on the 20th day of treatment. For the procedure, anesthetic eye drops of 1% tetracaine and 0.1% phenylephrine hydrochloride⁴ [Anesthetic® - 2 drops in each eye] were used. Scraping was performed with a hypodermic needle and, subsequently, the eyes were washed with povidone-iodine diluted in 0.9% saline solution (1 mL in 500 mL). After the ulcer had healed (Figure 3A & B), dexamethasone ophthalmic ointment was used to reduce the scar.

After 7 days of the initial treatment, the animal was reevaluated and, upon physical examination, bilateral tracheal and cranioventral pulmonary crepitation was observed, and bronchopneumonia was diagnosed. The following were prescribed: benzathine penicillin² [Penfort® - 40,000 IU/kg, IM, SID, for 3 days and 20,000 IU/kg, for another 4 days]; meloxicam² [Maxicam 2%®² - 0.5 mg/kg, IM, SID, for 3 days]. Two days later, it was observed that the mother was not allowing the calf to suckle and that the calf had become hypothermic, dehydrated and hypoglycemic. It was recommended that the calf be admitted to the veterinary hospital for stabilization and closer monitoring. The animal was warmed with hot compresses and after treatment with intravenous fluid therapy based on 0.9% NaCl and 5% glucose, its vital signs and behavior were reestablished.

After 12 days of treatment, the animal presented re-epithelialization and hair growth in the most dorsal regions of the body and head. In the most ventral regions of the abdomen and limbs, hair and skin loss

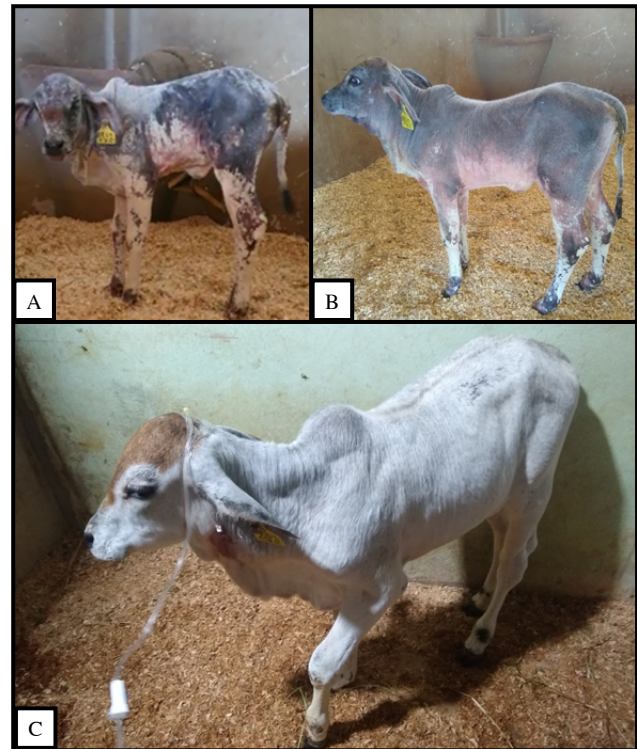


Figure 4. Tabapuã calf with hepatogenous photosensitization. A- Reepithelialization in the most dorsal regions of the body and head, but still with hair loss and skin loss in blocks, in the ventral part of the abdomen and limbs, after 12 days of treatment. B- Hair growth on the animal's back and abdomen after 30 days of treatment. C- Significant hair growth on the entire body, after 54 days of treatment.

continued in blocks (Figure 4A). After 30 days, hair loss no longer occurred, and re-epithelialization and hair growth continued (Figure 4B). After 54 days of treatment, the animal already presented significant hair growth (Figure 4C).

DISCUSSION

Brachiaria spp. species contain steroidal saponins. These are glycosides with a furostanolic or spirostanolic nucleus, which contain 1 or more sugar chains. The hydrolysis of the saponins of *Brachiaria decumbens*, mainly protodioscin, results in the saponogenins diosgenin and iamogenin, which, after being metabolized in the digestive tract of animals, result in the saponogenins epismilagenin and episarsasapogenin, respectively, which are responsible for the formation of bile crystals [25]. The mechanism of formation of these crystals involves the hydrolysis of the saponin sugars during rumen metabolism, followed by reduction, epimerization and, finally, conjugation with glucuronic acid. The glucuronides of epismilagenin and episarsasapogenin bind with calcium ions, forming insoluble salts that are deposited in the form of crystals [12].

The calf and its mother were grazing on *Brachiaria decumbens* pasture, and as is known, this is the species of *Brachiaria* spp. that has the highest amount of lithogenic saponins [7], which caused the disease in the animal. The crystals cause inflammation and obstruction of the biliary system, in addition to necrosis of periportal hepatocytes, resulting in jaundice, photosensitization and hepatitis [25].

Depigmented skin is more affected in cases of photosensitization, but animals with pigmented skin may also present symptoms. In the reported case, the calf is from a breed with more pigmented skin, the Tabapuã breed, and presented a severe form of the disease. There is a report of an outbreak of hepatogenous photosensitization in 320 Nelore animals, which also have pigmented skin, after entering a *B. decumbens* paddock. The animals began to present clinical signs, on average, 30 days after the pasture change [14].

The animal in the report was a suckling calf only 22 days old, and therefore its diet consisted mainly of breast milk. In suckling calves less than 30 days old raised with their mothers on pasture, the diet is almost exclusively breast milk. Thus, the explanation is that the toxic principle may pass from the mother's blood to her milk [30]. In Brazil, there is a description of an outbreak in suckling calves up to 6 months old, on *B. brizantha* pasture, and another outbreak in calves 30 to 60 days old, on *B. decumbens* pasture. In the episode that affected suckling calves up to 6 months old, the morbidity was 56% and the lethality was 35%. In the other outbreak, in which calves aged 30 to 60 days were affected, the morbidity was 13% and the lethality was 33% [28].

The calf had yellowish diarrhea, possibly due to the fact that saponins are irritating to the digestive system and can cause diarrhea [1,14].

When the calf was 1st seen, corneal opacity was observed in both eyes, and staining with 1% fluorescein ophthalmic solution revealed corneal ulcers. Ophthalmic changes, such as photophobia, corneal opacity [23], ocular secretions, and blindness, may occur in cases of hepatogenic photosensitization [16]. In some sheep and goats kept on *Brachiaria* hybrid cv. mulato I pasture, corneal tearing, opacity, and ulceration occurred [20].

The increase in the number of total leukocytes observed may be caused by the inflammatory process resulting from skin, liver and kidney lesions [14].

Another possibility would be the increase in total leukocytes and fibrinogen, due to secondary bacterial infection of photodermatitis lesions [10].

There is a significant increase in gamma-glutamyltransferase (GGT) and aspartate aminotransferase (AST) levels in cases of hepatogenous photosensitization, due to liver damage, which can aid in the diagnosis of this condition [3,6]. Total, direct and indirect bilirubin may also be increased [10]. In this case, it was not possible to measure these enzymes and bilirubin, however, the diagnosis could be confirmed by the anamnesis and confirmation of the ingestion of *Brachiaria* spp., in this case by the mother, associated with the characteristic clinical signs of the condition and response to the therapeutic measures implemented [23].

The mother and calf were transferred to a covered pen, where the mother's diet was restricted to corn silage and feed. When the animal is lactating, it is considered that the main means of ingesting saponins is via milk, therefore, when establishing the new management, the milk should come from a cow that does not consume *Brachiaria* spp. The main management for treatment consists of removing the animals from the *Brachiaria* spp. pasture and transferring them to a shaded place [19,26]. Removing the animal from exposure to the sun does not prevent the presence of clinical signs of poisoning, but exposure to sunlight exacerbates the clinical signs [22].

In this case, a vitamin and amino acid complex was used. This medication contains vitamins, minerals, amino acids and glucose, which aid in hepatic metabolism. It also contains choline, which is a lipotropic factor, due to its function of acting on lipid metabolism, accelerating the removal or decreasing the deposition of fat in the liver [17]. Due to liver damage in cases of photosensitization, the use of liver-sparing agents is recommended [26]. The solution containing acetylmethionine and choline chloride was used to assist in the treatment of a goat diagnosed with hepatogenic photosensitization by *Brachiaria decumbens* in serious condition [18]. It is also recommended to administer non-steroidal anti-inflammatory drugs parenterally [19]. In this case, the use of flunixin meglumine and later, meloxicam, was chosen.

Zinc oxide-based ointment was used on skin wounds to stimulate healing. Zinc accelerates wound healing, increases the speed of epithelial tissue repair and maintains cellular integrity [21].

Heterologous serum and 0.35% EDTA were used in the calf to aid in the corneal healing process. Autologous/heterologous serum is widely used in the treatment of corneal ulcers, as it contains factors that control inflammation, reduce pain and aid in the healing of the corneal epithelium [11]. 0.35% EDTA is capable of lysing collagenase, inhibiting this enzyme of bacterial origin and of the organism itself, which enhances the destruction of corneal tissue [27].

Eye drops containing the antibiotics ciprofloxacin, ofloxacin and moxifloxacin were used to control the infection. The change of bases was made due to a worsening of the condition of the ulcers. The use of eye drops from the quinolone group is indicated as antibiotic therapy in the clinical treatment of corneal ulcers with the aim of eliminating the infection [4].

Indolent ulcers are erosions of the epithelial layer of the cornea that do not respond adequately to clinical treatment. Grid keratotomy is one of the treatments indicated for indolent ulcers, in order to aid in healing [9]. In the case reported, the ulcers were classified as such because they did not respond well to topical treatment, and therefore grid keratotomy was chosen, with increasing improvement observed after its completion.

Topical application of chondroitin sulfate has a restorative effect, as it stimulates the synthesis of proteoglycans via intra and extracellular mechanisms. In addition, it reduces the inflammatory process by acting directly on enzymes, in addition to inhibiting the complement system and the action of plasmin, a fibrinolytic enzyme found in high concentrations in damaged corneas. In horses, the association of chondroitin sulfate in the treatment of corneal ulcers helped in the early reduction of clinical signs and in filling the ulcer bed with better quality scar tissue, achieving healing without leukoma in 80% of eyes within 14 days [31]. After healing of the corneal ulcer, the use of topical corticosteroids, such as dexamethasone,

can help in the reorganization of collagen, reducing corneal scarring [13]. In indolent corneal ulcers, such as those reported in this calf, it is important to consider the association of drugs that reduce the ocular scar remaining from the ulcer healing, providing a better quality of life for the patient.

It was recommended not to use the animal in question for breeding. The selection of resistant animals and the use of *Brachiaria* spp. species with low concentrations of saponins can contribute to the control of cases of poisoning by *Brachiaria* spp. In addition, there are ways to avoid poisoning through adaptation, placing young animals on *Brachiaria* spp. pasture on alternate days or placing them on pasture for 2 h per day for a period of 120 days [5]. Energy and protein supplementation at 2.4% of live weight is an efficient nutritional strategy to minimize the effects of poisoning in lambs fed *Brachiaria* spp. [9].

Hepatogenic photosensitization requires veterinarians to have knowledge of the epidemiology and pathogenesis of the disease, especially with regard to the involvement of calves on an exclusive milk diet. It is important to keep in mind the possibility of difficult-to-heal corneal ulcers in animals affected by hepatogenic photosensitization and to be aware of the treatment options available. The successful treatment of the case reported is attributed to the removal of the mother and calf from *Brachiaria decumbens* pasture and exposure to the sun, as well as to supportive drug treatment.

MANUFACTURERS

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