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Clinical Observations and Management of Ivermectin Toxicity in Camels (Camelus dromedarius): A Study from Algatroun, Southwest Libya

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A B S T R A C T

This study investigates the adverse reactions associated with intravenous (IV) injections of ivermectin in camels (Camelus dromedarius) presented to a veterinary clinic in Algatroun city. A total of 45 camels were divided into four groups and treated with 1% ivermectin via intravenous (IV) and subcutaneous (SC) routes. Group 1 consisted of three young camels administered 15 ml of ivermectin IV, while Groups 2, 3, and 4 included camels treated SC with doses of 5 ml, 10 ml, and 20 ml, respectively. Clinical signs of toxicity, including hypersalivation, ataxia, depression, and coma, were observed mainly in the IV group, with significant adverse effects noted at doses exceeding 7.5 times the recommended dosage. The study highlights the rapid onset of severe toxicity in young camels, with fatalities occurring within hours of administration. Treatments involving dexamethasone, isotonic solutions, and multivitamins showed beneficial effects in mitigating toxicity. This research stresses the critical importance of adhering to recommended dosing guidelines and the risks associated with improper administration practices by non-veterinarians.

Keywords: Camel, Ivermectin, Neurotoxicity, Algatroun, Libya.

الأعراض السريرية وعلاج سمية الإيفرمكتين في الإبل: دراسة من القطرون، جنوب غرب ليبيا

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الملخص

تبحث هذه الدراسة في التأثيرات السلبية المرتبطة بالحقن الوريدي للإيفرمكتين في مجموعة من الإبل عرضت على عيادة بيطرية بمنطقة القطرون جنوب غرب ليبيا. تم تقسيم الحيوانات (45 جملاً) إلى أربع مجموعات, عُولجت بالإيفرمكتين تركيز 1% عن طريق الحقن الوريدي (IV) وتحت الجلد (SC). تكونت المجموعة 1 من ثلاثة جمال صغيرة تم حقنها بجرعة 15 مل من الإيفرمكتين عن طريق الوريد، بينما شملت المجموعات 2، 3، و4 جمالاً عُولجت تحت الجلد بجرعات 5 مل، 10 مل، و20 مل على التوالي. تم ملاحظة علامات سمية سريرية تشمل فرط إفراز اللعاب، الترنح، الاكتئاب، والغيبوبة بشكل رئيسي في المجموعة التي تلقت العلاج عن طريق الوريد، مع ظهور آثار جانبية ملحوظة عند الجرعات التي تتجاوز 7.5 ضعف الجرعة الموصى بها. تسلط الدراسة الضوء على الظهور السريع للتسمم الحاد في الجمال الصغيرة، حيث حدثت حالات الوفاة خلال ساعات من الحقن. أظهرت العلاجات باستخدام الديكساميثازون، المحاليل متساوية الايونية، والفيتامينات المتعددة تأثيرات إيجابية في التخفيف من

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لتسمم. تؤكد هذه الأبحاث على الأهمية البالغة للالتزام بإرشادات الجرعات الموصى بها والمخاطر المرتبطة بممارسات الحقن غير الصحيحة من قبل غير المتخصصين.

الكلمات المفتاحية: الابل، إيفرمكتين، السمية العصبية, القطرون, ليبيا

Introduction

Ivermectin has been classified as a broad-spectrum antiparasitic drug, initially developed for the treatment of helminths, excluding cestodes. However, it was later found to be effective against external parasites such as lice and mites [1, 2]. Ivermectin is a semisynthetic formulation [3] derived from avermectins, which are macrocyclic lactones produced by *Streptomyces avermitilis* [4-6]. Ivermectin works by binding to glutamate-activated chloride channels in the nerve cells or muscles of invertebrates with high affinity, resulting in hyperpolarization of the muscle or nerve cells by increasing chloride ion permeability across the cell membrane. Subsequently, the organism becomes paralyzed and eventually dies [7].

Although ivermectin is highly toxic to insects, as GABA receptors are primarily located in the peripheral nervous system, adverse reactions to ivermectin in mammals at normal doses are rare [8]. In mammals, GABA receptors are located in the central nervous system, and ivermectin cannot easily cross the blood-brain barrier, being efficiently excluded from the central nervous system by a P-glycoprotein-mediated efflux mechanism [9]. A large dose of ivermectin may cross the blood-brain barrier and induce GABA-mimetic toxic effects [10-13].

Mutations in the multidrug resistance gene MDR1, which encodes P-glycoprotein in mammals, are also involved in ivermectin toxicosis [14], allowing the penetration of ivermectin across the blood-brain barrier due to P-glycoprotein dysfunction [15]. The standard dose of ivermectin in animals is 0.2-0.4 mg/kg [16]. Neurotoxicity is a major concern when using ivermectin for treatment, as it can cause hypersalivation, tremors, ataxia, respiratory failure, and death in most vertebrates [17].

Studies in camels have shown susceptibility to the acute toxic effects of ivermectin. A single dose of 5 mg/kg had no severe effects, and repeated monthly doses of ivermectin at 0.6 mg/kg produced no adverse effects. However, 10 mg/kg, which is the LD_{50} for rats, caused ataxia, severe depression, and death within 24 hours [1, 18]. Generally, no treatment is required for mild to moderate adverse reactions to ivermectin; however, in severe cases, the administration of steroids, antihistamines, paracetamol, and bronchodilators could be beneficial [10].

While ivermectin is generally safe when used correctly, accidental misuse or overdosing can lead to significant health risks. Therefore, this study was initiated following several cases of ivermectin toxicity in camels after intravenous administration presented to a veterinary clinic in Algatroun City, located in the southwest of Libya. The observed clinical signs and severity of toxicity prompted a systematic investigation to document and analyze these adverse reactions. Supportive treatments provided to affected camels and their recovery outcomes were also studied.

MATERIALS AND METHODS

This study was conducted in Algatroun City, located in the southwest of Libya (24°55′48″N 14°34′35″E), to evaluate the effects of ivermectin administration in camels (Table 1).

Table 1: Summary of treatment groups, including age, body weight, and administered doses of 1% ivermectin via different routes in camels.

Group	Number of Camels	Age Range	Body Weight (kg)	Route of Administration	Dose (mg/ml)
Group 1	3	9-12 months	100,130, 170	Intravenous (IV)	15 ml (150 mg/ml)
Group 2	3	5 months	60, 70, 75	Subcutaneous (SC)	5 ml (50 mg/ml)
Group 3	9	1-3 years	200-250	Subcutaneous (SC)	10 ml (100 mg/ml)
Group 4	30	4-5 years	300-350	Subcutaneous (SC)	20 ml (200 mg/ml)

In this study, camels in Group 1 received 15 ml of 1% ivermectin solution (Conmectin; from Concept Pharmaceuticals Ltd, Mumbai, India) intravenously through the jugular vein. Groups 2, 3, and 4 were treated subcutaneously with 5 ml, 10 ml, and 20 ml of 1% ivermectin, respectively, with Group 4 receiving repeat treatment after 10 days. Additionally, intoxicated camels were administered dexamethasone (BIO-DEXA; from Bio-Pharmachemic, Ho Chi Minh City, Vietnam) and multivitamins (Oligovit; from Vetos Farma Ltd, Bielawa, Poland). Severely affected camels received isotonic solutions both intravenously and subcutaneously.

RESULTS

The IV-treated camels exhibited various clinical signs, including hypersalivation, ataxia, depression, tremors, coma, and death. Specifically, three camels experienced ivermectin toxicity at doses of 1.5 mg/kg, 1.15 mg/kg, and 0.88 mg/kg. The camel that received 1.5 mg/kg collapsed within 20 minutes of administration and died four hours later, displaying clinical signs such as salivation, dullness, vomiting, and coma. The camel treated with 1.15 mg/kg also collapsed and exhibited dullness, loss of appetite, and subcutaneous edema in the ventral aspect of the neck. In contrast, the camel that received 0.88 mg/kg showed signs of incoordination but maintained a normal appetite.

No signs of toxicity were observed at four times the recommended subcutaneous dose of ivermectin. However, incoordination was noted at the same dose when administered intravenously. Recovery times varied: camels intoxicated through IV administration had longer recovery times compared to those treated subcutaneously. For example, intravenously intoxicated camels began eating within six hours of showing clinical signs and achieved full recovery within 48 hours.

Camels treated with dexamethasone, multivitamins, and isotonic solutions exhibited rapid health improvement. Recovery times were satisfactory, with the health of camels improving significantly between 6 and 48 hours.

DISCUSSION

The findings demonstrate that the severity of ivermectin toxicity in camels is influenced by both the route of administration and the dosage. Intravenous administration at high doses significantly increases the risk of acute toxicity, as evidenced by the severe outcomes in camels receiving doses of 1.5 mg/kg and 1.15 mg/kg. These results align with previous studies by Norman and Chaffin [19][20], which reported subcutaneous edema and neurological signs in cases of ivermectin toxicity in other species. The observed variation in clinical signs among camels receiving different doses highlights the importance of precise dosing and administration routes to mitigate toxicity risks. A previous study conducted by Abdou and Sharkawy [21] indicated that the administration of 4 mg/kg of ivermectin orally and 8 mg/kg subcutaneously resulted in toxicity, further demonstrating that toxicity is influenced by the route of administration.

This study corroborates earlier findings regarding the impermeability of the blood-brain barrier to ivermectin in vertebrates, which prevents toxicity under normal dosing conditions [22]. However, high doses can surpass the barrier's protective capacity, leading to GABA-mimetic effects. Young camels

appeared more susceptible to toxicity, consistent with findings in other species where younger animals exhibit heightened sensitivity to overdosing [23].

Supportive treatments, including dexamethasone [24][25] and multivitamins, proved effective in mitigating the effects of toxicity. This outcome underscores the importance of timely intervention in cases of accidental overdose. The rapid recovery observed in this study parallels findings by Hopper and Aldrich [26], who reported similar improvements with supportive care in ivermectin-intoxicated animals.

These results emphasize the need for strict adherence to recommended dosing guidelines and proper administration techniques to avoid accidental intravenous administration. Training for handlers and veterinarians is essential to reduce the incidence of such errors and improve animal welfare outcomes in camel herds.

Conclusion

Administration of 7.5 folds of 1% ivermectin intravenously can lead to signs of acute toxicity within 20 minutes or less and can result in the death of camels within 4 hours, particularly in young camels. Severe toxicity was indicated by symptoms such as salivation, vomiting, tremors, coma, and death, while sub-acute toxicity was associated with dullness, loss of appetite, incoordination, and subcutaneous edema. A dose of 4 times the recommended amount showed mild toxicity, including incoordination. However, toxicity was not observed when the same dose was administered subcutaneously. Treatment with dexamethasone, multivitamins, and fluid therapy proved beneficial.

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