GALLAMINE REVERSAL IN CUBAN CROCODILES (*Crocodylus rhombifer*) USING NEOSTIGMINE ALONE VERSUS NEOSTIGMINE WITH HYALURONIDASE

Mark Lynn Lloyd, DVM *
Roger Williams Park Zoo, 1000 Elmwood Ave, Providence, RI, 02905, USA

Timothy Reichard, DVM and R. Andrew Odum, Curator of Reptiles
Toledo Zoologic Society, 2700 Broadway, Toledo, OH, 43609, USA

Introduction

Gallamine triethiodide is a water soluble competitive neuromuscular blocking agent. It is excreted unchanged via the renal system in mammals. Its effect on skeletal muscle ranges from relaxation to complete paralysis. It does not provide analgesia, anesthesia, loss of proprioception nor consciousness. For this reason it is only suitable for procedures eliciting minimal pain if used alone however may be combined with local or general anesthesia for more invasive procedures. The dose and duration vary with species. Reversal can be achieved via neostigmine methylsulfate administration. In this study recovery time was monitored to evaluate the rate of absorption and response to the reversal agent neostigmine both with and without hyaluronidase. Hyaluronidase (purified bovine testicular hyaluronidase) hydrolyzes interstitial hyaluronic acid promoting spread and absorption of concomitantly injected substances. It is used to enhance the absorption of subcutaneously administered fluids and urographic contrast media to accelerate absorption in humans.

Materials and Methods

Four Cuban crocodiles (*Crocodilus rhombifer*), ranging in weight from 45 - 74 kg, were immobilized for physical examination, radiography, gastric coin removal per os, sexing, and transport to new enclosures. A total of 12 immobilizations were performed using gallamine; seven of these were recovered with neostigmine and hyaluronidase, five times with neostigmine alone. A dose of 75 mg hyaluronidase was mixed in the same syringe with the neostigmine in every dose independent of the total neostigmine dose or the weight of each animal.

Results (see fig. 1)

Recovery was based on the animal's ability to lift their body and ambulate effectively. The animals reversed with neostigmine in combination with hyaluronidase recovered significantly sooner than those reversed with neostigmine alone. No repeat doses of reversal agents were required for any of those animals augmented with hyaluronidase and all recovered within eight hours. Two of those given neostigmine alone, however, required three doses of neostigmine, five took greater than 24 hours to recover and one of those was still unable to effectively ambulate even at three days post procedure.

Discussion

Use of gallamine for immobilization of crocodilians, including Nile crocodiles (*Crocodylus niloticus*), caiman (*Caiman crocodilus*) and American alligators (*Alligator mississippiensis*) has been reported by numerous authors both with and without neostigmine reversal.[7,5,4,1,2] No reports of neostigmine in combination with hyaluronidase were found.

Excellent immobilization has been achieved over a dose range of 0.64 - 4.0 mg/kg I.M. in Nile crocodiles with minimal side effects. Side effects after gallamine administration included tachycardia, tachypnea, hypersalivation and gaping. It is unclear whether these are direct effects of gallamine or due to the procedure stimulation. Recumbency occurred from 8 - 30 minutes post injection, comparable to our results in Cuban crocodiles. Reversal with neostigmine was used in some but not all of these procedures. A dose range of 0.03 - 0.25 mg/kg neostigmine was used.[7,5,4,2] Recovery from the high dose was as short as 5 minutes post injection but the route was unspecified. This is comparable to the results we obtained with the I.V. dose of 0.063 mg/kg neostigmine with hyaluronidase in Cuban crocodiles (4 min). The shortest recovery without reversal in Nile crocodiles was 45 minutes, significantly shorter than specimens in our study.[7] Adverse side effects of neostigmine reversal are chiefly due to its muscarinic activity and may be manifested even at the low end of the dose range above.[5] These include emesis and lacrimation but may be avoided via atropinization if necessary.[4] By fasting the Cuban crocodile 24 - 48 hours prior to immobilization no regurgitation/ emesis was observed in our study. The exception is one individual which "rushed" the keeper leading it out into the immobilization area and snatched the bait rat from the tongs only to purge it post neostigmine administration. Fatalities were reported in Nile crocodile but were associated with drowning during an attempted aquatic immobilization or asphyxiation by a conspecific which laid on top of an unrecovered individual.[5]

Dosage of 50 mg/kg I.P. gallamine in *C. crocodylus* combined with pentobarbital resulted in apnea and required positive pressure ventilation, however these specimens were intentionally not recovered.[3]

Two American alligators receiving only 0.75 - 1.0 mg/kg of gallamine were given no reversal agent and did not survive. For this reason some authors do not consider gallamine safe in this species.[2]

Conclusions

Augmentation of the reversal agent neostigmine with 75 mg hyaluronidase may increase efficacy and speed recovery of Cuban crocodiles immobilized with gallamine.

ACKNOWLEDGEMENTS

Thanks to the reptile department of the Toledo Zoo for their great assistance in all the procedures performed.

Figure 1

RANGES AND AVERAGE VALUES FOR REVERSAL WITH AND WITHOUT HYALURONIDASE

	w/ H range	w/o H range	Ave H grp	Ave w/o H grp
Wt.(Kg)	45-74	45-68	54	53
total G dose mg/kg	0.60-0.77	0.91-1.28	0.70	1.07
recumbency (minutes)	21-103	30-130	42	58
time to reversal admin.(min)	95-331	173-405	257	304
total N dose(mg/kg)	0.04-0.07	0.07-0.17	0.06	0.11
time til ambulatory (min)	99-434 (1.7-7.2hr)	1440-2050 (24-34hr)	321 (5.4hr)	1867 (31.1hr)

KEY

total G dose - total dose gallamine, in all except one immobilization the total dose was given all at once

recumbency - time from gallamine dose to sternal recumbency and inability to stand or ambulate

time to reversal admin. - time from initial dose of gallamine to the administration of the reversal agent(s)

total N dose - total dose of neostigmine given to effect, reversal defined as ability to stand and ambulate, initial dose may have been repeated after several hours or days if insufficient response occurred

time til ambulatory - response to reversal agent(s) gauged by ability to stand and ambulate since initial gallamine administration

w/ H range and Ave H grp - range of values and average value for each parameter in immobilizations with hyaluronidase supplemented reversals in minutes with hour equivalents below

w/o H range and Ave w/o H grp - range of values and average value for each parameter in the immobilizations without hyaluronidase in minutes with hour equivalent below

LITERATURE CITED

1. Frye, FL. 1991. Biomedical & surgical aspects of captive reptile husbandry. Kreiger Publishing, Malabar, FL. Pp.421-424.
2. Jacobson, ER. 1984. Immobilization, Blood Sampling, Necropsy Techniques and Diseases of Crocodilians: A Review. J. Zoo An. Med. 15: 38-45.
3. Ilinas, R, C Nicholson, & W Precht, 1969. Preferred centripetal conduction of dendritic spikes in alligator Purkinje cells. Science, NY. 163: 184-187.
4. Loveridge, JP. 1979. The immobilization and anaesthesia of crocodilians. In: Olney, P.J.S. (ed.). International Zoo Yearbook. Zoological Society of London. Pp. 103-112.
5. Loveridge, JP & DK Drake, 1972. Techniques in the immobilization and handling of the Nile crocodile. *Crocodylus niloticus*. Arnoldia (Rhod.) 5: 1-14.
6. Strobel, GE & H Wollman. 1969. Pharmacology of anesthetic agents. Fedn. Proc. Fedn Am. Socs exp. Biol. 28: 1386-1403.
7. Woodford, MH. 1972. The use of gallamine triethiodide as a chemical immobilizing agent for the Nile crocodile (*Crocodilus niloticus*). E. Afr. Wildl. J. 10: 67-70.

Products Discussed

Gallamine triethiodide: Flexadil (R), Davis+Geck, American Cyanamid Co., Pearl River, NY, 10965

Neostigmine methylsulfate: Bristol-Meyers Squibb Co., Prinston, NJ, 08540

Hyaluronidase: Wydase (R), Wyeth Labs Inc., Philadelphia, PA, 19101