Evaluation of the Venom Ex apparatus in the initial treatment of puff adder envenomation

A study in rabbits

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Summary

The Venom Ex apparatus has been evaluated for the treatment of puff adder bite. Rabbits were injected with double the lethal dose of puff adder venom, followed by treatment with the Venom Ex cutting and suction apparatus. Controls received no treatment. The percentage of venom extracted as determined by radial immunodiffusion was very low after intramuscular injection and significantly higher after subcutaneous injection. However, all treated and control animals injected subcutaneously, recovered while all animals injected intramuscularly died, irrespective of treatment. Blood venom levels were extremely low in all animals. Venom Ex treatment did not improve survival or affect local necrosis significantly.


Puff adder (Bitis arietans) bite is the most common type of dangerous snakebite in southern Africa, causing death occasionally and permanent disability or serious local lesions frequently. It is therefore important to investigate new initial methods of treatment in order to improve results if possible. The Venom Ex cutting and suction apparatus is being promoted in the lay press for the early treatment of all types of poisonous snakebite. Previous studies indicated that this method could be of some value following Egyptian cobra bite if used very early and if the dose of venom was not too high. In this study the Venom Ex apparatus (Fig. 1) was evaluated for the treatment of puff adder bite.

Materials and methods

Sixteen healthy adult New Zealand White rabbits were used. They were housed under controlled conditions in a constant environment. The animals were divided into groups of 4. Puff adder venom was obtained by milking adult snakes. The pooled venom was freeze dried and stored at -20°C and reconstituted with physiological NaCl immediately before use. The same batch of venom was used for all the animals. Epidural anaesthesia was administered to the animals before treatment and all recovered from this within 1 hour or less without showing any untoward effects. As puff adder fangs are ±10-14 mm long, groups A and B were injected intramuscularly, 10 mm deep on the denuded left calf with 4 mg/kg (about double the lethal intramuscular dose) of puff adder venom. For comparison groups C and D were injected subcutaneously ±3 mm deep with the same dose.

Groups A and C received no treatment. Groups B and D were treated with the Venom Ex method 5 minutes after the venom had been injected. A venous tourniquet was applied to the thigh when treatment was started. The Venom Ex apparatus has a cutting head with six parallel blades, which were set at their maximum depth of 5 mm. The blades were retracted and the apparatus was applied firmly to the skin over the injection site, parallel to the long axis of the limb. The blades were then suddenly released by pressing the lever. This process was repeated 4 times, causing small lacerations over an area of about 30 x 45 mm on the right calf. Suction was then applied by means of a 10 ml syringe fitted with a suction cup and a spring. Suction was intermittently maintained for 15 seconds at a time for 15 minutes and the extracted fluid was placed in test tubes. The tourniquet was removed after treatment was completed. After treatment animals were closely observed and local and systemic reactions were noted. The circumference of the leg was measured at the injection site and also 1.5 cm above and below the injection site at regular intervals. Controls were monitored in the same way. Arterial blood was obtained from ear arteries at certain intervals for determination of blood levels of puff adder venom.

Fig. 1. Venom Ex incision apparatus with tourniquet and syringe with suction cup and spring to maintain suction.

Quantitative estimation of venom in Venom Ex extracted fluid and in blood samples was determined by single radial immunodiffusion. The linear correlation coefficient of the standard was \( r = 0.932, P < 0.001 \). Necropsies were performed on all animals which died.

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Results (Table I)

Group A received venom intramuscularly (depth 10 mm) but had no treatment. All animals in this control group died within 5 - 19 hours with extremely severe local cytotoxic effects and shock. Group B also received venom intramuscularly (depth 10 mm), followed by Venom Ex treatment, but only 2-7% of the venom could be extracted. The findings were similar to those obtained in the control group and all died within 5 - 44 hours in spite of treatment. All 8 rabbits (groups C and D) injected subcutaneously with 4 mg/kg, double the dose of venom which caused death when given intramuscularly, recovered.

In group D 50-55% of venom (and 65% in 1 case) was removed by applying the Venom Ex apparatus. Skin necrosis occurred but all animals survived and recovered with full function of the leg; however, this also happened in Group C where no treatment was administered. No aggravation of lesions was found in animals where a venous tourniquet was applied for 15 minutes.

There was no statistically significant difference between the treated and the control animals when local reactions, leg circumference, blood venom levels, clinical signs and symptoms and survival rates were taken into consideration.

Blood levels of venom in the treated and control groups were extremely low.

Autopsy findings

In groups A and B (venom injected intramuscularly) very severe local reactions were present. The left leg was oedematous from the foot to the thigh, with purpura and subcutaneous haemorrhages over the calf and the inguinal region in all animals. In some animals the scrotum and abdominal wall were affected in the same way. Extensive myonecrosis of the calf muscles and haematoma were present. No haemorrhages were found in the liver, kidneys, lungs or other organs or in the abdominal or thoracic cavities. In group B where Venom Ex was applied small skin lacerations were present over the injection sites. All other findings were similar in the two groups. In groups C and D no autopsies were performed as these animals all recovered.

Statistical analysis

Using the Kruskal-Wallis test the percentage of venom removed after subcutaneous injection was significantly higher than the venom removed after intramuscular injection ($P = 0.0020$).

After intramuscular injection all animals died irrespective of treatment while all survived following subcutaneous injection of the same dose. According to Fisher's exact test this difference was significant ($P = 0.0143$).

By using the Breslow test no significant difference was found when the survival times of the treated and control groups, after intramuscular injection, were compared ($P = 0.665$).

Discussion

All animals injected intramuscularly with double the lethal dose of puff adder venom died, with or without Venom Ex treatment, while all animals injected subcutaneously with the same dose recovered and there were no statistically significant differences between the treated and untreated groups. Previous reports showed that the Venom Ex cutting and suction method resulted in complete recovery or prolonged survival of most rabbits after subcutaneous administration of double the lethal dose of Egyptian cobra venom, providing treatment was started very early. These results differ from the findings recorded in this present study where puff adder venom was used. Egyptian cobra fangs have a length of about 5.5 mm but puff adder fangs are about 10 - 14 mm long. According to Visser and Chapman experience with adders suggests that the normal bite involves one-third to two-thirds of the total fang length; however, an enraged snake may sink its fangs to their full depth. In this study the venom was therefore injected intramuscularly (10 mm deep) in 8 rabbits and for comparison subcutaneously ($\pm$ 3 mm deep) in 8 rabbits. In the group injected 10 mm deep only 3 - 7% venom could be removed although treatment was started after 5 minutes. This indicates that the Venom Ex cutting apparatus with the blades set at the maximum depth of 5 mm, is unlikely to be very helpful in bites where the venom has been injected deeper than this.

As previously reported, trauma without removal of venom improves survival of rabbits by about 50% following injection of Egyptian cobra venom. Egyptian cobra venom causes minimal local reactions but is absorbed systemically, causing neurotoxic effects with respiratory failure as the cause of death. Local blunt trauma at the injection site without extraction of venom probably improved the survival mainly because systemic absorption of venom was impaired due to damage to the lymphatic and venous drainage systems and trapping of cobra venom in the haematomata. In this present study puff adder venom was used, which causes severe local reactions, while extensive systemic absorption could not be demonstrated and blood venom levels were extremely low. Local tissue damage appeared to be maximal due to the cytotoxic effect of the venom. In the present study the trauma plus extraction of tissue fluid and venom applied by means of the Venom Ex apparatus in the treated animals did not improve survival. It was therefore not considered worth while to apply blunt trauma only without removal of venom, as was done in the previous study.

Most authorities agree that cutting and suction of snakebite wounds should never be performed. However, according to the manufacturers, the Venom Ex method has been used successfully elsewhere in more than 34 patients following bites by a variety of poisonous snakes, including various vipers (A. Birchmeier — personal communication). Snake venoms are extremely variable and complex and the fangs of most snakes are much shorter than those of the puff adder. Rabbits have a thin, loosely attached skin with no subcutaneous fat and results obtained in these animals may differ from those found in humans.

<table>
<thead>
<tr>
<th>TABLE I</th>
<th>THE EFFECT OF VENOM EX TREATMENT ON RABBITS INJECTED WITH PUDD ADDER VENOM</th>
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<tbody>
<tr>
<td>Group</td>
<td>No. of rabbits</td>
</tr>
<tr>
<td>A</td>
<td>4</td>
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<td>B</td>
<td>4</td>
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(65 in one)
Conclusions

Subcutaneous injection of venom (3 mm deep) was followed by recovery of all animals, while the same dose invariably caused death when given intramuscularly (10 mm deep), despite the use of the Venom Ex apparatus.

Following subcutaneous injection, the percentage of venom extracted was significantly higher than the percentage removed after intramuscular injection.

Venom Ex treatment did not improve survival of rabbits nor did it affect local necrosis, after injection of puff adder venom, significantly.

Dr C. A. van der Merwe and Miss R. J. Dreyer of the Institute of Biostatistics of the South African Medical Research Council (Tvl branch) are thanked for the statistical analysis. The Venom Ex apparatus has been patented by: A. Birchmeier, Zürcherstrasse 8, 8952 Schlieren, Switzerland (US patent No. 4 417 580, 1983).

REFERENCES


The AS 800 artificial urinary sphincter in children with myelodysplasia

Preliminary results

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Summary

Ten children with myelodysplasia and intractable urinary incontinence have been implanted with an AS 800 artificial sphincter. Eight remain dry and 2 are improved over a follow-up period of 12 - 14 months. However, most have shown a reduction in bladder compliance, which suggests that further surgery may be necessary to maintain continence.


The past decade has seen major advances in the urological management of children with myelodysplasia. One of the most exciting is the development of the artificial urinary sphincter. An implantation programme has recently been established at this hospital, and the preliminary results in 10 children with intractable urinary incontinence are reported.

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Patients and methods

Nine boys and 1 girl aged 6 - 16 years (mean 11 years) were implanted with an AS 800 (American Medical Systems Inc., Minnetonka, Minnesota, USA) artificial urinary sphincter (Figs 1 and 2) between September and November 1984. All were born with a myelomeningocoele and remained severely incontinent of urine in spite of 2-hourly intermittent catheterization and the use of anticholinergic drugs. All were very keen to be dry.

Initial investigations included intravenous urography, micturating cysto-urethrography, rapid-fill cystometrography and flow rate measurement. Eight children had mild bladder hyper-reflexia but this was abolished in all cases by oxybutynin. Poor bladder emptying was not regarded as a contraindication to implantation provided the child was prepared to continue with intermittent catheterization. One child was found to have a refluxing left ureter which was reimplanted at the time of sphincter surgery. The upper tracts of the 9 remaining children were normal. The urine of all children was sterile for at least 72 hours pre-operatively. At surgery, the occlusive cuff was placed around the bladder neck and a regulating balloon with a 71-80 cm pressure range was used. Postoperatively amikacin, ampicillin and cloxacillin were given for 7 days and long-term oxybutynin 5 mg 3 times daily begun. The device was de-activated at the time of implantation and activated between 4 and 12 weeks later.

Results

All 10 children have retained their artificial sphincters and have been manipulating the control pump themselves during the follow-