WIDE LOCAL EXCISION OF THE VENOM INJECTION AREA; A POSSIBLE ALTERNATIVE METHOD TO ANTIVENOM APPLICATION IN THE TREATMENT OF CERASTES CERASTES ENVENOMATION IN ADULT ALBINO RATS

Soha K. Ashry[a]; Khaled M. Elsherbeny[b]; Ahmad Abdelbaset[c]; Sherif A. Elseginy[d]
[a]Department of Forensic Medicine and Clinical Toxicology, [b]Department of Plastic Surgery, , [c]Medical Research Center, [d]Post-graduate year 1/Masters student, Faculty of Medicine, Ain Shams University, Cairo, Egypt
Corresponding Author: Soha K. Ashry
E-mail: soha_ashry@med.asu.edu.eg Telephone: +20111404140
Postal address : Department of Forensic Medicine and Clinical Toxicology, Faculty of Medicine, Ain Shams University, Abbasia square, Cairo, Egypt.

ABSTRACT

Background: Viper envenomation is one of the common toxicities encountered in temperate countries; and one of the important causes of death. Egypt is one of the countries suffering from this problem. Cerastes cerastes is one of the most abundant venomous viper species in North Africa and the Middle East. Envenomation by vipers is characterized by prominent local tissue damage as well as systemic alterations in the form of coagulopathy that induces spontaneous hemorrhage. Antivenoms are the mainstay of treatment; however they are of little effectiveness in treating the local effects. Owing to their side effects and the decrease in their overall worldwide production, new therapeutic strategies are encouraged worldwide. The aim of the present work was to study the efficiency of wide local excision of the venom injection site in ameliorating the effects of Cerastes cerastes viper venom in adult albino rats. **Methods:** Six groups of adult albino rats; each comprising 6 rats of both sexes were used in this study. Three groups were used as controls. One group was injected with venom only, and two groups were injected with venom followed by the surgical procedure. An appropriate volume of the reconstituted venom containing the LD50 was injected subcutaneously to each rat. This was followed in the two groups by excision of a calculated area of the skin and subcutaneous tissue around the injection site. The skin defect was closed by undermining and direct closure in one group and by using Limberg flap in the other group. Healing and cosmetic results were compared in both groups. **Results:** The study groups with wide local excision of the venom injection area showed statistically significant correction of the blood picture, coagulation profile and CPK level when compared to the results of the group with unopposed venom effects. Local healing progressed normally in the surgically treated groups with a normal scar observed after complete superficial healing and there was no incidence of infection or skin edge necrosis. **Conclusions:** Wide local excision of the venom injection area was proved efficient in ameliorating the systemic alterations caused by Cerastes cerastes viper venom. It also produced a cosmetically appealing scar that is not reached with using other treatment strategies owing to the occurrence of the healing process in healthy tissues in our case. The use of Limberg flap produced better cosmetic results than direct closure

Keywords: Viper venom; Cerastes cerastes; wide local excision; Limberg flap.

INTRODUCTION

Snakebite is a well-known medical emergency in many parts of the world. Annually, there are 5 million recorded snakebite accidents resulting in 2.5 million envenomations, 125,000 deaths and about triple that number of permanent sequelae in the world **(WHO, 2007).** Cerastes cerastes is one of the most abundant venomous viper species in North Africa and the Middle East **(Harding & Welch, 1980).**

Envenomation by vipers is characterized by prominent local tissue damage as well as systemic alterations. Locally, viper snake venom causes pain and swelling at the bite site, bleeding and necrosis. In more severe cases blistering, bruising, active bleeding, darkening or liquefaction of skin could occur and this leads to permanent sequelae **(Kohli & Sakhuja, 2003; Arnold, 2016).**

Systemically, viper snake venoms induce spontaneous hemorrhage secondary to microvascular damage, coagulopathy and platelet dysfunction, together with cardiovascular shock and renal failure. The coagulopathy and hemorrhage are caused by venom components with proteolytic actions that are capable of degrading extracellular matrix proteins and blood clotting factors **(Ismail & Memish, 2003; Warrell, 2010).**

The combination of defibrination, thrombocytopenia and vessel wall damage results in massive bleeding, a common cause of death following bites by vipers. Patients may exhibit bleeding from the bite site or venipuncture sites, but more commonly there is also bleeding from the gums, and gastrointestinal tract bleeding (manifest as hematemesis or melena) and hematuria. Bleeding into a major organ or space (e.g., intracranial) could also occur **(White, 2005; Mohapatra et al., 2011).**

Antivenoms are the main line of treatment of snakebite envenomations, as they effectively neutralize systemically acting venom toxins and correct the systemic manifestations **(Gutiérrez et al., 1999; Bentur et al., 2004; Visser et al, 2008).** However, many studies proved that antivenoms are of limited value in correcting the local manifestations **(Ownby et al, 1997; Clissa et al., 2001; Zamuner et al., 2005).** The ineffectiveness of antivenom in treating the local effects of the venom is due to the difference in the pharmacokinetics between the venom and the antivenom. The time needed by the antivenom to reach maximum tissue concentration far exceeds that needed by the venom and the half-life of the antivenom is shorter than that of the venom and in addition to that, the inability of antivenom to cross the blood/tissue barrier **(Ismail et al., 1998; Anai et al., 2002).**

Antivenom administration has many adverse reactions where early anaphylactic, anaphylactoid or pyrogenic and late serum sickness reactions may occur **(Isbister et al., 2013).** According to World Health Organization, (WHO) (2010), skin test does not predict early or late antivenom reactions; thus it is recommended that antivenom should be used only in patients in whom the benefits of treatment are considered to exceed the risks of antivenom reactions. Furthermore, there is an international crisis in antivenom availability with the decrease in its overall worldwide production. The current annual need for the treatment of snake-bite envenoming amounts to ten million vials of antivenom, and unfortunately, the present worldwide production capacity

is well below these needs. This is due to the withdrawal of the big and most important manufacturing companies from the market owing to the high cost of the business **(WHO, 2007; WHO, 2010; Vaiyapuri et al., 2013).**

Adding the adverse effects of antivenom, its scarcity and its ineffectiveness in decreasing local tissue damage, studies based on new therapeutic approaches are encouraged worldwide **(Barbosa et al., 2008).** A Japanese team succeeded in treating five patients envenomed with Japanese viper by local ablation **(Fujioka et al., 2009).** Accordingly, and due to the vast variety of the lethality of different vipers' toxins, the present work aimed to study the efficiency of wide local excision of the venom injection site in ameliorating the effects of Cerastes cerastes viper venom in adult albino rats.

MATERIALS & METHODS:

Animals

Forty-four adult albino rats of both sexes and of average age of 3-6 months and weight of 180-220 grams were chosen for this experiment. Both sexes were included to bypass the effect of sex on the toxic response, and pregnant rats were excluded from the experiment to avoid the effect of pregnancy on the tested parameters. Animals were housed in standard conditions and received normal balanced diet and tap water. The experiments took place in the Medical Research Center, Ain Shams University.

Venom

The crude venom of Cerastes cerastes was supplied by the Medical Research Center, Ain Shams University in a powder form. Cerastes cerastes species was chosen because it is the most abundant species of vipers in Egypt **(Saleh, 1997).**

Dose of the venom: The dose of the venom was calculated according to the LD_{50} which was already calculated by Abdel-Aal and Abdel-baset (2010) for the same species in Egypt, and which was equal to 0.950 mg/kg. In order to confirm the correct value of LD50, a pilot study was conducted where 4 rats were given this dose subcutaneously and were inspected after 24 hours and 50% of them were recorded dead. This LD50 was used throughout the experiment.

Preparation of the venom reconstitute: The powder venom was weighed by the microbalance and a multiple of the LD50 was prepared. Just before its use, the powder venom was reconstituted by appropriate mixing with normal saline. The same reconstitute was used throughout the experiment to assure equal concentration of the injected venom. The volume of saline used was calculated so that each ml of the reconstitute would contain the exact concentration of the venom LD50.

Venom injection was administered once for each animal as the snakebite is an acute insult. The injections were given subcutaneously in the lower right quadrant of the back of the animal**.** The subcutaneous (S.C.) route was chosen to simulate the natural event as most bites pour the venom subcutaneously **(WHO, 2007).** Each animal was weighed and the appropriate volume of the reconstituted venom containing the LD50 was administered.

Study Groups

The rats were divided into 6 groups where each group comprised 6 rats (3 males and 3 females). Group I was the negative control group that received nothing except food and shelter. Groups II, III were the positive control groups,

where group II was given S.C. injection of normal saline and group III was given ether by inhalation. These two groups (II and III) were treated with saline alone and ether alone in order to check if saline and/or ether have an effect on the tested parameters.

Group IV was the venom group and was given S.C. injection of the venom. Groups V was the direct suture group and group VI was the skin flap group. Both (group V and VI) were given S.C. injection of the venom followed after 30 minutes by excision of the skin and subcutaneous tissue (while using inhalational anesthesia with ether) of the injection site, and surgical interference was done in group V by direct sutures and in group VI by skin flap.

Calculation of the area to be excised

A pilot study was conducted in order to clinically determine the extent of the area to be excised. Four rats were given S.C. venom injection, and sacrificed after 30 minutes. The subcutaneous area of edema and hemorrhage was measured and an average was decided with an addition of a safety margin of 5 mm. This was the standard area (as shown in Figures 1 & 2) excised in all animals throughout the experiment and it measured 2.5 cm x 3.5 cm.

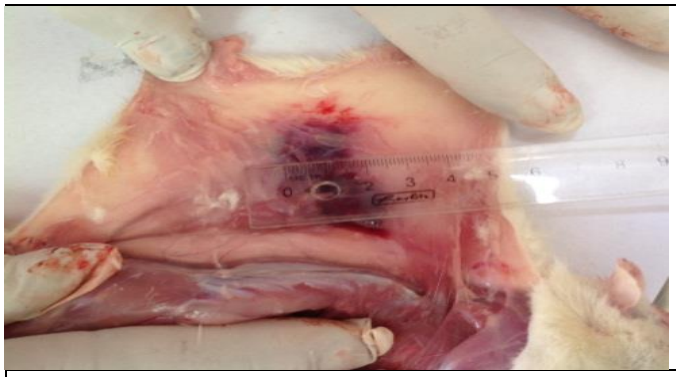

Figure (1): Local effect of the venom (width)

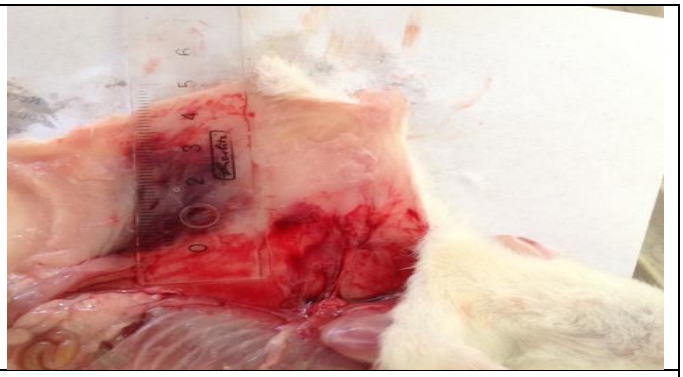

Figure (2): Local effect of the venom (length)

Methodology and technique of excision and wound care

For groups V and VI excision of the standard area was done followed by good hemostasis by pressure dressing until sutures were done. The excision created a defect that was closed by undermining and direct closure in group V while in group VI Limberg flap was created to close the defect. The skin marking for direct suture and Limberg flap are shown in Figures 3 & 4 respectively. Wound care was done for both groups where the wounds were left open and dressings were applied. The healing process and monitoring of possible complications have been followed-up for four weeks, after which the rats were sacrificed and the inner aspect of the skin was inspected for healing.

Figure (3): Marking for direct sutures

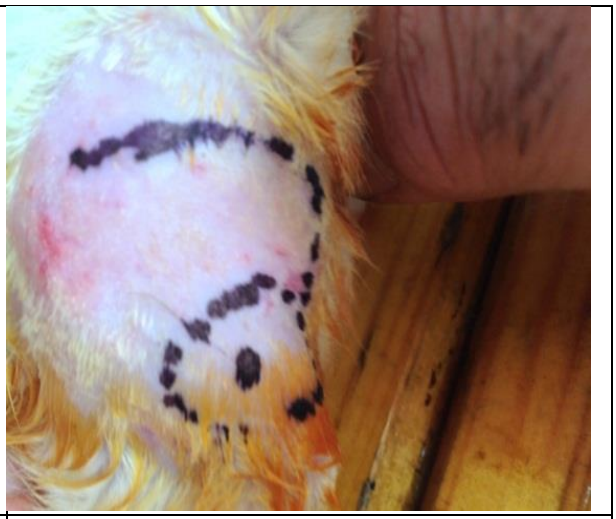

Figure (4): Markings for Limberg flap

Sample collection and lab tests

Three hours after injection according to Barbosa et al. (2003), venous blood samples were collected and the laboratory data were determined for each group. The tested parameters were complete blood count (CBC), prothrombin time (PT), partial thomboplastin time (PTT), fibrinogen level, fibrin degradation products (FDPs) and creatine phosphokinase (CPK). The rats of the venom group IV were sacrificed after sample collection and the other groups were followed up for four weeks.

Statistical analysis

All the obtained data were recorded, presented as mean ± SD and were statistically analyzed using analysis of variance (ANOVA) and t-test. Chi-Square test was used to test the association variables for categorical data and Fisher's exact test was used in tables containing values less than 5. A P value less than 0.05 was considered as significant.

Ethical considerations

All experiments complied with the ARRIVE guidelines and were carried out in accordance with the EU Directive 2010/63/EU for animal experiments.

RESULTS

3.1. Control groups lab results

There were no significant differences (P value >0.05) between the negative control group (I) and the two positive control groups (II & III) regarding the laboratory tested parameters (Tables 1 & 2).

Table (1): Comparison between the control groups (I, II, III) regarding blood laboratory results

	Group I		Group II		Group III		
Variable	**Mean**	**±SD**	**Mean**	**±SD**	**Mean**	**±SD**	**P-value***
RBCs ($x10^6$/µl)	8.38	0.67	8.14	0.64	8.20	0.76	0.821
Hemoglobin (g/dL)	14.38	1.19	14.28	1.19	14.33	1.42	0.991
WBCs ($x10^3$/µl)	7.83	0.804	7.65	1.21	7.47	0.48	0.775
Platelets ($x10^3$/µl)	841.67	72.56	848.67	66.63	839.17	82.89	0.974
PT (seconds)	13.72	0.48	13.6	0.39	13.38	0.58	0.501
PTT (seconds)	21.38	1.26	22.48	1.23	22	1.97	0.475
Fibrinogen (mg/dl)	224.67	15.32	226.33	24.04	226.83	6.46	0.973
CPK (U/L)	180.83	23.05	185.67	20.55	193.67	15.87	0.547

***Statistically significant at p value <0.05**

Table (2): Comparing the levels of FDPs in the six groups

FDPs	Group I	Group II	Group III	Group IV	Group V	Group VI
<5	6	6	6	0	3	3
5 to 20	0	0	0	0	3	3
>20	0	0	0	6	0	0
X^2_1	.	.	.	*	32.9	32.9
P_1	.	.	.	<0.0001	<0.0001	<0.0001
X^2_2	*	*	*	.	*	*
P_2	<0.0001	<0.0001	<0.0001	.	<0.0001	<0.0001

X^2_1: Chi square comparison with control group
X^2_2: Chi square comparison with venom group
*: Fisher's exact test

Effects of Cerastes cerastes venom application and its comparison with the negative control group

The unopposed effects of Cerastes cerastes viper venom were studied in the venom group (IV) and were compared to the negative control group (I). A severely deteriorated blood picture was observed in which statistically significant decrease in the RBCs count, hemoglobin concentration and platelets count and a statistically significant increase in WBCs count were observed. There was also a significant deterioration in the coagulation profile. Statistically significant prolongation in PT and PTT, a decrease in fibrinogen level and an increase in FDPs level were observed. There was also a statistically significant elevation in CPK level (Tables 2 & 3).

Table (3): Comparison between the negative control group (group I) and the venom group (group IV) regarding blood laboratory results.

	Group I		**Group IV**		
Variable	**Mean**	**±SD**	Mean	±SD	P-value*
RBCs (x10^6/µl)	8.38	0.67	6.15	0.34	<0.0001*
Hemoglobin (g/dL)	14.38	1.19	9.92	0.48	<0.0001*
WBCs (x10^3/µl)	7.83	0.804	9.63	2.04	0.0719
Platelets (x10^3/µl)	841.67	72.56	409	145.55	<0.0001*
PT (seconds)	13.72	0.48	23.92	3.29	<0.0001*
PTT (seconds)	21.38	1.26	52.22	2.72	<0.0001*
Fibrinogen (mg/dl)	224.67	15.32	153	13.25	<0.0001*
CPK (U/L)	180.83	23.05	1963	203.08	<0.0001*

***Statistically significant at p value <0.05**

Naked eye examination for the venom injection area in the venom group revealed the presence of edema and areas of hemorrhage on the outer surface of the skin while on the inner surface of the skin areas of tissue necrosis were observed in addition to edema and hemorrhage. The injection area in the negative control group was normal in appearance.

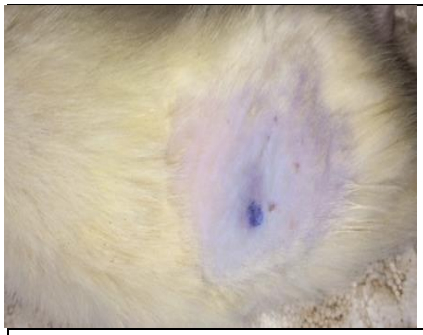

Figure (5): Edema and hemorrhage on the outer surface of the skin (Group IV, the venom group)

Figure (6): Edema and hemorrhage on the outer surface of the skin partially dissected (Group IV)

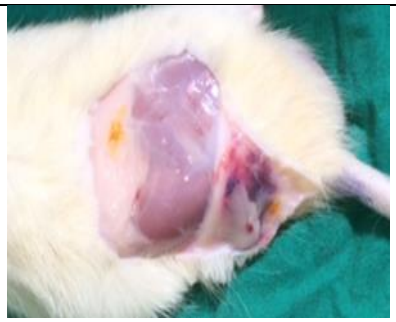

Figure (7): The inner surface of the skin dissected to show edema and hemorrhage seen on the outer surface (Group IV)

The effects of wide local excision of the venom injection site

Group V (the direct suture group):

The lab results for the direct suture group showed improvement of blood picture and coagulation profile when compared to the venom group (IV) where there was a statistically significant increase in the RBCs count, hemoglobin concentration, and platelets count whereas there was a statistically non-significant decrease in WBCs count. There was also an improvement in the coagulation profile, where there was a statistically significant decrease of PT and PTT, and FDPs level and a statistically significant increase in the fibrinogen level and decrease in CPK level (Tables 2 & 4).

Table (4): Comparison between the venom group (group IV) and the direct suture group (group V) regarding blood laboratory results

	Group IV		Group V		
Variable	Mean	±SD	Mean	±SD	**P-value***
RBCs (x10^6/µl)	6.15	0.34	7.46	0.85	0.0057*
Hemoglobin (g/dL)	9.92	0.48	13.2	1.05	<0.0001*
WBCs (x10^3/µl)	9.63	2.04	9.42	0.68	0.809
Platelets (x10^3/µl)	409	145.55	803.83	67.55	<0.0001*
PT (seconds)	23.92	3.29	16.52	0.82	<0.0001*
PTT (seconds)	52.22	2.72	29.32	2.86	<0.0001*
Fibrinogen (mg/dl)	153	13.25	215.17	9.11	<0.0001*
CPK (U/L)	1963	203.08	901.33	167.96	<0.0001*

***Statistically significant at p value <0.05**

Group VI (the skin flap group)

The lab results for the skin flap group showed improvement of blood picture and coagulation profile when compared to the venom group (IV) where there was a statistically significant increase in the RBCs count, hemoglobin concentration, and platelets count whereas there was a statistically non-significant decrease in WBCs count. There was also an improvement in the coagulation profile, where there was a statistically significant decrease of PT and PTT, and FDPs level and a statistically significant increase in the fibrinogen level. There was also a statistically significant decrease in CPK level (Tables 2 & 5).

Table (5): Comparison between the venom group (group IV) and the Limberg flap group (group VI) regarding blood laboratory results.

	Group IV		Group VI		
Variable	Mean	±SD	Mean	±SD	**P-value***
RBCs (x10^6/µl)	6.15	0.34	7.40	0.57	<0.0001*
Hemoglobin (g/dL)	9.92	0.48	13.17	0.70	<0.0001*
WBCs (x10^3/µl)	9.63	2.04	10.8	1.59	0.291
Platelets (x10^3/µl)	409	145.55	838.33	69.99	<0.0001*
PT (seconds)	23.92	3.29	16.13	0.68	<0.0001*
PTT (seconds)	52.22	2.72	29.6	2.32	<0.0001*
Fibrinogen (mg/dl)	153	13.25	210.33	11.48	<0.0001*
CPK (U/L)	1963	203.08	902.83	208.28	<0.0001*

***Statistically significant at p value <0.05**

Comparison between group V (the direct suture group) and group VI (the skin flap group) regarding local healing of the excision area

Local healing progressed normally in both groups and a normal scar was observed after complete superficial healing. Serial daily photographs were taken to both groups during the healing process until superficial healing was observed (figures 5-13). The resulting scar width ranged from 1.25 mm to 2 mm in group V and from 0.58 mm to 1 mm in group VI. The resulting scar was compared using the width of the scar in group V versus (counter base scar) in group VI where the width of scar in group V was more than that of group

VI.

Complications in the form of infection and necrosis were monitored where there was no incidence of infection or skin edge necrosis either in Group V or in Group VI.

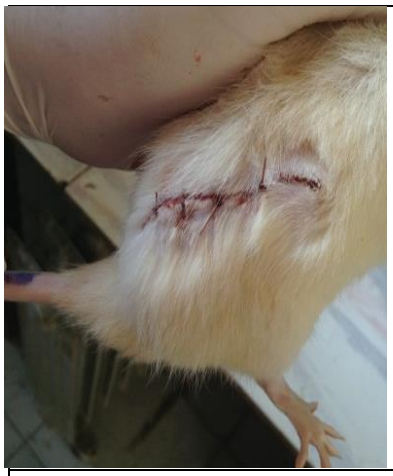

Figure (8): Direct sutures - day 4 (group V)

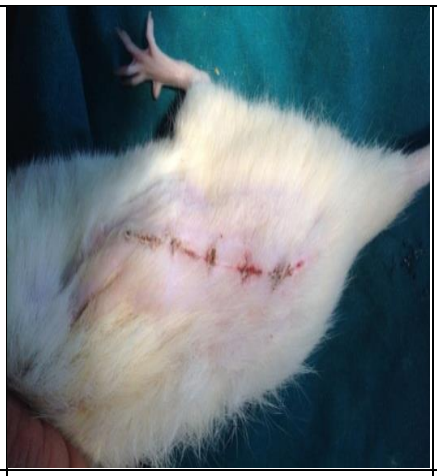

Fig (9): Direct sutures-day 9 (group V)

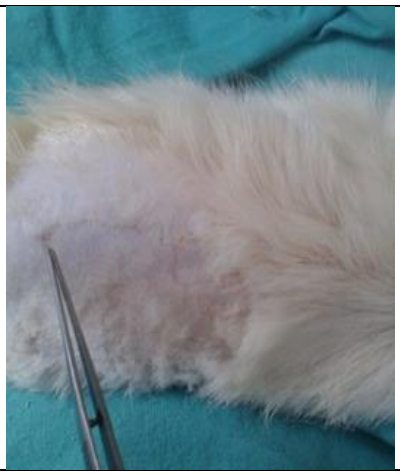

Figure (10): Direct sutures-day 28 (group V)

Figure (11): Limberg flap-day 4 (group VI)

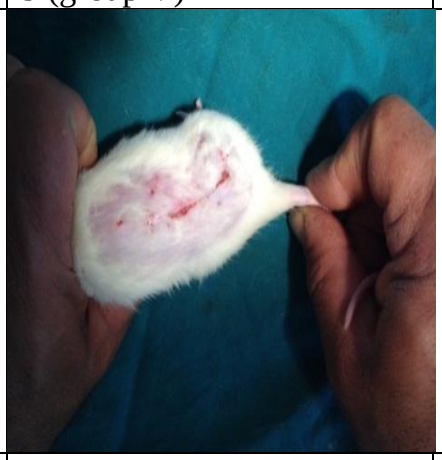

Figure (12): Limberg flap-day 9 (group VI)

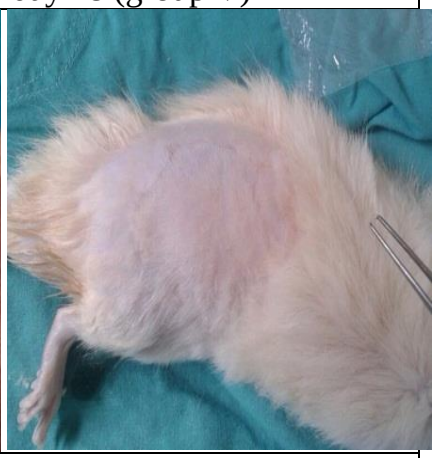

Figure (13): Limberg flap-day 28 (group VI)

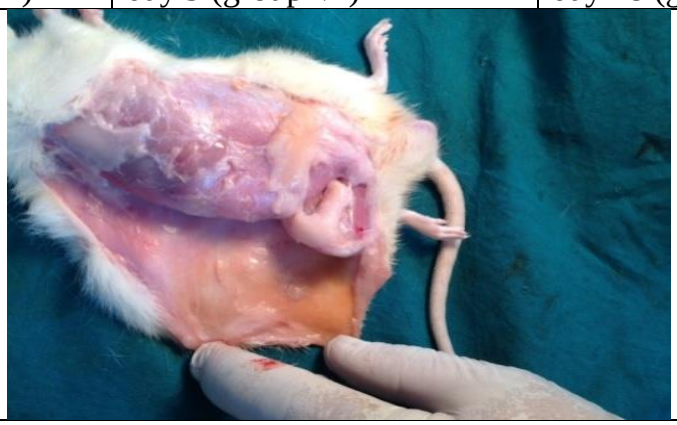

Figure (14): Inner aspect of skin after healing (group VI)

DISCUSSION

Egypt is one of the countries suffering from recurrent viper envenomation where different lethal viper species are distributed in desert areas **(Saleh, 1997; WHO, 2007).** According to the Poison Control Center in Ain Shams University (PCC-ASU) which serves the surrounding area in Cairo, an average of 190-200 snake bite cases are seen annually, and this number is prone to increase with the expansion of housing projects that invades the desert; the snakes natural habitat **(PCC, 2009; PCC, 2013).**

In the present study, there was no effect for saline or ether observed in the laboratory results of the control groups (groups II and III). In Group IV, after subcutaneous injection of Cerastes cerastes venom in the rats, local edema and hemorrhage were observed by the naked eye in the area of injection and were confirmed by dissecting the skin and inspecting the inner surface. These local findings are part of the classic picture of local effects of viper venom that was described by **White (2004) and Warrell (2012)** reporting that the local action of toxins on muscle, skin and blood vessels, causes edema, bleeding and necrosis of skin, subcutaneous tissues and muscle which may result in permanent sequel.

Systemically, in the present study, Cerastes cerastes viper venom caused a state of coagulopathy which was proved by altered laboratory results in the venom group. There was a decrease in RBCs count, hemoglobin level, platelets count, an increase in WBCs count, increase in the level of CPK, and FDPs as well as prolongation in PT and PTT.

These findings are in accordance with **Warrell (2004) and Bhaumik (2013)**, who stated that viper snake venoms are known to induce spontaneous hemorrhage secondary to microvascular damage, coagulopathy and platelet dysfunction, together with cardiovascular shock. The coagulopathy and hemorrhage are caused by venom components with proteolytic actions. According to **Corneille et al. (2006)** these effects lead to a decrease in RBCs count and hemoglobin levels and an increase in WBCs count, a decrease in the platelets count and an prolongation in PT and PTT as well as a decrease in fibrinogen level and an increase in FDPs as well as an increase in CPK level.

In the present study, wide surgical excision of the venom injection site was decided in order to excise the local venom depot in a trial to ameliorate its systemic effects. The technique resulted in relative correction of most of the altered laboratory findings caused by the venom, where there was a statistically significant difference in all the laboratory studied parameters in groups V and VI in comparison to the findings in the venom group IV. There was a statistically significant increase in the RBCs count, hemoglobin concentration, platelets count as well as a statistically significant decrease of PT and PTT, and FDPs levels and a statistically significant increase in the fibrinogen level. There was also a statistically significant decrease in CPK level when compared to the venom group. The only parameter with a non-significant change was the WBCs count. This finding is in accordance to **Pardal et al. (2004)** who reported non-significant decline of WBCs count after administration of enough neutralizing treatment.

According to **Seifert and Boyer (2001)** and **Ismail and Memish (2003),** viper venom is known to be slowly

absorbed, that's why some apparently mild cases turn severe, and others deteriorate after initial good response to treatment. This is due to the continuous absorption of venom from the bite site. This explains the correction of most of the laboratory findings after excising the venom injection site in the present study.

Rucavado et al. (2000) stated that the observations in mice and rats, concerning the need of an immediate administration of venom inhibitors, should not be simply extrapolated to human cases. It is suggested that the time course of local tissue damage in humans is not as rapid as in rodents and, therefore, the time lapse in which inhibitors injection may be beneficial is likely to be more prolonged. These findings make the obtained results from the present study applicable in real life as the area excised in rats would not be reflected as a percent area from total body area to be applied on humans and the time of surgical intervention in humans would be more prolonged than 30 minutes.

In the present work, none of the rats in all groups died. This proves the possibility of high effectiveness of the surgical treatment used in ameliorating the effects of Cerastes cerastes viper venom. This could also be beneficial in cases of envenomation in areas where the antivenom is not available as well as decreasing the needed therapeutic antivenom dose if it is available. According to **Pardal et al. (2004),** most of the cases are bitten in remote areas away from the medical services and there is always a recorded delay of more than 10 hours before receiving efficient treatment **(Pardal et al., 2004).**

In the present study, groups V and VI with the surgical excision of the injection area have been followed up for three weeks until complete superficial healing occurred. Healing is a condition that restores the internal and/or external physical integrity of body structures and includes complex interactions between cells and several other factors. It is a dynamic and complex process, consisting four highly integrated and overlapping phases: hemostasis, inflammation, proliferation, and tissue remodeling. The healing process comprises the extracellular matrix, cytokines, blood cells, and growth factors **(Gosain & DiPietro, 2004).**

According to **Edward and Harding (2004) and Bishop (2008)**, good oxygenation and the absence of infections are two crucial factors for successful wound healing without complications or disfigurements. These factors are highly compromised in cases of viper envenomation due to the local venom damage resulting in local healing with disfigurements in most cases. **Gutiérrez and Rucavado (2000)** stated that viper venom causes local extravasation of plasma and blood into the bitten area, inflammation and tissue necrosis. In the present study the excision of the damaged tissues gave the chance to the healing process to take place in the healthy skin areas; thus leading to successful healing, less complications and better cosmetic results. In addition, the resulting scar width observed in Group VI with Limberg flap was less than that observed in Group V with direct sutures giving better cosmetic results.

Other studies tried local excision. **Fujioka et al. (2009)** tried fang mark excision in five patients where in two patients delayed grafts were done and in the other three patients, the wound was left to heal by secondary intention.

In both scenarios, although the aim was excision of skin, that contains venom and necrotic and inflamed tissues, both techniques have caused a delay in healing for at least two weeks. Furthermore, in some cases, a secondary procedure was needed. Excision and primary closure or immediate reconstruction that was used in the present study could spare that time and produce better cosmetic results with minimal scar tissue.

CONCLUSIONS

In the present study, wide local excision of the venom injection site and immediate closure of the resultant defect resulted in amelioration of the local and systemic effects of viper envenomation. The study proved the efficacy of this method, as there was improvement of all laboratory results as well as absence of infection and edge necrosis in the local area of venom injection. In addition, no deaths were recorded in both treated groups of the study. This method could be used as an adjuvant or substitute to current treatment strategies used to treat the effects of viper envenomation.

RECOMMENDATIONS:

Based on the outcomes of the present study the following are recommended:

- Experimental trial of the treatment strategy used in the present study with venoms of other viper species.
- The use of wide local excision of the bite site and immediate closure of the resultant defect in human clinical trials as an efficient treatment strategy for viper envenomation.
- The use of Limberg flap for wound closure for less wide scar and better cosmetic results.

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الإستئصال الموضعى للجلد فى منطقة حقن سم الحية كطريقة مساعدة أو بديلة لإستخدام الترياق فى علاج حالات التسمم بسم الحية المُقَرنة فى فئران التجارب

يعتبر التسمم الناتج عن عض الحيات أحد المشكلات الطبية الشائعة في البلدان الحارة، وأحد الأسباب الهامة للوفاة. مصر هي واحدة من الدول التي تعاني من هذه المشكلة. الحية المُقَرنة هي واحدة من أنواع الحيات السامة المتواجدة بكثرة في شمال أفريقيا والشرق الأوسط. تظهر أعراض التسمم بعض الحيات فى هيئتين أساسيتين. تتمثل الأولى فى التأثير الموضعى الذى يشمل التورم والنزيف وتلف الأنسجة، فى حين تتمثل الثانية فى خلل فى عملية التجلط فى الجسم ينتج عنها تأخر تخثر الدم ونزف مستمر داخل الجسم وخارجه. يعتبر الترياق هو حجر الركن الأساسى فى علاج هذه الحالات ومع ذلك فإن قدرة الترياق على علاج الآثار الموضعية للسم تعتبر ذات تأثير محدود. ونظرا لوجود بعض الآثار الجانبية الضارة للترياق وإنخفاض معدل إنتاجه العالمى، لذا ينادى المهتمين بهذا المجال على العمل على إيجاد طرق جديدة للعلاج.

تناولت هذه الدراسة التجريبية العلاج الجراحى لهذه الحالات عن طريق حقن مجموعتان من فئران التجارب البيضاء بسم الحية المُقَرنة، ثم إستئصال الجلد فى منطقة الحقن وإغلاق المنطقة مرة بالغلق المباشر بالغرز بالجراحة التجميلية للجرح فى مجموعة ومرة أخرى بإستخدام طريقة ليمبرج التى تستخدم رقعة من الجلد ثم إغلاق الجرح بالغرز بالجراحة التجميلية فى المجموعة الأخرى. تم إحتساب مساحة الجزء الذى سيجرى إستئصاله من الجلد بعد إجراء دراسة تجريبية مصغرة يتم حقن الفئران فيها بالجرعة المميتة من سم الحية ومراقبة المساحة التى يتكون فيها النزيف تحت الجلد وقياسها، ثم أخذ متوسط المساحة فى كل الفئران المستخدمة فى التجربة. تم عمل إختبارات معملية عبارة عن صورة دم وإختبارات التجلط ومقارنة نتائج المجموعتان بنتائج المجموعات الضابطة.

أظهرت الدراسة وجود فروق إحصائية واضحة فى نتيجة التحاليل المعملية بين مجموعتى الفئران المعالجة جراحياً ومجموعة الفئران التى تم حقنها بالسم فقط، كما أظهرت أن نتائج التحاليل المعملية للمجموعات المعالجة جراحياً تقارب النتائج الخاصة بالمجموعة الضابطة السليمة.

أما بالنسبة لنتيجة الجراحة، فبعد مراقبة إلتئام الجروح لمدة أربعة أسابيع وجد أن الجروح التأمت بطريقة طبيعية فى المجموعتين بدون حدوث عدوى أو نخر فى حواف الجلد ولكن الشكل الجمالى للمجموعة التى إستخدمت الرقعة بها كان أفضل من الذى تم إغلاقه مباشرة بالغرز.

وعليه فإن الدراسة خلصت إلى أن العلاج الجراحى بإستئصال الجلد فى المنطقة المصابة فى حالات التسمم بعضة الحية يمكن أن يستخدم كمساعد للترياق أو بديل له فى حالة عدم وجوده وأن إستخدام طريقة ليمبرج فى غلق الجرح الناتج عن إستئصال الجلد يعطى نتيجة جمالية أفضل من إستخدام الغرز المباشرة.