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Mini Review

An Appeal to the World Health Organization (WHO) to Stop the Lethal Snakebite Antivenom Treatment, and to Start a New Suggested Treatment. Mini Literature Review

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Abstract

Snake envenomation represents an important health problem in much of the world. In 2009, it was recognized by the World Health Organization (WHO) as a neglected tropical disease and in 2017, it was elevated into Category A of the Neglected Tropical Diseases list. The French scientist Albert Calmette developed the first antivenom in 1895 (against the venom of the cobra). Antivenom, the serum of animals immunized with venom, is the only available treatment for poisoning with snake venom. It is proved that antivenom is more dangerous than the snake's venom itself. Its harm is greater than its health benefit and this treatment (antivenom) should be stopped and even rejected completely, as physicians declared.

Keywords: *World Health Organization (WHO); Snakebite; Antivenom Treatment*

Introduction

Snakebites are a significant risk to health and well-being for 5.8 billion people around the world and for those affected carry a high financial burden that often cannot be met (Dr Tedros Adhanom, Director -General, WHO) [1].

Snake envenomation represents an important health problem in much of the world. In 2009, it was recognized by the World Health Organization (WHO) as a neglected tropical disease and in 2017, it was elevated into Category A of the Neglected Tropical Diseases list. The French scientist Albert Calmette developed the first antivenom in 1895 (against the venom of the cobra). Antivenom, the serum of animals immunized with venom, is the only available treatment for poisoning with snake venom. It is proved that antivenom is more dangerous than the snake's venom itself. Its harm is greater than its health benefit, and this treatment (antivenom) should be stopped and even rejected completely, as physicians declared. Also, despite guidelines and recommendations of the World Health Organization in the annual meetings and conferences for decades, all these activities did not provide any new method regarding the discovery of new treatment to replace a current lethal antivenom. Since the first trial by Calmette in 1895 and the first production of antivenom, no other qualitative experiments having new hypothesis, was fulfilled in order to get new successful antivenom. It is still produced by the same method that was developed in the 1895. The main goal of this mini literature review is to prove definitively that the existing antivenom is dangerous and lethal. The researchers followed one wrong pathway in the production of this fatal antivenom. In order to get a solution and a new treatment for snakebite venom, it is mandatory to change your old method. The appropriateness of researchers' pathway is null and the effectiveness of their existing antivenoms is zero. The proverb stated: The one who lack the thing cannot give it to others.

What is known about?

Snakes and snake bites

The world Health Organization (WHO) estimates that every year, about 5.8 million snakebites occur worldwide. These cause up to 2.7 million envenomings, almost 138,000 deaths, and 400,000 cases of sequelae or disabilities (WHO 2019).

Snakes form a sub-order of the reptiles and have definite characters, the more important poisonous snakes are distributed among the following families and subfamilies: Elapidae, Viperidae, crotalidae, colubridae and hydrophiinae [4].

The snakes have different names according to their venom, anatomy, shape and place (country). Some of them are: Egyptian cobra (*Naja haje*), King cobra, carpet viper (*Echis pyramidum*), puff adder (*Bitis arietans*), Saharan horned viper (*Ceraster ceraste*), Black mamba (*Dendroaspis polylepis*), Black-necked spitting cobra, Death adders and many others.

Snake-bites are well-known medical emergencies, it constitutes an important health problem in many countries of the world, especially in rural areas. Agricultural workers are the most affected persons [2,3,6].

Snake venom and its composition

Snake venom is a mixed saliva composed of the secretion of the serous venom gland together with that of certain supralabial mucous glands. These glands produce a viscous yellowish liquid which contains both poisonous and non-poisonous proteins as well as, other organic and non-organic substances [2,3].

It is a mixture of mostly enzymes and non-enzymatic proteins or peptides constituting 90% to 95% of the venom's dry weight. Other components include carbohydrates, lipids, metal ions, and inorganic anions. These proteins have either (a) enzymatic activities such as metalloproteinase, serine proteinase, phospholipase A2 (PLA2), acetylcholinesterase (AChE), L-amino-acid- oxidase (LAAO), or hyaluronidase or (b) Non-enzymatic properties like natriuretic peptides, three-finger toxins, C-types lectins, proteinase inhibitors, and bradykinin-potentiating peptides [8]. c) Pathophysiological and pharmacological actions of snake venoms.

The major categories include [12]:

- Cytotoxins: Cause swelling and tissue damage wherever you've been bitten.
- Haemorrhagins: Disrupt the blood vessels.
- Anti-clotting agents: Prevent the blood from clotting.
- Neurotoxins: Cause paralysis or other damage to the nervous system.
- Myotoxins: Break down muscles.

ABO blood groups

The ABO blood types were first discovered by an Austrian Physician Karl Landsteiner working at the Pathological-Anatomical Institute of the University of Vienna (now Medical University of Vienna), in 1900. The determination of the ABO blood group system is used to denote the presence of one, both, or neither of the A and B antigens on erythrocytes. And by detecting the presence or absence of anti-A and/

or anti-B antibodies in the plasma. The Rh blood group is one of the most complex blood groups known in humans. The Rh antigens are highly immunogenic, and most of the Rh antibodies should be considered as potential causes of hemolytic transfusion reactions. O negative blood contains no A, B, or Rh antigens. Almost anyone with any blood type can receive these red blood cells. A person with group(O) negative blood is a universal donor [9-11].

What did they write about antivenom treatment?

English physicians who are honest in their profession have said that treatment must be stopped [5]. They wrote: surprisingly few deaths have been reported but some anaphylactic deaths may have been wrongly attributed to envenoming. In England the death of an asthmatic boy from anaphylaxis induced by antivenom in 1957 led to wholesale rejection of treatment on the ground that the bite was less dangerous than the treatment [6]. The physicians in their clinical managements of the bitten cases were afraid from the result of allergy test reaction and waiting to see its positive or negative response, losing time before giving antivenom [5,7]. Also, physicians after long practice and due to the lack of confidence in this antivenom refrain from giving this antivenom because of its danger, and waiting hours to see if there will be an appearance of clinical manifestations on patients from the toxicity of snake venom.

It is not accepted to delay antivenom treatment though it is lethal for 20 or 30 minutes to read the results of sensitivity tests. And waiting hours to observe if there will be antivenom reactions.

Animals and the researchers experiments [13]

Since the discovery of this product (antivenom) by the scientist Alberto Calmette in 1895, numerous animal species (Other than Calmette's horse) have been undergone for experimental purposes and for the production of large volumes of antivenom. The animals, birds and rodents that were used for experiments are: horses, sheep, goats, donkeys, rabbits, hen, camels, llamas, Ponies, Mules, dogs cats, sharks, ticks, fleas and others. The selection of the animal species by researchers was based on the following criteria and considerations: availability in the region, adaptation to the local environment, domestic, big size, and cost. Unfortunately, the criteria given by researchers are totally non convincing at all. What is the link between blood, serum, antibodies, etc. and the availability of the animal and its cost and size. What are the common biological characteristics and traits of a horse, rabbit and a tick? How could a horse and a mouse produce the same antivenoms? Unfortunately, this takes place under the umbrella of WHO experts everywhere in the world as they encourage such nonscientific experiments, with good intention. What are the control of such experiments, their variables, and their hypotheses? Researchers choose, only, what is available from these different kinds of animals and birds for their futile, unsuccessful experiments. There are uncountable theoretical reasons, medical and scientific evidences, that prevent the continuation of antivenom treatment and support its cessation. The astonishing news was that a doctor said that she needs support and fund from the World Health Organization to produce an antivenom to snake bite envenomation from bacteria. The strange thing is that the WHO experts believe this nonsense and may respond to it. In fact, these are experiments on humans, not on animals.

Discussion

This short review enabled me to find out most of the errors in regarding this drug since its discovery, and to put a number of logic, scientific and medical questions, as follows: 1) How could researchers or WHO experts determine that there are no differences between the blood of different animals in one side and the blood of animals and humans in the other side? As far as I know from my medical study and medical information written in hematology references that there is slight difference in the components of blood of the same humankind, (between the blood of a male and female), it is widely known that there are differences in the number of RBCs and WBCs and other minerals…etc. also there are different human blood groups, while in the other side the researchers determined, with no scientific base, that there is no difference between the blood of animals and humans. Current efforts of researchers aimed to discover a new treatment,

but they cannot, simply, because they are walking in the same wrong old street, they are rotating in the same vicious circle. They cannot achieve lifelong success or progress unless they change their path and method in studying this health problem.

Einstein stated: Insanity, doing the same thing over and over again and expecting different results. This is true 100% (This is Albert Einstein wisdom). What did researchers change in their method and variables, in order to have new antivenom? 2) How could I accept this lethal antivenom extracted from rabbits or mice? while I cannot even change the engine oil of my car with another different type of oil? Also, I cannot donate my son drops of my blood if it is not matching his blood group. Here I will give you an example (we apply part of it in the disputed paternity in forensic medicine): If my blood group is type (AB), and my wife is group (O). So, our son will be either (A) or (B). In this case, of any of the two groups for my son, I can't donate my son a drop of my blood, while my wife can donate him a blood. Also, I can receive a blood from my child, while my wife cannot receive a drop of her son's blood. 3) Who determined that this antivenom which is extracted from animals blood, is the effective and appropriate treatment to humans suffering from snakebites venom?

Alfleesy new suggested treatment

Regardless of the increasing knowledge about the composition of snake venom and its mode of action, and a sound understanding of clinical features of envenoming, management of snakebites remains a challenge in the Region (Dr Poonam, Regional Director) [1]. The researchers repeated animal experiments and studies with the same method, since the first experiments by the scientist Alberto Calmette in 1895. This first experiment on horse has failed to have health benefit to humans with this antivenom product. It is unequivocal that there is strong evidence which indicates the risk of antivenom for humans and its danger clearly outweighs its health benefit. During this long journey of clinical managements of bitten patients, nothing supports the use of existing antivenom at all. The ineffectiveness of antivenom treatment was due to the blood of the horse and other animals which (blood) is not appropriate for the production of suitable antivenom for humans. The discovery of diphtheria antitoxin (1892) by the scientist Emil von Behring has paved the way for researchers to conduct their experiments on animals, and Calmette's horse was the first winner to give its serum (antivenom) for snake bite venom. Taking into account the success of the experiment in extraction diphtheria antitoxin, does not mean that another horse is suitable for producing another effective antivenom for snake bite venoms. WHO still emphasizes to design a mixture of snake venoms that can be injected in animals to make appropriate antivenom. The great Arab scientist Al-Hasan Ibn Al-Haytham, who proved the fact that light comes from objects to the eye, and not from the eye to the object, as they were thinking. The same story is repeated here, the problem is not the mixture of snake venoms and to include or exclude some venoms to get appropriate mixture in order to inject in the horse's blood, as WHO experts believe, but the problem is the horse's blood itself and other animals blood. How long will this method and this lethal antivenom treatment continue? Why WHO did not pay attention to all these errors, and stop antivenom treatment, in spite of: 1- Unequivocal proof that antivenom is dangerous to life. 2- Certainly, its harm is greater than its health benefit, 3- The treatments for an allergic reaction are another dangerous drugs. There is a cocktail of dangers: (a) Deadly snake venom. (b) Antivenom is more dangerous than snake venom. (c) Allergy test and its complications. (d) And the drugs used as prophylaxis for this complications (steroid, adrenaline, hydrocortisone, epinephrine…..etc). Albert Calmette has failed to hit his target (Even Homer sometimes nods), because of a number of factors and reasons, some of them are: 1- Calmette did not succeed in choosing the horse or other animals and birds. 2- His discovery in (1895) was before Landsteiner discovery of ABO blood groups in (1900). 3- The researchers were unable to communicate with each other, as it happens now, because was no communication or feedback to know the clinical results of snakebite treatment on the ground of practice as it is happening now. Moreover, the scientific informations of the scientists at that time regarding blood and its reactions (allergy, anaphylaxis… etc.), were limited. Look to the medical references at that time. Finally, and after a review of this health problem, since my higher study in Jordan (1989) my study fortunately was at the expense of WHO, my interest and suggested thesis was about snake bite, but fortunately and unfortunately after gathering some references and researches I selected the general examination because of other considerations. With reference to all of the foregoing matters which I have explained, my new suggested treatment is based on a number of: (theoretical

reasons, clinical observations, scientific facts, medical evidences, Physicians' clinical work and managements of bitten cases) and Declarations of: (WHO experts, physicians and researchers), ineffectiveness and lethality of the antivenom. I propose a new treatment (alfleesy treatment) for snakebite venom: (1) Transfusion of blood group type (O) negative. (2) Isotonic fluid and other suitable fluid (according to the evaluation of the physician). (3) Analgesics (according to the evaluation of physicians). 4) Diuretics (if needed) according to the estimation of the medical specialist be careful of overloading fluids, you have to take every case upon its own merits. The treatment must be under the supervision of medical specialist.

Conclusion

It is true that medicine is a field of possibilities and probabilities, and thousands of hypotheses, theories, experiments and (drugs) that were successful for a period of time, later on have been proven incorrect, invalid, and have dangers, side effects after their temporary success and propaganda, they have been dropped and cancelled [14]. So, antivenom treatment must be dropped as soon as possible.

Why did not the World Health Organization intervene to stop and prevent this harmful antivenom from being sold in the medical stores, the same question for U.S. FDA? Because the honesty of the manufacturers is absent, they have no control and they are selling death to poor patients. All these disadvantages in concern to antivenom, mentioned previously, where can World Health Organization experts can them?

Recommendation

It is my appeal to WHO experts committee to stop the treatment by this lethal antivenom extracted from the horse and other animals as soon as possible. The ethical duty and the humanitarian responsibility necessitate WHO and make it imperative to stop the existing antivenom for snakebites venoms. Even if there is immediately no other new treatment instead of (Alfleesy treatment), it is advised to let the bitten patients depend on their own immunity (antibodies). At least: (What cannot be cured must be endured). The other appeal is directed to the U.S. Food and Drug Administration (FDA). FDA is the government agency responsible for reviewing, approving and regulating medical products, including pharmaceutical drugs before they can be sold to the public. Also, FDA's Center for Drug Evaluation and Research (CDER) evaluates new drugs before they can be sold. A team of CDER physicians, statisticians, chemists, pharmacologists and other scientists review all the data and collect reports. FDA review the safety and effectiveness of new drugs that manufacturers wish to market in U.S. FDA works with manufacturers to recall problematic products and collect reports and adverse events, side effects caused by drugs and vaccines. If the agency decides these reports are serious, it may issue a safety communication and warn the public When needed. Here, again the question puts itself: How this Agency (FDA) which was established in 1906, with its doctors, researchers and scientists could not know anything - during more than (115) years - about the danger of antivenom and its lethality. If they did not know, now, I am reporting them on behalf of all the farmers in the poor countries who are suffering from snakebites, and saying that the antivenom is ineffective and unsafe treatment.

Comment

In May 2019, the World Health Organization (WHO) launched a program to prevent and control snakebite incidents and to have new effective and safe treatment. Really, I don't know what the word "prevent" means in the dictionary of WHO experts? How will you prevent farmers from snakebites in south Yemen, Abyan governorate and Hassan valley? The declarations are not enough, an ounce of deed is better than a ton of words. With no doubt there is a lack of interest and indifference on the part of the World Health Organization towards this health problem. It is clear, there is no seriousness, that is probably the cause for putting this health problem in neglected diseases of the world.

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