Original Research Articles

Received on 10.11.2016, **Accepted on** 26.11.2016

Indian Journal of Emergency Medicine
Volume 2 Number 2, July - December 2016
DOI: http://dx.doi.org/10.21088/ijem.2395.311X.2216.1

Assessing the Efficacy of Haemostatic Dressing Axiostat® In Trauma Care at a Tertiary Care Hospital in India: A Comparison with Conventional Cotton Gauze

Patel Ketan*, Patel Anjali, Patel Rignesh**, Patel Bhavika**, Parmar Priyank***, Patel Dev******

Author's Affiliation:
*Consultant and Head, **Consultant, ***Registrar, Department of Emergency Medicine, Apollo hospitals, Bhat, GIDC Estate, Gandhinagar - 382428, Gujarat, India. ****Specialty Doctor, Dept. of Emergency Medicine at Glan Clwyd Hospital, UK.

Corresponding Author:
Ketan Patel, Consultant & Head, Department of Emergency Medicine Zydus Hospitals, Zydus Hospital Road Ahmedabad – 380054 Gujarat, India.
E-mail: haemostatindia@gmail.com

Abstract

First aid is most urgent need to stabilize patient condition before any kind of intervention is sought. Scientists estimate the volume of blood in a human body to be approximately 7 percent of body weight. An observational study of 61 patients with bleeding wound chosen by random assortment was carried out. All patients were divided in two groups: Group - I, Axiostat® (Chitosan Haemostatic Dressing) and Group - II, Conventional Cotton dressing. The patients were divided in both groups by 1:1 randomization. A total of thirty patients in group – I and thirty one patients in group –II were subjected to the study. A standard pattern was followed for application of dressing to bleeding wound in both groups and different parameters were recorded. Results showed that haemostatic time in group-I (Axiostat®) was 2.125±1.35 minutes where in group-II (cotton gauze) it was 13.08±6.40 minutes. Only 61% of patients who were applied with cotton gauze showed no rebleeding after removal whereas 83% patients showed no rebleeding after removal of Axiostat® in 30 minutes. Axiostat® could be easily applied and removal was also effective by application of saline where about 63% of patients showed an excellent ease of removal when only 10% of patients applied with cotton gauze showed excellent removal. The aim of this study was to evaluate the efficacy and safety of use of external haemostat Axiostat® to control the flow of blood and attain haemostasis in comparison with conventional cotton gauze dressing.

Keywords: Axiostat®; Bleeding; Chitosan; Cotton; Dressing; Trauma.

Introduction

Accidents occur not only due to ignorance but also due to carelessness, thoughtlessness and over confidence. Human, vehicle and environmental factors play roles before, during and after a trauma event. Trauma in India is an increasingly significant problem, particularly in light of rapid development and increasing motorization. India leads world in road deaths. Thirteen Indians die every hour due to an accident. 1,14,590 people died in road traffic accidents in India (2007), highest in the world. Fatalities due to road traffic injuries in India are projected to increase by 150% by the year 2020 [1]. The nature of injuries sustained due to trauma is well understood; however, the causality of injury is less well understood. In India, systematic and scientific efforts in injury prevention and control are yet to begin [2].

Severe bleeding or uncontrolled bleeding is the major cause of death in traumatic conditions. Appropriate management to stop bleeding and to attain hemodynamic stability is the need of the hour and one method to counter this problem is the use of haemostatic dressings as a first line of treatment before further interventions are sought. The ideal wound dressing material should have characteristics like create a moist, clean, warm environment, provide hydration, remove excess exudates and protect the periwound area, should allow for gaseous exchange, have anti-microbial properties, should be free of toxic or irritant particles and should not release particles

or fibers, should conform to the wound site and have minimal pain during application and removal and finally should be easy to use and be cost effective [3]. Generally in the traumatic injury cotton with pressure is used to control bleeding from wound and its takes more time or not able to control to stop bleeding.

The main goals of wound care and management are prevention of infection, maintenance of a moist environment, protection of the wound and achievement of rapid and complete healing with the minimum scar formation. Chitosan, as a cationic natural polymer, has been widely used as a topical dressing in wound management owing to its haemostatic, stimulation of healing, antimicrobial, nontoxic, biocompatible and biodegradable properties.

The Chitosan dressing is a haemostatic dressing that was designed to stop hemorrhage that cannot be controlled by the use of a tourniquet because of the location of the injury. This dressing has CE approval for external use on human patients and has currently been used with success on wounded soldiers in a pre-hospital combat setting [4]. The aim of this study was comparative evaluation between Axiostat® (Chitosan Haemostatic Dressing) and Conventional Cotton Gauze dressing to control bleeding from wound.

Materials and Methods

Patients

The study was approved by Ethics Committee - Apollo Hospitals International Ltd. Either sex, more than or equal to 18 years of age with bleeding wound in upper and/or lower extremities were included in this study. The selection of wound size was based on proper covering through dressing materials.

Inclusion/exclusion Criteria

The inclusion criteria for the study involved age greater than or equal to 18 years. Patient and/or patient's legal representative and/or impartial witness have been informed of the nature of the study and agree to its provisions and have provided written informed consent as approved by the Ethics Committee of the investigative site. Patients with bleeding wounds in upper and/or lower extremities due to any injury. The wounds must be bleeding at the time of baseline assessment/randomization. The targeted wound size should be such that it should be covered by single available size of the study device as per the instructions for use.

The exclusion criteria for the study involved prior diagnosis of disease or medical condition affecting the ability of blood to clot (e.g., hemophilia). Patients with known sensitivity to Chitosan (shellfish) or the gauze dressings used in this study. A non-survivable injury as per the investigators' discretion. Patients who in the opinion of the investigator may not complete the study for any reason, e.g. Patients requiring immediate suturing. Infected wounds that may reasonably be expected to require multiple debridement procedures prior to clearance of bacteria and non-viable tissue from the wound. Patient is currently participating in an investigational drug or device study that has not yet completed its primary endpoint or interferes with procedure and assessments in this trial. Pregnant women were excluded from the study. Patients with Surgical/ iatrogenic wound were also excluded from the study. Patients with a head injury, spinal injury, neck injury, abdominal injury, deep wound injury, fracture, hemorrhagic shock, foreign materials inside the study wound like stab injury were excluded.

Wound Dressing Materials

In group-I, Axiostat®[1]- a sterile, single use dressing made from Poly [β-(1,4)-2-amino-2-deoxy-D-glucosamine] commonly known as Chitosan, a natural biomaterial was used. The Poly [β-(1,4)-2-amino-2-deoxy-D-glucosamine] is a linear polysaccharide which is structurally similar to cellulose and poly cationic in nature. It is highly bio-adhesive and readily binds to negatively charged surfaces such as mucosal membranes. The dressing bypasses the natural clotting mechanism to create a temporary clot. The dressing works on the basis of electrostatic interactions and has an extremely positive charge on its surface which interacts with the tissue and blood cell components which are negatively charged (due to the presence the glycosidic acid moieties on the surface). The highly porous dressing absorbs the blood and the blood cells get trapped in the interconnected structure of the dressing. It also initiates the platelets and other blood components which forms the natural clot thereafter. Being pH sensitive, dressing can be easily detached using few drops of saline. In group – II, standard cotton gauze was used. The size of the dressing was 5 x 8 cm in both groups.

[1]Axiostat® -Axio Biosolutions Private Limited, Ahmedabad, Gujarat, India

Application Procedure

The wound was assessed for inclusion in the study. The dressing pack was opened carefully which contained either Axiostat® or Cotton gauze and applied on the bleeding wound. The dressing was applied such that it covered the contour of the wound leaving only one centimeter from each side. Manual pressure was applied with fingers for about two minutes until the dressing sticks to the wound site and stayed in position. The time for haemostasis was observed. If bleeding did not stop after the application of the first dressing, a second application was provided with the same previous application procedure. The time at which blood oozing through or from periphery of the dressing stops, was considered as achieving complete haemostasis and was noted as the efficacy endpoint. In both groups, the dressing was kept for further 30 minutes after complete haemostasis was achieved. Axiostat® was removed by applying saline and gently lifting it off. After removal, wound site was checked for rebleeding. Cotton gauze was removed as per institutional standard. After the removal of the dressing, the patients were further treated as per institutional standard of care.

Parameters

Primary End-Points

Efficacy End-Points

The time to achieve haemostasis (The time from application of dressing at the target bleeding site to the achievement of haemostasis).

Safety End-Points

1. The occurrence of rebleeding after Axiostat®/ Cotton gauze dressing was removed from wound after 30 minutes of achieving haemostasis.
2. To check the sensitivity of dressing to skin peripheral to the wound.

Secondary End-Points

1. To assess comfort levels of treating doctors and patients treated with Axiostat® dressings as compared to cotton gauze dressings.

Stastical Analysis

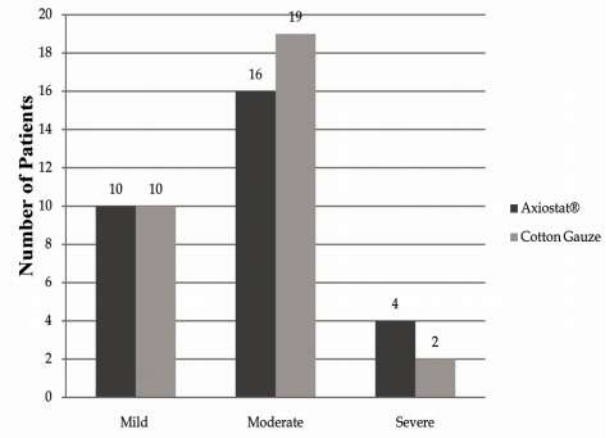
The resulting differences in the two groups for parametric data (time for haemostasis) were expressed as mean ± standard deviation (SD). Categorical variables (gender, ease of application and removal) were expressed as absolute frequencies and percentages.

Results

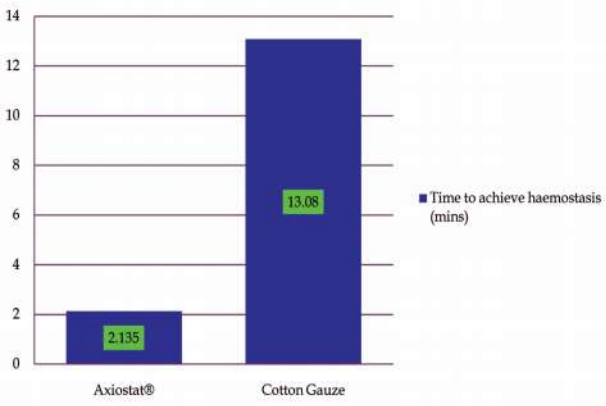
Results were drawn from Axiostat®)/Cotton gauze dressing applied in all sixty one patients with wound bleeding in both groups. The randomization of the patient was nearly equal to male and female in the both groups. A ratio for male and female allotments of patients in group-I was 4:1 and in group-II it was 3:1 (Table 1).

Based on severity of bleeding, bleeding from wound was classified as Mild, Moderate and Severe. Both groups had equal number of cases with mild bleeding. Moderate bleeding was seen in 16 and 19 patients in group –I and group – II respectively. Severe bleeding was seen in 4 patients in Group - I and 2 patients in group – II. Results show that there was not much difference in both groups during randomization of the patients based on of severity of bleeding from wound (Graph 1).

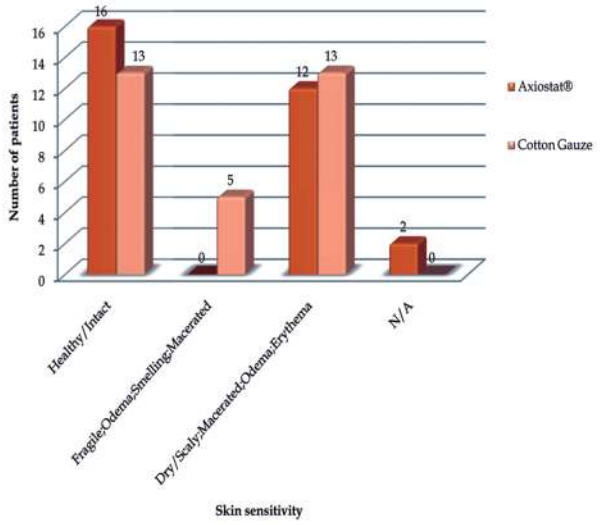
Average number of Axiostat® haemostatic dressing used to control bleeding was 1.2 as compared to standard cotton gauze which was 2.9.



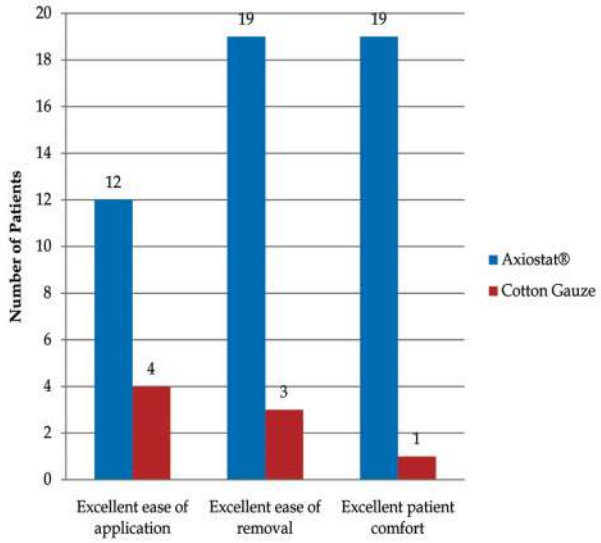
Graph 1 : Distribution of bleeding from wound based on severity in both groups



Graph 2 : Average time (minutes) to control bleeding from wound in both groups



Graph 3: Sensitivity to surrounding skin 30 minutes post haemostasis



Graph 4 : Comfort Level for using Dressing

Table 1: Outline of Study data and comparative results of various parameters in group – I (Axiostat®) and group- II (Cotton Gauze)

Sr. No.	Parameters	Group- I (Axiostat®)	Group-II (Cotton Gauze)
1.	Number of subjects	30	31
2.	Mean age (years)	36.5	37.6
3.	Male	24	23
4.	Female	6	8
5.	Number of dressing required to achieve haemostasis	1.2	2.9
6.	Average time to achieve haemostasis (minutes)	2.125 ±1.35	13.08 ± 6.40
7.	Rebleeding at 30 minutes post haemostasis	5 (17 %)	12 (39 %)
8.	Excellent ease of application	12 (40 %)	4 (12 %)
9.	Excellent ease of removal	19 (63 %)	3 (10 %)
10.	Excellent adherence to wound	10 (33 %)	2 (6 %)
11.	Excellent ability to manage exudates	6 (20 %)	0
12.	Excellent ability to manage odour	9 (30 %)	0
13.	Excellent conformability of dressing to wound	12 (40 %)	0
14.	Excellent ability to remain in position	16 (53 %)	1 (3 %)
15.	Excellent Patient Comfort	19 (63%)	1 (3 %)

The average time to control bleeding from affected wound in group-I (Axiostat®) was recorded 2.125±1.35 minutes, where as in group- II (cotton gauze), it was 13.08±6.40 minutes (Graph 2).

Rebleeding was assessed in both groups after 30 minutes of achieving haemostasis. Axiostat® was removed using saline and it was observed that in group-I only five patients showed rebleeding as compared to twelve patients in group-II.

Different sensitive reactions to skin surrounding wound were monitored after 30 minutes of haemostasis and it was observed that 16 patients in group-I had healthy and intact skin as compared to 13 in group-II. Other reactions like macerated, oedema, dry/scaly, erythema, smelling and fragile were also observed. Overall, group-I (Axiostat®) shows minimum tissue reactions in comparison with group-II (cotton gauze) (Graph 3).

The dressing was removed after 30 minutes post haemostasis and evaluation for comfort level in removal of dressing was monitored. Overall patient as well as doctor's comfort for application and removal of dressing was excellent in group- I (Axiostat®) as compared to group- II (Cotton Gauze) (Graph 4).

Discussion

In India, the motor vehicle population is growing at a faster rate than the economic and population growth. The surge in motorization coupled with expansion of the road network has brought with it the challenge of addressing adverse factors such as

the increase in road accidents [5]. The leading cause of death for trauma patients in both civilian and combat setting is uncontrolled haemorrhage [6]. In our study Chitosan based haemostatic dressing used to control the bleeding wound has CE approval.

Chitosan is a blood clotting accelerator, and there is also good evidence that chitosan can beneficially influence every separate stage of wound healing. Chitosan and its derivatives could accelerate wound healing by enhancing the functions of inflammatory cells, such as polymorphonuclear leukocytes (PMN) [7-10], macrophages [7,11,12] and fibroblasts [7,13-15] or osteoblasts [16].

In this study sex distribution was found more towards males. This is probably because men were found to be involved in accidents and thus exposed to risk-factors [17]. Wound healing, as a normal biological process in the human body, is achieved through four precisely and highly programmed phases: haemostasis, inflammation, proliferation, and remodeling [18]. In this study haemostasis of bleeding wound was achieved in 2.125±1.35 minutes using Chitosan haemostatic dressing (Axiostat®).

Chitosan, a natural cationic polysaccharide, has received considerable attention as a functional, renewable, nontoxic and biodegradable biopolymer for diverse applications, especially in pharmaceutics[19], food [20] and cosmetics [21]. In the medical field, chitosan has been developed not only as artificial skin, absorbable surgical suture, and a wound healing accelerator, but also as new physiological materials due to their antitumor, immunoenhancing, antimicrobial and hypocholesterolemic properties [22].

Research showed that whole blood formed a coagulum rapidly upon exposure to Chitosan [23]. The various studies have shown that chitosan acts as a haemostatic agent and may be used in various wound healing applications such as haemostatic bandages [24-26]. However, chitosan, only in its purest form, has an internal haemostatic dressing potentiality, as a drug delivery agent, tissue scaffolding and numerous other health related products [27,28].

Even in a therapeutically anticoagulated (heparinized) rabbit model, chitosan treatment could effectively bring bleeding time within the normal range [29]. A fly-larva shell-derived chitosan sponge (CS) was evaluated as an absorbable surgical haemostatic agent in a rat hepatic hemorrhage model [30], indicating that CS was a suitable implantable haemostatic material when compared to gelatin sponge or oxidized cellulose in both acute and chronic bleeding models.

Chitosan's haemostatic mechanism seems to be independent of the classical coagulation cascade [27]. It has been found that coagulation factors could not be activated by chitosan and its derivatives [31], and no activation of the intrinsic pathway was observed by Benesch *et al [32].* Chitosan's putative capacity to induce clot formation in the absence of coagulation factors could prove to be useful for patients with coagulopathies or those who are therapeutically anticoagulated, since chitosan keeps ability to maintain haemostasis in the presence of heparinized blood. Most of all, numerous articles reported the interactions between chitin/chitosan and platelets [33-35]. Chitin and chitosan directly influenced platelets by themselves and this effect was enhanced in the presence of plasma. Some researchers regarded that chitosan likely function independently of platelets because it could induce clot formation in the absence of platelets [31,36]. However, over time, more and more researchers admit that the haemostatic effects of chitosan are related to both platelets and erythrocyte aggregations.

Overall, the study data and comparative results of various parameters between group-I (Axiostat®) and group-II (Cotton gauze) (Table -1) shows that using Axiostat® was better than the use of cotton gauze in fresh bleeding wound to control the bleeding with minimum time, less tissue reaction and easy to use for patients and doctor.

Conflict of Interest

Axiostat® (Axio Biosolutions Pvt. Ltd, India) is an external haemostatic dressing that is CE approved and was provided at no cost from Axio Biosolutions as a part of the authors research work. The authors of this study do not have any financial interests in Axio Biosolutions Pvt. Ltd. and did not receive any fellowships or support from them in the conduction of this study, collection of data and preparation of manuscript. There is no any conflict of interest among the all authors in this research study.

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