Regulatory Guidelines for Burn Dressings and Advanced Wound Care

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Abstract: Burn and wound injury is a prevalent and burdensome critical care issue. Furthermore, burn wounds are complex and present unique challenges that require specialized care to protect from microbial infection. According to the World Health Organization (WHO), more than 3,00,000 deaths occur each year as a consequence of fire-induced burns. The burden of such injuries generally fall on poor patients as they cannot afford costly treatment. A primary contributing factor that leads to infection and finally to death in this population, is poor hygiene.[4-5] Burn injury management is challenging, due to significant fluid loss, tissue damage and deep wounds, thus contributing to death. It is estimated that there are about 7 million burn injuries in India annually, of which 7,00,000 require hospitalisation and 1,40,000 are estimated to be fatal. According to the National Burns Programme data 91,000 of these deaths are of women. In cases of surgical site infection, the mortality rate resulted in 70-80%, where deep and extensive infection takes place during surgery. The high prevalence and death rate due to burn mandates the need for guidelines.

Key Words: Burn and wound injury, World Health Organization (WHO), Regulatory Guidelines for wound and burns.

I. INRODUCTION

1.1 Wound and burn

A wound is generally defined as a disruption in the continuity of the epithelial lining of the skin or mucosa.[11] Wound is found to be of many types and has multiple causes of occurrence.[11-12] The healing of a wound is very complex process. To prevent microbial infection and to facilitate the body's natural healing mechanisms, an optimal healing environment and an appropriate wound dressing is often required.[13-14] Burn is a most common injury characterised by severe skin damage that causes the affected skin cells to die. Burns are generally classified on the basis of degree on burning *i.e.* first, second, third and fourth degree. The first degree of burn is the most minor and fourth-degree being the most severe. The symptoms occurring during burn generally define the degree *e.g.* red, non-blistered skin represents first -degree burn, blisters and some thickening of the skin represents second-degree of burn and third- degree burn is as when widespread thickness with a white, leathery appearance occurs. The fourth-degree burn includes all of the symptoms of a third-degree burn and also extends beyond the skin into tendons and bones.

1.2 Prevalence, death rate due to burn and wound injury

Majority of the death occurs in low and medium income countries. In India, over 10,00,000 people get moderate and severe burns every year. In other countries such as Pakistan, Egypt, Columbia and Bangladesh 17% of children with burns have temporary affliction and 18% of them have a permanent affliction. Burns are the second utmost commonly reported injury in the countryside of Nepal, considering disabilities of 5%.[3-4]

The mortality rate is also high in India when burn injuries are taken into account. Large population and congested habitat results in the prevalence of such injuries. The occupation of many people falls in high-risk jobs such as cracker manufacturing, acid manufacturing, chemical manufacturing and road maintenance. The high cost of treatment, rehabilitation and shortage of dedicated burn units plays a major role in the increased mortality rate.[16] The high cost of treatment, rehabilitation and shortage of dedicated

burn units plays a major role in the increased mortality rate. It is very difficult to cater huge population with less number of beds per hospital especially with infectious diseases .[17]

Table 1: Estimated prevalence and growth rate of various types of wounds from 2012-2020[4]

Wound type	Worldwide prevalence (thousands)	CAGR (2012-2020)
Surgical wounds	114271	3.6%
Traumatic wounds	1627	1.7%
Lacerations	20645	1.2%
Burn wounds	10221	1.2%
Chronic wounds	40400	7.6%
Carcinoma	618	3.0%
Melanoma	103	3.2%
Skin cancer	103	3.1%

Table: 2 List of microorganisms responsible for infection in burn and wound patients

Infection Type	Name of the microorganism
Viral infections	*Cytomegalovirus*
Fungal infections	*Candida sp, Aspergillus sp.* *Alternaria sp, Fusariumspp, Rhizopus sp, and Mucor sp*
Bacterial infection	*Pseudomonas aeruginosa* *Staphylococcus aureus*
Sepsis and toxic shock syndrome	*TSST-1 toxin*

1.3 Wound and burn healing

Wound healing is a process that involves tissue regeneration and a response to injury.[11, 24] A wound can be described as a defect or a break in the skin, resulting from physical or thermal damage or as a result of the presence of an underlying medical or physiological condition.[25]

It is a quite challenging process as an acute wound may transform to chronic one if left unattended or because of lack of "ideal" wound-healing environment. Huge figures of burns, ulcers and diseases (diabetes) cases worldwide are making wound healing a topic of large research and debate. Healing occurs through a series of biochemical processes including 4 key phases: hemostasis, inflammation, proliferation and remodeling. Variety of cellular and matrix components act together to re-establish the integrity of damaged tissue and replacement of lost tissue.[26-27] If this process becomes distracted, healing process ceases and results in chronic wounds. In order to bring the wounds into healing cascade, wound dressings are the first line treatment, although many wound care products are also there in use.[28-29]

II. METHODOLOGY

2.1 Wound and burn dressings: A dressing is a medical device that is used to cover the wound and burn injuries, to promote healing and further prevent harm. They are also called as surgical dressings or bandages but generally, they are different from bandages because they are designed to be in direct contact with the skin.[30]

Wound and burn dressing includes a first layer which remains in direct contact with the wound and is made up of material which should be bio absorbable, porous and adapted for serving as a scaffold for cell attachment and proliferation. The second layer which is in direct contact with the first layer comprises an absorbent, gel- forming material, which serves as a barrier to cell adhesion and penetration.[11]

The key objectives of wound care and burn dressing are the reduction of infection and pain as well as healing of wounds. Various types of materials have been used for the manufacturing of these dressings. In ancient times, natural materials like honey paste, plant and animal materials and clothes have been used for the healing purpose. [11, 31] Nowadays, novel materials like synthetic bio-compatible polymers and natural polymers are being used to improve the wound healing

performance. Natural polymers having good adhesive and permeability properties like chitin and chitosan have been well investigated for wound healing. Synthetic polymers like polypeptide- poly (ethylene glycol) and copolymers have been reported to have suitable properties for wound care and burn treatment.[11, 31] The wound dressings that are prepared from synthetic polymers are generally called as advanced dressings. Various types of advanced dressings/modern dressings are now being used like hydrocolloids, hydro fibre, silicons, alginates and polyurethane etc.[31] There are other dressings like paraffin dressing, gauze and silver sulfadiazine (SSD) called as traditional dressings but they are under criticism for causing dryness at wound site and not supporting proper healing.[32] In comparison to traditional dressings, advanced dressings have own features in achieving optimal healing and in the prevention of burn infection *e.g.* hydrocolloid dressing, one of the advanced dressing contain gelatin, pectin and sodium carboxy methyl cellulose in an adhesive polymer matrix. When the matrix comes in contact with the wound they form a gel that further facilitates autolytic debridement of wounds. Polyurethane films have their own advantage as they are permeable to water vapor, oxygen and carbon dioxide but not to pathogenic bacteria and viruses and they are not supposed to be used for wounds that are likely exudating.[33]

Traditional dressings like cotton gauze, non-woven dressings and other fibers dressing are generally used to absorb exudate and allowed for a dry site, hide the wound from view and provide a barrier to contamination. These dressings are very less preferred as compared to advanced dressings which provide a wet environment that heals wounds quickly as compared to dry state.[34]

Reasons for use of advanced dressing over traditional dressings:

1. Advanced dressings provides a wet environment to wounds
2. Can be used in chronic wounds
3. High absorption rate further reduces the accumulation of exudate at the wound site and thus overcomes microbial attack
4. Do not stick to skin and therefore no pain or trauma occurs while removing the dressing
5. Protects against microbial infection
6. Proper exchange of gases leads to quick healing of wounds

Traditional dressings have a lot of limitations but they are still being used as they are low-cost dressings.[11, 35]

2.2 Ideal properties of wound and burn dressings

Dressings are generally made up of different type of material, therefore they possess different properties. Hence, selection of dressing is required while treatment of particular type of wound. Not all dressings have all properties associated with them but an 'ideal' dressing should have following properties:

1. It should maintain a moist environment around the wound
2. Permit diffusion of gases as this is required for regeneration of skin
3. Provide mechanical support
4. Help in maintaining temperature and pH
5. Low cost and commercially available
6. Should be elastic and biocompatible
7. Should be inert and not cause skin irritation
8. Easily removable and require less frequency of change
9. Help in minimizing pain and give relief to patients
10. Easy to handle
11. Protect wound from external contamination like foreign particles and microorganisms
12. Help in exudate management and prevent saturation of dressing from the external environment

It has been reported in several studies that wound healing generally takes place faster in moist environment *e.g.* provided by hydrogel dressings as compared to gauze dressings.[11, 35-36]

2.3 Types of wound and burn dressings

There are basically various types of wound and burn dressings. Some are used for short-term application and some are used for long-term application. They can be further subdivided on the basis of application like partial thickness until healing occurs and full thickness wounds until autografting.[37]

Dressings can be categorized in many ways but the

most preferred dressing classification is based on the nature of the material as conventional, biological and synthetic dressings. They are sub-categorized as primary dressings, secondary dressings and island dressings.[11, 38]

Primary dressing
Dressings that are used directly and comes in physical contact with injured skin.

Secondary dressing
These are the dressings that are used to cover the primary dressings.

Island Dressing
These are the dressings that are made up of a central absorbent core surrounded by an adhesive portion.[11]

2.3.1 Advanced dressings
The advanced dressings have been named according to the materials from which they are produced including like hydrocolloids, alginates and hydrogels etc.[39]

2.3.1.1 Impregnated gauze
These are the dressings that are non-adherent and moderately occlusive. Gauze dressings are impregnated with substances such as petroleum, iodine, bismuth and zinc *e.g.* Paraffin Gauze.[11, 40]

2.3.1.2 Transparent film dressings
These are thin flexible transparent sheets with the adhesive back, made up of polyurethane or co-polyester. Film dressings can be used as primary or secondary dressings and also as an outer layer in foams, hydrocolloids, composite and hydrogel dressings. Film dressing is permeable to water vapor, oxygen and carbon dioxide but impermeable to bacteria and water.[11, 41]
They have the advantage that they retain moisture at the wound site and also promote autolytic debridement. Film dressings can be used to cover sutures following surgery. They have the limitation of being non-absorbable and cannot be used in wounds with excessive exudates. Moreover, they are prone to bacterial growth because of lack of adequate drainage.

2.3.1.3 Foam dressings
Foam dressings are made up of a polyurethane base and are permeable to both gases and water vapour. Foam films help in reducing the risk of bacterial contamination. It works incredibly well for wounds of varying degrees of severity, as well as for injuries that exhibit odours. It absorbs exudates from the wound's surface, creating an environment that promotes faster healing. Their water vapor permeation property helps in keeping the area moist, promoting faster healing and prevents bacteria from entering the affected area. These dressings come in various sizes and shapes as well as in a range of adhesive and non-adhesive options *e.g.* Allevyn (Smith & Nephew), Biatain (Coloplast), Mepilex/ Mepilex Border (Molnlycke), Tegaderm foam (3M). It limits its use in wounds that dry out if there is no or too little exudate to be absorbed.

III. RESULTS AND DISCUSSIONS

3.1 Regulatory status of wound and burn dressings in India
Prior to 2018, India categorized these types of dressings as drug and thus regulated as per The Drug and Cosmetic Act, 1940. The dressings that are already approved in other countries are directly eligible for sale and distribution in India.[73] Recently, the new Medical Devices Rules, 2017 has been released by the Ministry of Health and Family Welfare in Gazette of India, Extraordinary Part II, section 3, subsection (i), vide notification no G.S.R. 983(E), implemented since 01 January 2018.[74]

Table: 3 Types of advanced wound care and burn dressings

Type of dressing	Examples/ product brand names	Components	Intended use	References
Advanced wound dressings:				
Foam dressings	Biatain, Tegaderm, Restore, Optifoam, Mepilex, PolyMem, Cura form (3M)	Polymers, often polyurethane	For use beneath compression stockings, for patients with venous leg ulcers	48-50
Hydrocolloid dressings	Biopad, Tegasorb, Comfeel, Hydrocoll, Varihesive E, Medihoney tube (Coloplast/Sween)	Adhesive, absorbent, and elastomeric components, carboxymethyl cellulose	Intended for use on light-to-moderate exuding, acute or chronic partial- or full-thickness wounds	48-50
Film dressings	3M Tegaderm, Pro-clude, Polyskin II, ProCyte film (proCyte)	Single thin transparent sheet of polyurethane coated on one side with an adhesive	Superficial wounds with little exudate, secondary dressing to attach a primary absorbent dressing	48-50
Hydrogel	Aquasite, ReliaMed, Anasept, Flex derm, Nu-Gel (Dow Hickam, Johnson &Johnson)	Three-dimensional networks of cross-linked hydrophilic polymers	Used to retain the gel in shallow wounds	
Alginate dressings	Bioguard Roll gauze, Kerlix AMD, Algicel, Melgisorb (Kendall)	Calcium or calcium-sodium salts of natural polysaccharides	For moist, moderate-to-heavy exuding wounds	48-49,51
Collagen	Prisma, Promogran, Stimulen (Systagenix)	Collagen	Wounds with minimal, moderate or heavy drainage	48-49,51
Therapy device:				
Negative pressure wound therapy (NPWT)				
Conventional NPWT	Vacuum Assisted Closure (VAC) therapy, Vista Versatile (Boehringer Wound Systems LLC), Engenex®	Consist of three components: porous non adhesive packing material, occlusive seal, air tight container system	Potential to accelerate healing process	48,52-55
Oxygen and hyperbaric oxygen equipment	OxyHeal (OxyHeal Health Group)	Hydrogel sheet containing glucose and an enzyme oxidase	Stimulates wound healing	48,51,53
Electrical stimulation devices	POSIFECT (Biofisica LLC)	Derived from two 3-V nominal lithium coin cell batteries that deliver electric current to the wound bed	Stimulates the wound healing process	48,53,56-58
Active wound care device:				
Artificial skin and skin substitutes	Biobrane, TransCyte (Smith & Nephew)	Biosynthetic skin substitute	Provides protection from bacterial influx and mechanical coverage	51-53

Table: 4 Upcoming innovative advanced dressings

Product	Innovator/Company	Material	Clinical trial	References
Dissolvable dressing	Boston University (USA)	Hydrogel	Under trial in lab rats with second degree burns	61
Colour change dressing	University of Bath (UK)	Hydrated Agarose film	Funds granted for further trials, Plans has been developed. But trails has not yet been started.	
Fish skin dressing	Federal University of Ceara (Brazil)	Tilapia Fish Skin	Trials on-going on 56 burn patients in 2017	62
Smart bandage	MIT - USA	Hydrogel and LED indicators	Under trials	63
Microlyte AG wound dressing	Imbed Biosciences (USA)	Ultrathin polymeric film with metallic silver coating	In 2017, FDA cleared MicroLyte™ Ag for use	64
Strata graft	(Stratatech Corporation, (UK)	Living tissue of human cells	Got fast track boost from USFDA	65
Omega3-rich fish skin	Keresis (USA)	Omega3-rich fish skin	Under clinical trials since 2016	66
Restorative oxygenation technology	Mednoxa (USA)	Oxygenation in skin	Received funds to develop the technology in 2017	67
Smart scar pad	Department of Rehabilitation Sciences, PolyU(China)	Pressure therapy and silicone gel	Clinical trial (2017) results showed the pads are effective	68
Wood based gel dressing	IIT Kharagpur, (India)	Unique water-based gel, wood is the main component	Under clinical trials	69

3.2 Need of quality guidelines for wound and burn dressings in India

It was estimated that there are an estimated 7 million burn injuries in India annually, of which 7,00,000 require hospital admission of which (1,40,000) are estimated to be fatal. According to the National Burns Programme data 91,000 of these deaths are of women. In cases of surgical site infection, the mortality rate resulted in 70 - 80%, where deep and extensive infection takes place during surgery. The high prevalence and death rate due to burn mandates the need for guidelines to be identified. The "WHY-5" concept was designed (Fig1) and applied to check the most common cause of death due to burn and wound injury and necessity of regulatory guidelines in India.

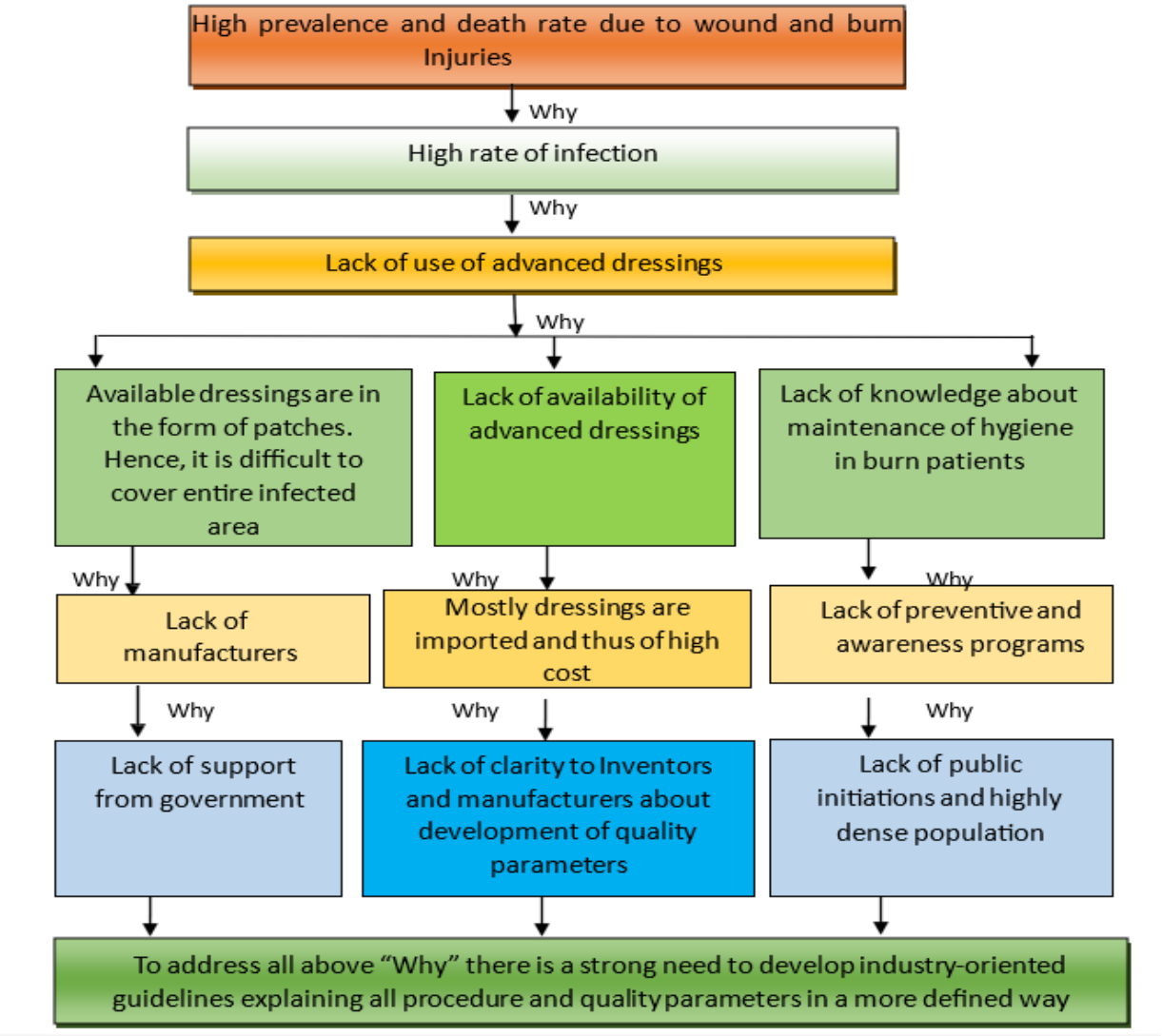

Fig.1. Need of guidelines for wound care and burn dressings

IV CONCLUSION

Burn and wound injuries are recognised as a serious health problem.[9] Various reported study details that burn and wound injuries have a major contribution in death occurring each year.[10] According to the WHO every year more than 3, 00,000 individuals died of fire-related burns and 95% of these deaths occurred in low and middle-income countries.[2] Despite having recent advancement in medical sciences the infection caused during the injury is still uncontrolled. For the successful management of burn injuries and to prevent death and deformity following burns, the systemic study of death reasons following burns and wounds has

not yet been carried out so far. Therefore, an attempt has been undertaken with a view to fill up the lacuna in regard to knowledge about burns and associated problems.

The present study offers an overview of the significance of regulatory guidelines for marketing authorization of advanced dressings for wound and burn care in India. It is important to note that burn is a serious hazard and prone to infections that can finally lead to the death of the patient. Deaths due to burn are a major public health problem in a developing country like India.[3-4] Moreover, poor sanitation of burn care centers further aggravates the situation.

One of the major causes behind this is the quality and cost of advanced dressings that are being marketed in India. These are either imported or manufacturers trying to get it approved in EU/US. Further maintaining their standards related to infrastructure, approval fee, renewals finally led to increased cost of the product. India is lacking behind of their own quality regulatory standards for advanced dressings.

Hence, the treatment becomes further very costly as the dressings need to be changed regularly. This makes the purchase of such dressings non-affordable. Ultimately, this may lead to serious infection or death of the patient. Despite such alarming situation that occurs not due to the burn but due to the costly therapy. So, there is an urgent need for the development of advanced dressings without compromising its quality which is totally ignored by the Indian regulatory bodies.

Keeping all the facts, the aim of the present study is to develop quality regulatory guidelines for advanced wound care and burn dressings.

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