

Evaluation of Lyme Disease

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Abstract

Lyme disease is a rapidly spreading infectious disease that is widespread in large parts of temperate Eurasia and North America. About 80% of patients have an erythema migrans rash, which can look like the traditional target bull's-eye lesion or unrelated lesions. This rash is linked to early infection and is present in a variety of patients. Methods. The general public's capacity to recognise different erythema migrans manifestations from non-Lyme rashes was tested through a survey. By N-deacetylating chitin with a strong alkali, chitosan, a non-toxic, biocompatible, and biodegradable polymer, is created. As a bilayer skin-regenerating template, chitosan can serve as a scaffold for regeneration. Integra is a two-layer skin regeneration system made of a crosslinked fibre matrix that serves as a scaffold for renewing dermal skin cells. The "gold standard" for short-term treatment of clean burn wounds is human skin allografts (HSAs). Objectives. This study aimed to evaluate the in-vivo, preclinical biocompatibility of the Integra, HSA, and Chitosan skin-regenerating templates (SRT). Methods. To implant test materials, paravertebral subcutaneous niches were developed. After 4, 7, 14, 21, and 28 days, implants were removed.

Keywords: Biodegradable polymer; Erythema

Introduction

A significant source of infection in endemic areas of North America and Eurasia, Lyme disease (LD), which is brought on by the tick-borne spirochete *Borrelia burgdorferi*, has a strong seasonal pattern, with the majority of cases occurring from May through August. In North America, more than 90% of cases are reported from the East Coast of the United States, however considerable numbers of cases are also documented from the upper Midwest of the United States, several regions of Canada, and the West Coast [1]. The United Kingdom, Germany, Norway, and other temperate nations have all documented incidences in Eurasia. At least 80% of people with LD will develop erythema migrans, which is the most prevalent LD symptom. A round red area that is characteristic of EM steadily grows over time, usually enlarging to a minimum of 5 cm. If left untreated for days or weeks, the localised rash that develops three to thirty days following an infected tick bite will go away naturally. Although it has been shown that EM can present in a variety of ways, the typical "target" shaped EM is the most well-known in the literature and is most frequently seen on public health materials. In reality, only 20% of EM patients experience a traditional target EM, with the remainder of cases lacking the core clearing or ring-within-a-ring pattern [2].

In many regions of the world, including temperate Eurasia and North America, LD is an infectious disease that is on the rise. LD is the third most prevalent infectious illness to be reported in the Northeast and Mid-Atlantic regions of the US and the most frequently reported vector-borne disease overall. As a result, many individuals are concerned about LD's impact on public health, particularly in the periurban residential areas of the northeast and the Mid-Atlantic [3]. However, a review of the published LD research shows that the EM rash of LD is both under- and overdiagnosed. A research also revealed that when shown both EM and other rashes typical of an ambulatory population, up to 72% of physicians questioned were unable to accurately identify the EM accompanying LD.

For many years, fundamental research has been drawn to the allure of using skin substitutes to promote early burn wound closure or to treat chronic wounds. There isn't a widely used product that possesses all of the required features, despite the fact that many products have been launched to the market for wound treatment. A skin substitute must perform similarly to actual skin while causing the least amount

of inflammation possible [4]. A substance that improves the function of the epidermal barrier and is absorbed into the healing wound is needed for wound closure. The substance should also improve the conditions for epidermal renewal and act as a barrier against infection and water loss. Its functional and structural properties should closely resemble those of autograft skin in order for it to be a successful skin substitute. Additionally, it must be pliable, light-weight, odourless, and microorganism-impervious. In order to allow exudates to leave the wound, the material should be adequately permeable to water vapour [5]. As the material restores the skin's normal function, it would also be advantageous for it to be transparent, hemostatic, and biodegradable. Nothing that comes close to the properties of autogenous material has been developed as a substitute or replacement for the patient's own skin up to this point.

A naturally occurring and widely accessible carbohydrate, chitin is derived from the exoskeleton of crustaceans. It is a biodegradable, biocompatible, and nontoxic polymer. Chitosan can also form films and is employed in the creation of film dosage forms and medication delivery systems. Additionally, it exhibits hemostatic properties and has been suggested for use as a topical treatment in tissue repair [6]. Additionally, chitosan has been demonstrated to have antibacterial, haemostatic, fungistatic, antitumoral, and anticholesteremic effects. Due to the numerous ways in which its biological, physical, and chemical properties can be manipulated and altered under benign circumstances, chitosan is a common choice as a tissue support material.

The synthetic skin substitute Integra artificial skin, created for use in burn patients, is currently the most generally accepted [7]. A silicone membrane that performs the function of the epidermis is coated on one side of the bilaminar structure of Integra, which is made

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of crosslinked bovine collagen and glycosaminoglycan. The hole size has been created to enable the migration of fibroblasts and endothelial cells from the patient. Fibroblasts, macrophages, lymphocytes, and capillaries originating from the wound bed are infiltrated into the collagen dermal replacement layer using it as a matrix. The dermal layer of Integra is destroyed concurrently with the fibroblasts' deposition of an endogenous collagen matrix as the healing process advances [8]. The temporary silicone layer is removed after the dermal layer has vascularized sufficiently and donor autograft tissue is available.

Although Integra has several benefits, it is also claimed to have a steep learning curve and significant first failure rates. Integra has the advantages of enhanced elasticity and cosmesis over ultra-thin split-skin grafts and lower donor-site morbidity than standard-thickness split-skin grafts. Human skin allograft has been utilised in wound covering for as long as autogenic skin transplantation has been practised. Reverdin also spoke about allogenic transplantation when he reported on the first autologous skin transplant in 1869 [9]. Menzel noted in 1882 that after being covered in cadaver skin, burn wounds healed more quickly. When smallpox was spread from one severed limb to four patients through skin transplantation, the first side effects from cadaver skin transplantation were also documented in 1882. It has also been demonstrated that the recipient bed's granulation tissue can be enhanced and prepared with human skin allograft (HSA). The wound bed was discovered to be more suitable for autografting by the investigators. Improved fibroblastic and capillary ingrowth was said to be the cause of this. By getting encased in recipient epidermal cells, some allograft dermis fragments were integrated into the recipient tissue. Frozen skin from an allograft seems to desquamate from the recipient skin without eliciting a strong cellular immune response. The most effective treatment for severe burn wounds is human skin allograft [10]. HSA costs little money, is simple to use, and provides a wide range of advantages. Today, it is employed for the management of nonburn wounds because it has withstood the test of time. It has also been demonstrated that the recipient bed's granulation tissue can be enhanced and prepared with human skin allograft (HSA) [11]. The wound bed was discovered to be more suitable for autografting by the investigators. Improved fibroblastic and capillary ingrowth was said to be the cause of this. By getting encased in recipient epidermal cells, some allograft dermis fragments were integrated into the recipient tissue [12]. Frozen skin from an allograft seems to desquamate from the recipient skin without eliciting a strong cellular immune response. The most effective treatment for severe burn wounds is human skin allograft. HSA costs little money, is simple to use, and provides a wide range of advantages [13]. Today, it is employed for the management of nonburn wounds because it has withstood the test of time.

Material and Methods

Instrument Development

A study of the literature was done to find papers on EM and accounts of EM being misdiagnosed as LD in order to create the LD rash survey. In addition, when selecting instances of both classic target and nonclassic EM, professional advice from established authority in the field was sought out. The survey covered EMs as well as non-Lyme lesions. The chance of LD may then be determined, along with which non-Lyme lesions might cause an incorrect self-diagnosis of LD and which EMs are most likely to alert a potential surveyor to such a possibility.

Skin Substitutes Used

The SIRIM Advanced Material Research Centre created the

chitosan SRT that was used in this work. It was composed of an outer layer of film and an inner layer of porous sponge. It is believed that this structure can conceal wounds and promote the growth of new skin. The exterior film layer serves as a barrier to ward off bacterial invasion and regulate water loss, while the inner porous sponge layer serves as a template for the growth of cells and capillaries. With a molecular weight (M_v) of 6 105 daltons and an acetylation level of 89%, the chitosan was of pharmaceutical quality. A 2% (w/v) chitosan solution was created by dissolving the chitosan in 1% (v/v) acetic acid [14].

Histopathologic Analysis

After being longitudinally cut, the tissues were submitted for tissue processing in accordance with industry standards. Each tissue block yielded six histological sections. A light microscope was used to view each segment after it had been stained with Hematoxylin and Eosin (H&E) (X400). Recorded information included the quantity of inflammatory cells, any signs of angiogenesis, the number of granuloma and large cells, and the depth of infiltration of the surrounding tissue.

Results

Regardless of the type of lesion, there was a lot of uncertainty in the poll. The uncertainty rate for the traditional target EM was 18.1%, but it was 43.8% for the vesiculopustular EM, 44.0% for the consistently red EM, 40.5% for the dispersed EM, and 47.1% for the blue-purple EM. Among those rashes not brought on by LD, a large percentage also exhibited doubt. There was doubt regarding the small tick bite reaction (51.1%), the *Staphylococcus aureus* rash (48.5%), the hand, foot, and mouth rash (37.8%), the attached tick's rapid skin reaction (43.5%), the poison ivy rash (37.9%), the shingles rash (39.6%), and the cellulitis rash (47.6%). HSA, on the other hand, caused a more significant inflammatory response. At day 4, there were 2.9 au of inflammatory cells, and by days 7 and 14, there were 4.8 au of inflammatory cells. At day 21 and day 28, the amount of inflammation steadily decreased to 2.1 au and 1.1 au, respectively. Additionally, HSA did not exhibit a protracted or excessive inflammatory response. At day 28, there was a statistically significant difference in the levels of inflammatory cells between Chitosan SRT and HSA at days 4, 7, 14, and 28. Angiogenesis in chitosan SRT gradually decreased to 4.0 au at day 7 before plateauing at 2.0 au moving forward. By day 7, the angiogenesis around Integra samples has decreased from 4.8 to 2.1.

Discussion

Although LD is the most widespread vector-borne disease in the United States and early treatment is linked to better results, it's critical that the general public is informed about LD and knows how to spot the infection's earliest symptoms. Without understanding of the EM rash, the most typical LD symptom, it is doubtful that people will recognise the rash and seek out the proper medical attention. The purpose of the current survey study was to find out whether a convenience sample of people who visited a website for LD information could correctly distinguish between the classic and nonclassic rashes of LD and rashes caused by other non-Lyme skin disorders.

Overall, the findings suggest that most survey respondents (73%) were able to recognise the traditional. These people might seek out services needlessly when there is a false-positive error (i.e., when they believe a rash is EM when it is not), especially if the finding from this study is true and the most typical misidentification is for a benign, uninfected tick bite. The second option—seeking assistance when it is not necessary—is better for patients and the general public's health since it results in better treatment being provided. But by needlessly

seeking care, these people have added to the expense of those services and perhaps taken resources away from those who might have benefited from them more quickly. The poll's findings confirm the necessity for expanded efforts to inform the general population, in particular those living in endemic regions of the nation, about the many EM symptoms. It is advised that as research advances, future studies use techniques for gathering demographic data, including the geographic location of respondents. This would make it possible to do geographic analysis to see whether or not people living in Lyme endemic regions are more or less aware of the various EM symptoms. Additionally, it's crucial to ask each person about their chance of consulting a doctor if they develop a specific rash.

Conclusion

Public health education campaigns can be established and targeted to solve the shortcomings with more understanding of the general public's proficiency in correctly detecting EM and seeking out services for medical care [15]. Despite the fact that this poll did not specifically target medical professionals, there is some evidence to show that doctors have difficulty appropriately identifying the EM that is accompanied by LD. Investigating the ability of health professionals to correctly recognise EM would be another subject for future research. Those results might be used to inform the development of training programmes for front-line healthcare professionals in Lyme-endemic regions. These programmes would help these professionals become more familiar with the various EM manifestations. We discovered that Chitosan SRT, Integra, and HSA did not cause severe and protracted inflammatory responses [16]. All three test substances were well tolerated in this animal model and none of them induced a negative foreign body reaction. There is evidence of biocompatibility for all three skin substitutes.

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Conflicts of Interest

The author has no known conflicts of interest associated with this paper.

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