Cellular technologies in the treatment of scalded patients: Literature review

Ten Dmitriy Olegovich*
Fergana Medical Institute of Public Health, Ferghana, Uzbekistan
*Corresponding author

Abstract---Over the past decades, new methods of treating burn wounds based on biotechnology have appeared. The review presents the main materials for the treatment of burns, which were created using tissue engineering - biological wound dressings and skin substitutes.

Keywords---wound dressings, cellular technologies, thermal burns, skin substitutes, biotechnology.

Introduction

Since the creation of the emergency medicine service, one of the important areas of this system has been the combustiology service (Alekseev, 2015; Alekseev, 2010; Almazov, 2015). Since one of the most common types of injuries in peacetime in many countries is a burn injury. Thus, according to WHO, from all types of peacetime injuries, thermal injuries account for 6%, while the number of victims is increasing every year (Alekseev, 2010). A special place in the problem of combustiology is occupied by the choice of therapeutic tactics for burn injury in the acute period, which consists in assessing the timing and volume of this assistance, especially when signs of the development of a burn disease appear. According to various authors, the reason for this is accompanied by disorders of the vital functions of the body, the complexity of treatment, a high percentage of disability and mortality (Abugaliev, 2015; Akopyan, 2006; Barinov, 2003). Is a clinical manifestation that is severe and high. There is an acute issue of local treatment of burns, which depend on an objective assessment of the area of burns and the depth of damage, the stage of the wound process, as well as the severity of the condition of the victims, which makes it easier to choose the right treatment tactics. This once again emphasizes the relevance of the problem of thermal damage (Alekseev, 2012; Alekseev, 2009; Ankin, 2004).
Materials and Methods

Thanks to the progress of surgery and pharmacology, cell technologies are increasingly used in modern combustiology (Alekseev, 2012; Saver, 2006; Kolokolchikova, 2011; Bowe, 2018; Haslik, 007), injuries, the most interesting are the world developments of temporary biological coatings using cellular technologies. In many Considering the severity of the research engineering design. The selection of components for this kind of coating is carried out depending on the composition and condition of the wound surface, as well as the tasks set. The composition of the complex wound dressing may include keratinocytes, fibroblasts, collagen matrix, cell growth factors (Gryazin, 2004; Matveev, 2013; Revenko, 2004; Bowe, 2018). Modern developments in cellular technologies and wound dressings are moving towards the creation of three-dimensional scaffold structures with a specific set of. These technologies are certainly promising, but combustiological practice as allofibroblasts has not yet been widely used.

The traditional surgical approach with a large area of deep burns, according to the authors, does not give the desired results. Therefore, cellular technologies are one of the possible directions for optimizing the wound process in the complex surgical treatment of burn patients with the treatment of thermal lesions, especially with a shortage of donor resources. Autokeratinocytes as a morphological substrate are most suitable for wound surface repair, however, this is a rather expensive method for wide clinical use and requires special conditions for transplantation and wound preparation. Cultured allofibroblasts are part of multicomponent wound dressing complexes and are increasingly used in the treatment of wound defects of various origins (Lapotko, 2001; Gusak, 2000; Yurkevich, 2012; Bottcher-Haberzeth S. 2010). Allogeneic fibroblast culture transplantation is used as a method of preparing wounds for autodermal transplantation and stimulating delayed reparative processes in severe thermal injury. Basically, allofibroblast transplantation, according to the authors, is used for temporary wound closure after necrectomy. Conducted clinical and laboratory studies have proven the effectiveness of allofibroblast culture in the treatment of extensive deep burns. Allofibroblasts transplanted onto a burn wound provide a faster change in the cytological pattern in a burn wound, which is manifested by the transition of a degenerative and inflammatory type of cytogram to an inflammatory-regenerative one (Gilevich, 2017; Gusak, 2000; Markelova, 2012; Nagaychuk, 2005; Smolyaninov, 2013; Burd, 2002). Thanks to the bank of cell cultures in the leading burn centers, it is possible to create a large number of biological wound coverings in a relatively short time (Aleinik, 2015; Dmitriev, 2008; Dantlez, 2007). For example, in the laboratory of tissue and cell cultivation of INVH, 100 days is possible for the preparation of doses of allofibroblasts. In conditions of mass influx of victims from extensive burns, this figure can significantly optimize surgical treatment. Some centers use biosynthetic burn wound closures such as Integra, which consist of collagen and silicone film. It also contains a suspension of keratinocytes and allofibroblasts. In the presence of a significant amount of wound discharge, long-term use of film wound dressings is impossible, in addition, such wound dressings are quite expensive.
Results and Discussions

The beginning of the era of biotechnology in the creation of wound coverings based on living cells was the work of Rheinwald J. (1975). Technologies for culturing human cells have improved every year. The high cost of cultivating keratinocytes, the sensitivity of the culture to external influences contributed to the creation of relatively cheap structures consisting of a three-dimensional collagen gel with fibroblasts (Dantez, 2007; Fu, 2009). For many years, the authors have successfully used a gel composition with cells for application to burn wounds at the rate of 5 ml per 150 cm of the wound surface. The cell product was closed with an atraumatic mesh wound dressing followed by isotonic saline dressings. During the first day, the dressings were moistened with sterile saline (Fu, 2009). Such a technique, in our opinion, is convenient for use on extensive wound surfaces, is easy to perform, and can be used with a complex relief of the wound surface. The most effective time of cultured fetal allofibroblasts, since the method is 15-20 times cheaper than the cultivation of keratinocytes (Dantez, 2007). In the works of the authors, the cost of cultiving embryonic allofibroblasts and further stages of transplantation was calculated. It has been determined that with the same clinical efficacy, the use of human embryonic fibroblasts is more appropriate for economic reasons. In addition, we found quite a lot of works devoted to the use of various combinations of mesenchymal stem and embryonic cells to modulate the wound process in a burn wound (Aoki, 2004; Burd, 2002).

Kharkov combusiologists used a culture of allofibroblasts to close wounds after early necrectomy, to stimulate reparative processes in a burn wound with their long-term existence, to combine with autodermotransplantation with a high splitting factor, which is especially important when there is a shortage of donor resources. According to the published literature data from foreign sources, the treatment of severely burned skin cells with cultured skin cells at the beginning of the development of the application technique will not always give good results (Abugaliev, 2015; Aleinik, 2015; Alekseev, 2009; Almazov, 2015; Berezenko, 2007). At the first stage, the authors performed fascial necrectomy on the injured, then a suspension of autologous keratinocytes in fibrin glue was transplanted onto the wound surfaces, and microautodermotransplantation combined with xenotransplantation of autodermal grafts was also performed. Transplantation of cell cultures ended in failure, while the combined use of cell technologies with autodermotransplantation and keyenoplasty ended with the restoration of the skin (Vysotsky, 2004; Grigoryeva, 2012; Zinoviev, 2007). The authors of split transplantation emphasize the advantage of combinations of various methods of autodermal transplantation and xenotransplantation in the simplicity and reliability of the method. In patients with extensive burns, the most optimal option in the treatment of extensive burn wounds outside functionally important areas is autodermotransplantation with a high cleavage coefficient, a cell culture is applied to the cells of the graft, and the wound is covered with a xenograft to prevent drying out.

The use of cultured autokeratinocytes is possible only on prepared clean granulation wounds in an abacterial environment, which is possible after removal of the necrotic scab, at least after the third week of treatment and in "clean
rooms" (Zorin, 2009; Kovalevsky, 2007; Ledovskoy, 2008; Branski, 2008). Unfortunately, creating conditions for an abacterial environment in burn hospitals is quite difficult and requires significant material costs. At the same time, with a mass admission of victims with extensive burns, cell cultures will be required for several patients at once and earlier after the injury. Therefore, victims of man-made accidents and catastrophes need more accessible cell technologies. Allofibroblasts can already be used on the first day when performing early necrectomy and do not require special conditions for the patient to be in the intensive care unit. The only condition: do not use an antiseptic solution on the transplantation site and moisten the bandage with saline every 3-4 hours.

Many works emphasize that the transplantation of cultured allogeneic fibroblasts on borderline burns improves the clinical indicators of the course of the wound process, reduces the time of epithelialization of burn wounds (Bigunyak, 2007; Ostrovsky, 2007; Atiyeh, 2005). When conducting research, the same authors prove that allogeneic fibroblasts in a burn wound contribute to the positive dynamics of the cytological picture, which manifests itself in a faster change in the type of cytogram from inflammatory to inflammatory-regenerative (Bigunyak, 2004; Smolyaninov, 2013). This fact allows you to quickly prepare a burn wound for autodermotransplantation after removal of the necrotic scab and achieve maximum engraftment of the cytological graft.

Modern cellular technologies are needed to influence the course of wound healing in burn patients with combined and associated trauma, but there are few publications on this issue in the literature (Zinoviev, 2016; Zhernov, 2013). The volume of surgical intervention and the timing of the implementation are quite different for each author. This is explained by the fact that the authors et al., The volume of surgical intervention solves individual problems at each stage of treatment, from closing burn wounds after early necrectomy, and to stimulate the processes of epithelialization of burn wounds. However, at the present stage of development of residual combustiology, it is impossible to imagine the treatment of extensive burn wounds without the use of biological equivalents.

**Conclusion**

Thus, the literature data indicate that the arsenal of specialized care for patients with skin burns in recent years, using new effective methods, the use of which allows to achieve an increase in the anti-stress, adaptive, regenerative capabilities of the body, reduce the risk of infection or accelerate secession, significantly improve the replenishment of complex therapy, the course of the wound process and reduce the time for complete recovery of the skin. According to the literature, the application of cellular technologies significantly expand the possibilities of influencing the course of the wound process in a burn wound, however, the question of choosing the optimal method of treatment remains open and requires burn wounds, to date, further study.
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