The extracellular matrix (ECM) is a network of macromolecules that includes structural proteins, enzymes and soluble factors, which interact with surrounding cells, in order to maintain tissue structure and homeostasis.

The properties of regenerating agent therapy (RGTA) permit the reconstruction of the ECM, restoring biochemical and structural functions, and facilitating the processes of tissue regeneration and repair.

Preclinical studies demonstrate the efficacy of RGTA in acute or chronic oral ulcers, oral mucositis, as well as its potential as a skin protector following radiotherapy [1,2]. RGTA reduced bone loss to a hamster chronic periodontitis, leading to the restoration of alveolar bone and the regeneration of a periodontal ligament [3-5].

RGTA is already used in clinics in two commercially available products (OTR4120, alpha-1-6 polycarboxyl-methylsulfate glucose), CACIPLIQ for the treatment of chronic skin lesions, and CACICOL for the treatment of corneal lesions.

The modern regenerating agent therapy represents the first ophthalmic matrixial therapy and an alternative to what usually would be an ophthalmic surgical case. The use of Cacicol® is beneficial in a wide variety of corneal lesions. The evidence of corneal healing through RGTA is already used in clinics in two commercially available products (OTR4120, alpha-1-6 polycarboxyl-methylsulfate glucose), CACIPLIQ for the treatment of chronic skin lesions, and CACICOL for the treatment of corneal lesions.

Two cases of painful ocular surface lesions in which we achieved successful results only after the use of a topical regenerating agent, Cacicol®. Written informed consent was obtained from these two patients for the treatment and publication of this report.

The first case was about a 31-year-old man with corneal chemical burn with an unknown substance (spray). Clinically, there was a central corneal ulcer within the superficial stroma.
The second case was a 35-year-old man, contact lens wearer who appeared in the ophthalmology department with ocular pain, photophobia and decreased vision, symptoms secondary to a long trip which instituted poor personal hygiene. The visual acuity was very low, the patient’s visual acuity was only hand movements. The biomicroscopic evaluation demonstrated a profound corneal ulcer with a risk of perforation. The pathogen of staphylococcus into the patients conjunctival secretions was identified.

Results and discussions

To the first patient the conventional treatment did not lead to the expected results, the epithelialisation was slow (3 weeks) and the stromal defect persisted. The use of a tissue regenerating agent administration - Cacicol®, one drop/week, lead to the remodeling of the cornea and to restitutio ad integrum. The visual acuity progressed from 0.1 at the beginning of treatment, to 1.0 after the cessation of treatment.

To the second patient the local treatment administered was Netilmicin for 10 days, hourly for 48 hours and then every 3 hours for 7 days. Because there were stagnant secretions, the treatment was switched to Vigamox for 7 days, Tobrex ointment and Indocollyr for the inflammation.

When the secretions disappeared, re-epithelisants like Thealoz duo and Corneregel were administered. The scar was severe, that is why the RGTAs were administered, one drop of Cacicol® per week for 5 weeks. The result was total epithelialization after 2 weeks. Figures 1 and 2 demonstrate the favorable evolution of the scar.

There was insignificant evolution to conventional treatment in these cases, so, the therapeutic alternative to favor and ameliorate the scar was the Cacicol® matrix therapy. The chronic inflammatory component was associated with the lesion. Pain relief was alleviated after 2 weeks under the new RGTAs treatment with the restoration of the extracellular matrix which surrounds the sensitive nerve endings onto the cornea. The restitutio ad integrum was gained at the end of the therapy in the first case. In the second case, the improvement in visual acuity was 80% and the patient did not have any pain. The superior and paracentral parts of the cornea remain leukemic, under supervision.

The new therapeutic class of RGTA is a new and different promising healing agent from any product on the current market and their innovation consist in creating a new micro-environment because of their content in heparin-sulphates [8].

The idea of recreating a new micro-environment due to the heparin-sulphates is a real innovation. RGTA regeneration agents replace the degraded glycosaminoglycans such as heparin-sulphates and will furthermore settle on the matrix proteins and are resistant to the remodeling enzymes because they are not destroyed by proteolytic enzymes such as heparinases, thus providing protection for the stromal extracellular matrix environment and other components involved in tissue healin [9].

The RGTA attached to the matrix proteins will allow the growth factors and cytokines to act on the injured area leading to the restoration of the matrix comparable to physiological conditions.

Heparin-sulphate and their analogues obstruct in vivo the proteolytic enzymes like elastase, plasmin, cathepsin G [10,11].

RGTA have the potential of healing chronic wound problems of the entire body [12]. In order to promote epithelial wound healing, they contour a bio-skeleton which will activate cell adhesion and will be ready for the adhesion of growth factors onto the surface. RGTA job is to link different structural proteins such as collagen, elastin and fibronecin, thus assisting in the formation of the corneal matrix architectonics and can also restore the intercellular communication for the normal tissue regeneration, thus providing a strong mechanical protection for degradation.

By this way, restoration of ECM (stromal extracellular matrix) scaffolding properties and process take place and the RGTA reestablish the micro-environment.

Thus, this bio-skeleton being made, the micro-environment is just perfect to promote the healing through re-epithelialization and to secure the stromal extracellular matrix plan which will alleviate the pain. An anti-fibrotic response is done by decreasing the synthesis of collagen type III, decreasing the tissue edema and inflammation and reforming the collagen reorganization [13].

Oral mucositis is a complication of cancer treatment. Chemotherapy and radiation treatment cause oral mucosal atrophy and ulcerations, increasing the risk of infection and affecting the quality of life. RGTA prevented mucositis in 50% of treated hamsters and significantly reduced the mean lesion volume in the remaining animals [2].

Conclusions

The conventional treatment given in both cases did not lead to the expected results, which warranted new RGTA treatment, Cacicol®, which was introduced and the improvement of the lesion was immediate and evident through the alleviation of the pain and the evolution of the scar. Cacicol® was very well tolerated, did not have any local or general allergic reaction, nor side effects. The proteolitic enzymes like elastase, plasmin, cathepsin were not destroyed and further settle on the matrix proteins and are resistant to the remodeling enzymes because they are not destroyed by proteolytic enzymes such as heparinases, thus providing protection for the stromal extracellular matrix environment and other components involved in tissue healin [9].

RGTA controls ocular surface inflammation and enhances corneal healing. As a result, RGTA are the best choice to use for long lasting corneal lesions [18-21].
Studies demonstrate that RGTA matrix based therapy is an efficacious and non-invasive approach to treat various injuries affecting the cornea, muscle injuries, acute or chronic ulcers, oral mucositis, reduced bone loss in chronic periodontitis [18-25].

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