

Efficiency assessment of topical fetal human cord blood serum on alkaline corneal epithelial defects healing in a rabbit model.

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Abstract: One of the important tasks of the cornea, creating a normal vision by reflection light rays on the lens and retina. Defects in this organ can occur by many factors such as trauma, infections and chemical agents. Alkali substances are one of important factor that causes serious damage for cornea. In this situation rapid and effective treatment is important to obtain the function of this organ. This study has been planned and implemented to investigate the efficacy of fetal human umbilical cord serum on healing of alkali corneal damage in rabbit model. An experimental study design was conducted on 32 eyes (16 rabbit) that assigned by simple random sampling in two intervention and control group. In intervention group, human fetal umbilical cord blood serum and in control group artificial tear drops use 4 times a day for total 14 day. Slit lamp examination was performed daily and result register for each rabbit in record sheet. Then data enter in SPSS software version 11.5 and analyzed by repeated measurement method. Statistics test was F statistics and considered Significance level was 0.05. The average wound healing rate in the intervention group based on of defect diameter was 0.77(SD= 0.013) mm/day and in the control group was 0.73 (SD 0.018) mm/day. This study showed that fetal human cord blood serum compared with artificial tears increased rate of corneal alkali wound healing in the rabbit model. More evaluation based on extracted cord blood serum was suggested. This study showed that fetal human cord blood serum compared with artificial tears increased rate of corneal alkali wound healing in the rabbit model. More evaluation based on extracted cord blood serum was suggested.

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1. Introduction

The cornea is the organ with lucid and smooth surface that conducted light array to the lens and retina. Any damage to the layers, distorted transparency and ability of its protection task (1 and 2). Defects in the corneal surface could be due to trauma, infection, inflammation, defects in the eyelid and eyelashes, deficiency in tear or reduce in sensation or due to chemical agents (3). Corneal alkali Ulceration injury is one of the most common eye damage. Symptoms based on the cause of the injury, the severity and duration of exposure can vary widely from a mild redness of the eyes to complete loss of vision (4 and 5). Any persistent injury of corneal epithelium can lead to loss of sharpness of vision (6). Cornea healing can occur by two or combination of two methods: migration of peripheral epithelial cells or development of blood vessels from the conjunctiva. Superficial small ulcers heal rapidly by the first method. However, larger or deeper ulcers often require the presence of blood vessels to supply inflammatory cells (Wikipedia). Primary principal in corneal epithelial healing is growth, differentiation of

limbos cells and infiltration of this cells to conjunctiva and corneal surface (3). this process is mediated by many proteins that facilitate migration, proliferation and limbos cell differentiation. These proteins include epithelial growth factor (EGF), fibroblastic growth factor (FGF) and platelet growth factor (PGF), which distribute on corneal surface in soluble water (7). Diagnosis of corneal ulcer is done by direct observation under magnified view of slit lamp revealing the ulcer on the cornea. Exposed corneal stroma is taken up fluorescein stain, and appears green color. This method helps in defining the margins of the corneal ulcer, and can reveal additional details of the surrounding epithelium. Accepted classical methods to help repair the defects of corneal contains: topical treatment (ocular lubricants), contact lenses - medical, laser treatment, drug treatment (botulinum toxin), Tarsoraphy, cornea brushing and corneal transplants. In recent year's use of new methods such as serum drops, amniotic membrane graft, stem cells cause in sensible progress in prognosis and correction of visual acuity of patient with corneal ulcers. yoon et al 2005, evaluated effect

of blood serum of embryonic human umbilical cords on treatment of persistent corneal epithelial damage. Blood serum and especially embryonic umbilical cord blood serum contains many growth factors that may be effective in corneal defect healing (9-12). growth factor concentration of embryonic umbilical cord blood serum is much more than blood serum. Furthermore it seems and expected that embryonic umbilical blood serum cause faster and more effective in healing of corneal ulcers.

On previous studies that conducted to evaluated treatment effect of embryonic umbilical blood serum on corneal ulcer healing, damages with vary cause and epithelial size was evaluated and by this reason the accuracy of study was decreased(8). furthermore for control of other confounder factors we decided for more controls on assessment of efficiency and precision evaluation of our study, conducted this control experimental study with fixed size epithelial effect and with restricted cause of damage and with fixed of concentration of agent and fixed of exposure duration time to alkali chemical agent in rabbit model. Because of performed study in sterile conditions and minimize role of infection in study, there was no require to prescript antibiotic eye drop.

2. Materials and methods

This randomized double blinded experimental study was carry out in spring 2010 in medical university of science of kohgilueh & boyer-ahmad province in southern part of Islamic republic of Iran after proposal accepted in research committee and obtain acceptance from ethics committee. study unit was rabbit eye and total sample size contains 32 eyes in 32 male albino rabbits, weight 2-3 kilo gram, new Zealand race (for ethic issue each eye in each rabbit). Animals tested in this study based on the ARVO statement on the use of animals in research and compliance data were used for research. Rabbit subject numbered from one to 36 and then assigned randomly in two groups, intervention and control group. 16 rabbit (16 eye) in each group. After induce sedation in rabbit subject with intramuscular ketamine injection with total dose 30 mg per kilogram, one rabbit eye was anesthesia with topical tetracaine eye drop and then alkaline corneal damage is induce by use of filter paper contains one molar concentration of alkali, with a circular damage with diameter mm on central cornea. Ulcer size was controlled with use of fluorescing dye and slit lamps by ophthalmologist. Exclusion criteria after induced corneal ulcer consist any defects in epithelial larger than 6.1 mm or smaller than 5.9 mm in diameter, perforation of corneal, infection or old scarring on the cornea. During the period of study, the rabbit eyes observed and examined for irritation, corneal or

conjunctiva infection.

To prepare serum, use of human blood serum obtained from human fetal cord blood and reserved in freeze status at 0-8 Celsius degrees. Freeze blood serum in room temperature centrifuged with 1500 cycle per minute for 20 minute. Obtain suspension diluted 20 percent and reserve in little bottle and protected from sun light and UV radiation. We use fetal human umbilical serum in intervention group and artificial tears in control group four times per day in each group. The diameter of corneal ulcers controls during the study for each rabbit daily by slit lamp for 14 day and results for each rabbit was recorded in paper sheet. Data entered in SPSS soft ware version. 11.5 and analyze by using repeated measurement method (MANOVA). significance level for interpretation considered 0.05.

3. Results

Measure the diameter of wound reveal that on the first, second and fourth day there is no Significant differences in wound size between the two groups ($p > 0.05$), but on other days were significantly difference between two groups (p-value). The average rate of wound healing based on diameter in the intervention group and the control group was estimated 0.77 mm/day (SD =0.013) and 0.73 mm/day (SD 0.018) respectively. We comprise two curves and trend of treatment in two groups (averages) for the effect of fetal cord blood serum on corneal wound healing.

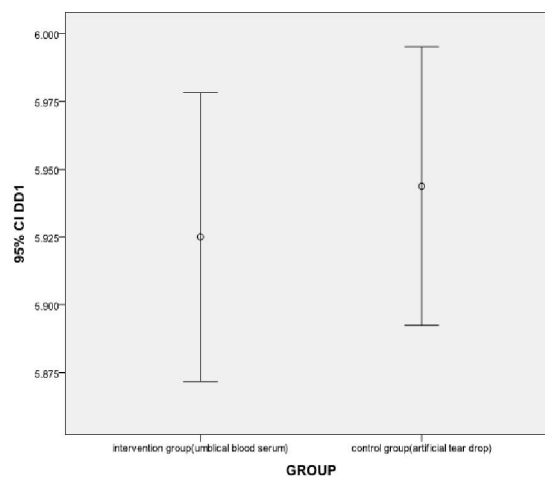


Figure 1. Graphical Comparison of corneal wound healing during the study period.

The results show meaningful difference. In intervention group the slope of the recovery curve was faster than the control group, shown in Figure 1 as a model.

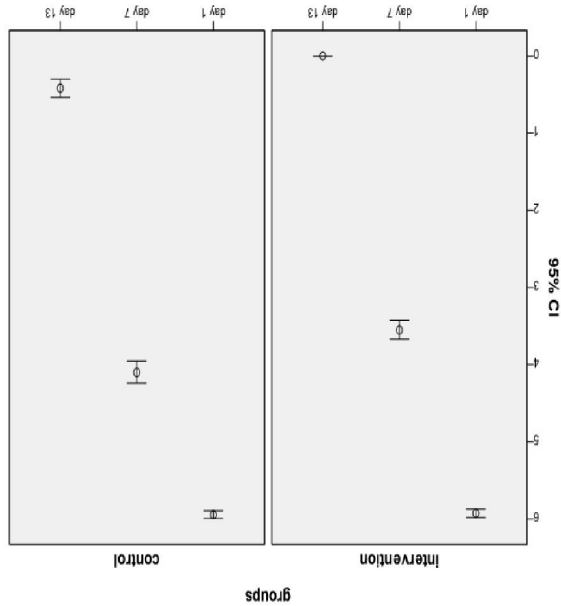


Figure 2. Error bar chart for comprise trend of treatment in first, seventh and fourth day of treatment.

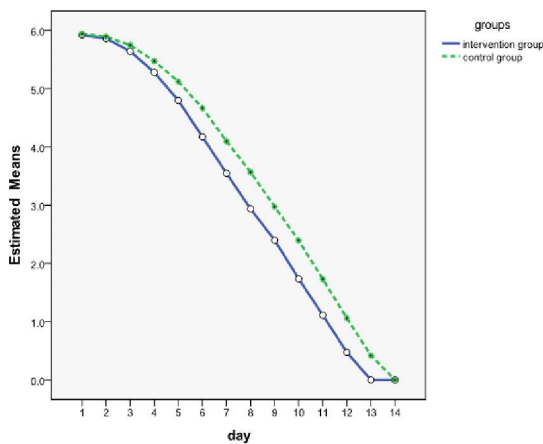


Figure 3. Trend of wound diameter in two groups.

4. Discussion and Conclusion

Because of importunacy of corneal in normal visual acuity, corneal ulcer management is permanently concerns in ophthalmology field. Alkali corneal ulcer can lead to more sever epithelial inflammation and damage than other chemical agents. This severity of inflammation could be due to Inhibit the growth of normal epithelium and can lead to fibrosis or scarring of the cornea (14).The proposes of this study was investigated effect of embryonic human umbilical cord serum on alkali corneal ulcer healing in rabbit model. Results of this study reveal that embryonic human umbilical cord serum cause rapid healing in comparison to the artificial tear drop. All corneal ulcers in intervention

group healing before 13th day after treatment without any complication. All control group corneal ulcer healing at 14th day after treatment. Youn eat al study 55 eye in 31 patients for investigate effect of umbilical serum in corneal healing and reported that all cases after 2 month have considerable recovery. They also reported that umbilical cord blood serum can use in treatment of signs and complication of dry eye syndrome and in epithelial keratopathy without any side effect.

In another study effect of human umbilical cord in treatment of persistent epithelial defect was evaluated and reported that 42.9 percent of patients relative recovery and no effects on 14.2 percent of patients.(8). Wachpaii et al 2003 conducted a randomized control clinical trial in 60 eyes with corneal ulcer and compare fetal human cord blood serum with autologe blood serum and reported that mean decrease in defect size in intervention group were significantly higher than control group that their finding are compatible with our finding(13). Shahriari et al 2008, compare effect of amniotic membrane suspension therapy, artificial tears and autologous serum in treatment of alkaline corneal ulcers. the average decrease in diameter of the wound in the intervention group is higher than amniotic membrane suspension group (5). A result of this study shows that fetal human umbilical cord blood serum can effectively and without any complications use in alkali corneal ulcer in albino news land race rabbit model. Also this study revealed that this intervention can improve healing of corneal ulcer s but this finding clinically is not considerable and need to conduct many study with extract substance in fetal umbilical blood serum for determine main factors that effect in this results.

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