

EFFECTS OF PLATELET-RICH PLASMA ON WOUND HEALING IN NASAL MUCOSA

PLATELETTEN ZENGİN PLAZMANIN NAZAL MUKOZADA YARA İYİLEŞMESİNE ETKİSİ

Bilal SARATAŞ¹, Mustafa TÜZ², Mehmet Emre SİVRİCE², Hasan YASAN², Kemal Kürşat BOZKURT³,

¹ Rhino-Laryngology and Head&Neck Surgery, Malkara State Hospital, Tekirdağ, Turkey

² Department of Oto-Rhino-Laryngology and Head&Neck Surgery, Faculty of Medicine, S.Demirel University, Isparta, Turkey

³ Department of Pathology, Faculty of Medicine, S.Demirel University, Isparta, Turkey

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Öz

Amaç

Plateletten Zengin Plazmanın nazal mukozada yara iyileşmesi üzerine olan etkilerini incelemek.

Gereç ve Yöntem

Çalışmamızda ağırlıkları 2.8-3.5 kg (ortalama 3.2 kg) ağırlığında 32 adet erkek Yeni Zelanda beyaz tavşanı kullanıldı. Sağ nazal kavitelere girilerek interdental fırça yardımı ile (brushing technique) septum, konka ve lateral nazal duvarlarında mukozal hasar oluşturuldu. Hayvanlar birinci hafta ve üçüncü hafta olmak üzere iki gruba ve bu iki grup da kontrol ve PRP olmak üzere iki alt gruba ayrıldı.

Bulgular

Histopatolojik skorlama sonuçlarına göre birinci hafta grubunda inflamasyonun şiddeti parametresinde belirgin düşüş izlendi ve bu düşüş istatistiksel olarak anlamlıydı (p=0,009). Mukozal ödem yaygınlığı, ciliyalı hücre kaybı derecesi, fibrozis yaygınlığı, goblet hücre hiperplazisi, inflamasyon yaygınlığı, konjesyon ve squamoz metaplazi açısından birinci hafta ve üçüncü hafta gruplarında istatistiksel olarak anlamlı fark saptanmadı.

Sonuç

Sonuçlarımız PRP'nin yara iyileşmesinin erken aşamalarında inflamasyonu azalttığını göstermektedir. PRP'nin nazal mukozal yara iyileşmesi üzerindeki etkilerinin anlaşılabilmesi için ileri çalışmalara ihtiyaç olduğu düşünülmektedir.

Anahtar Kelimeler: Plateletten zengin plazma, nazal mukoza, inflamasyon

Abstract

Objective

Study the effects of platelet-rich plasma (PRP) on wound healing in nasal mucosa.

Materials and Methods

Thirty two adult New Zealand white rabbit of male sex were used for this study each weighing between 2800 and 3500 grams. Mucosal damage was created by interdental brush (brushing technique). The animals were randomly distributed into two groups as first week group and third week group. This two groups were subdivided into two subgroups as control and PRP.

İletişim kurulacak yazar/Corresponding author: emresivrice@gmail.com

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Results

According to the histopathologic scoring results, in first week group inflammation severity decreases between PRP and control subgroups and this decrease was statistically significant ($p=0.009$). No statistically significant difference was observed between the other groups in terms of mucosal edema severity, loss of cilia degree between ciliary cells, fibrosis severity, goblet cell hyperplasia, inflammation severity, congestion and squamous metaplasia.

Conclusion

Our results show that PRP reduces inflammation in early stages of wound healing. We believe further more studies are needed to understand the effects of PRP on nasal mucosal wound healing.

Keywords: Platelet-rich plasma, nasal mucosa, inflammation, wound healing

Introduction

The first stage of acute wound healing is hemostasis and establishing transient wound matrix which occurs shortly after tissue damage and completed within hours. Platelets are one of the pioneer cells which plays crucial role in acute wound healing. In the first ten minutes of hemostasis, platelets secrete many proteins from the granules. These proteins bind to cells involved in the wound healing process and regulate processes such as cell proliferation, matrix formation, osteoid formation, and collagen synthesis.

PRP is an autologous product obtained from peripheral blood in vitro. PRP is used for the accelerating effect on wound healing in maxillofacial surgery, ophthalmology, neurosurgery, orthopedic surgery, plastic and reconstructive surgery and dental surgery (1).

Nasal mucosal injury is seen in many surgical procedures such as septoplasty and sinus surgery. In our research we aimed to obtain a treatment method that would enable mucosal wound healing to be faster and better, and thus to keep the complications at minimal level.

Materials and Methods

Thirty two adult New Zealand white rabbit of male sex were used for this study each weighing between 2800 and 3500 grams. Permission was obtained from Süleyman Demirel University Medical Ethic Board for all experimental methods. The animals were cared for under standardized conditions for a period of 3 weeks before surgery. They had access to pelleted food and water throughout the experiment. Rabbits were anesthetized by intraperitoneal administration of 35 mg/kg ketamine hydrochloride (Ketalar® 500 mg injectable Vial, Pfizer Inc, Turkey) and 20 mg/kg xsilazin (Alfaz-*yne*® 2 % injectable vial, Ege vet Hayvancılık San. ve Tic. Ltd. Sti. Turkey) and mucosal damage was created by interdental brush (brushing technique) on

the right nasal cavity and nasal bleeding and mucosal damage was observed with 0.9 mm nazal endoscope after mucosal damage on every animal. In the PRP subgroups, ten minutes after the mucosal damage, PRP is prepared by taking blood from the ear marginal veins of the animals and applied topically to the right nasal cavities. The animals were randomly distributed into two groups as first week group and third week group. This two groups were subdivided into two subgroups as control and PRP. No difference was observed on weight and health conditions in groups during our study. Animal numbers in each subgroup was decided by Ethic Board. No other drug or agent was administered during study.

First and second group animals (equal numbers of rabbits) were sacrificed by administering high-dose anesthetic agent (Ketalar® and Alsazin®) respectively on seventh and twenty first days of the study. The head was removed, soft tissue trimmed, and the skull placed in 10% neutral buffered formalin. After formalin fixation, a tissue specimen comprised of the sinuses and nasal septum was prepared. The tissue specimens were decalcified in decalcifying solution (Christensen's fluid-equal volumes of 40% formic acid and 6.8% sodium formiate) until softened at room temperature. The sinuses and nasal septum were dissected in coronal plane, with the intervals of 4 mm, from choanae to nares. Then, the removed segments of tissues were embedded in paraffin. Light microscopy slides were prepared from the specimens stained with Hematoxylin-Eosine and Masson's trichrome. The slides were labelled randomly by the investigator and presented to the pathologist for interpretation. The slides were evaluated in blinded fashion and differentiated according to histopathologic findings. The histopathologic examination was performed, blindly, regarding mucosal edema severity, loss of cilia degree between ciliary cells, fibrosis severity, goblet cell hyperplasia, inflammation severity, congestion and squamous metaplasia by light microscopy (Nikon Optiphod-B, Japan). The scoring for the histopathologic

examination were graded semiquantitatively as grade 0 (normal), grade 1 (mild), grade 2 (moderate) and grade 3 (severe) (2).

Statistics

Statistical analysis was performed using SPSS version 21.0. For comparison between histopathologic parameters we used Kruskal Wallis test and p values <0.05 were considered statistically significant.

Results

According to the histopathologic scoring results, in first week group statistically significant difference was observed in term of inflammation severity between PRP and control subgroups ($p=0.009$). Figure 1 shows reduced inflammation in PRP subgroup and Figure 2 shows severe inflammation in control subgroup. Table 1 shows results of inflammation severity in the first week group. No statistically significant difference was observed between the other groups in terms of mucosal edema severity, loss of cilia degree between ciliary cells fibrosis severity, goblet cell hyperplasia, congestion and squamous metaplasia in first week group. In third week group no statistically significant

difference was observed between the other groups in terms of mucosal edema severity, loss of cilia degree between ciliary cells fibrosis severity, goblet cell hyperplasia, congestion, squamous metaplasia and inflammation severity.

Discussion

Cellular growth factors are signal proteins which controls wound healing and tissue repair. It has been shown that growth factors enhance wound healing by increasing angiogenesis, epithelialization, granulation tissue formation, and bone maturation when applied topically to the wound (3-5). PRP is an autologous product obtained from peripheral blood in vitro. The proteins and growth factors identified in PRP are TGF- β , VEGF, PDGF, EGF, IGF, platelet factor 4 (PF-4), interleukin-1 (IL-1), platelet derived angiogenesis factor (PDAF), epithelial cell growth factor, osteocalcin, osteonectin, thrombospondin-1, fibrinogen, fibronectin and vitonectin (6). PRP is used for its accelerating effect of wound healing like maxillofacial surgery, ophthalmology, neurosurgery, orthopedic surgery, plastic and reconstructive surgery and dental surgery (1).

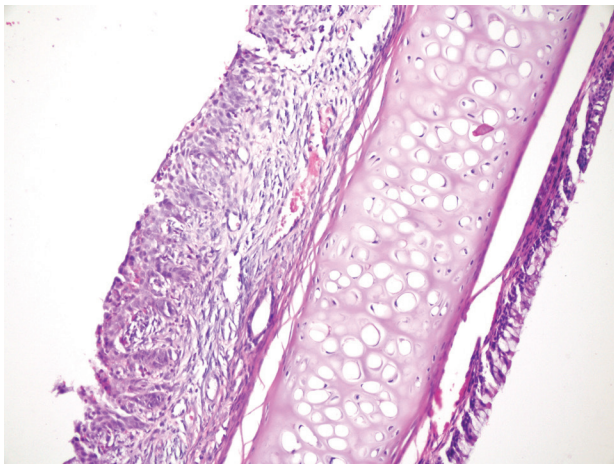


Figure 1: Reduced inflammation in PRP subgroup

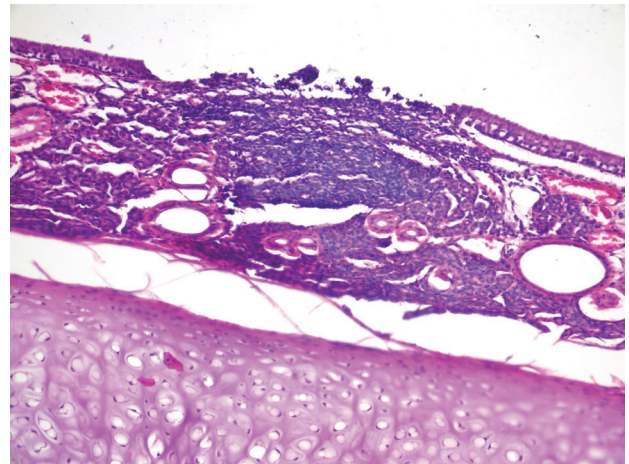


Figure 2: Shows severe inflammation in control subgroup

Table 1

Results of inflammation severity rates of in the first week group (n (%))

| | Control (%) | PRP (%) |
|---------|-------------|---------|
| Grade 0 | 0 (0) | 0 (0) |
| Grade 1 | 1 (12.5) | 6 (75) |
| Grade 2 | 4 (50) | 2 (25) |
| Grade 3 | 3 (27.5) | (0) |

Erkilet et al studied the effect of PRP on healing in experimentally generated rat tympanic membrane perforations. In this study, closure time of the perforations between the control and PRP groups were compared. It was observed that PRP accelerates the closure time. The difference between groups was statistically significant. There was no statistically significant difference between the control group and the PRP group in terms of lamina propria edema, neovascularization, fibroblast reaction and inflammation severity (7). In our study, we found that PRP reduces inflammation in the first week of nasal wound healing but not accelerates the healing time.

In the upper airways, ciliary cells and goblet cells has very important roles such as cleaning and protecting the mucosal surfaces. Mucociliary activity plays a crucial role in the wound healing of normal nasal mucosa and in the cleaning of nasal secretions. Especially in the postoperative period, nasal mucociliary dysfunction causes mucosal crust which can cause nasal obstruction and synechia (8). Salaheldin et al studied the effect of PRP on nasal mucociliary clearance after submucous diathermy of inferior turbinate. After 2 months follow up there was a significant increase in mucociliary function in PRP-treated nasal cavity group compared to the control group. Also in the same study, postoperative mucosal crust and bleeding were significantly lower in PRP-treated nasal cavity group. PRP has been evaluated as a treatment modality that will both increase the success of the surgery and enhance patient comfort (9). In our study, ciliary cell loss was observed to be less in the PRP group than the control group, especially in the first week but this difference was not statistically significant. Goblet cell hyperplasia was evaluated and an increase was observed in the PRP group in the first week compared to the control group, but this difference was not statistically significant, either.

One of the most important problems related to nasal mucosal wound healing in the postoperative period is the formation of synechia in the nasal cavity. After operations such as septoplasty and endoscopic sinus surgery, nasal synechia can cause recurrence of the disease and diminish surgical success. In the first instance, we thought that PRP could shorten the healing period by affecting wound healing positively and eventually reduce the formation of synechia. However in our study we didn't observe nasal synechia in any group. We believe that the wound model (brushing technique) we use is not successful in creating synechia. In order to understand the effect of PRP on nasal synechia, more studies should be done with other wound modals.

Conclusion

We believe that the effects of PRP could not be clearly monitored in our study since it was topically applied on an active ciliary surface such as nasal mucosa in a single dose. We suggest that the histopathological effects of PRP on the nasal mucosa can be better understood by new studies with different wound models and repetitive doses.

Compliance with ethical standards

Conflict of interest None.

All procedures performed in studies involving animals were in accordance with the ethical standards of the institution or practice at which the studies were conducted.

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