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Original Article

Long-Term Results of Fine Needle Diathermy Occlusion of Corneal Vessels in the Treatment of Herpetic Corneal Neovascularization

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ABSTRACT

Objective: This study aimed to evaluate the long-term results of fine needle diathermy (FND) in the treatment of corneal neovascularization (CoNV) due to herpetic keratitis.

Methods: We retrospectively reviewed the data of patients with herpetic keratitis CoNV who underwent FND. The demographic data, intraoperative and postoperative complications, preoperative and postoperative best corrected visual acuity (BCVA), and the number of FND procedure were recorded.

Results: Twelve eyes of 12 patients with herpetic keratitis CoNV were included in the study. Two patients (16.7%) were females and 10 were males (83.3%). The mean age was 56.75±13.24 (39–88) years. The mean follow-up period was 20.58±9.79 (12–42) months. The mean number of FND was 1.33±0.65. The mean preoperative BCVA was 1.40±0.44 log MAR, and the mean postoperative BCVA was 1.11±0.52 log MAR (p=0.018). All eyes with herpetic CoNV were categorized based on the resolution of corneal vascularization and visual acuity improvement into complete regression (n=6, 50%), partial regression (n=4, 33.3%), and no regression (n=2, 16.7%). Subconjunctival hemorrhage developed in 2 patients (16.7%). Corneal perforation developed in 1 patient (8.3%) and was treated conservatively. During the follow-up period, no patient had CoNV activation after FND.

Conclusion: Our results indicated that FND treatment in CoNV due to herpetic keratitis was effective in preventing CoNV recurrence, and the visual acuity gained after FND treatment was preserved in the long-term follow-up.

INTRODUCTION

Avascularity of the cornea is important for its transparency and preserves a degree of immune privilege.[1] In infection, allergic, and toxic conditions, vascularization develops in the cornea as a host defense response and contributes to the healing of the cornea.[2,3] However, when the disease process is over, these active vascular complexes sometimes do not regress and cause lipid accumulations in the cornea or loss of corneal transparency, resulting in decreased visual acuity.[4]

Various treatment options have been used in the prevention of corneal neovascularization (CoNV) by providing direct or indirect occlusion of the corneal vessels. Topical steroids, anti-VEGF agents, argon laser, yellow dye laser, radiation, and cryotherapy have also been applied to obliterate corneal vascularization.[5–10] Many studies reported that fine needle diathermy (FND) treatment is a newer, easier-to-apply, low-cost, and more effective option in the treatment of CoNV compared with other treatments.[11,12]

Herpes simplex virus (HSV) is one of the most common infectious causes of keratitis corneal blindness.[13] HSV may present in a wide spectrum such as epithelial keratitis, neurotrophic keratopathy, necrotizing stromal keratitis, immune stromal keratitis, and endotheliitis.[14] Immunoinflammatory lesions in the corneal stroma cause visual loss by creating stromal scar and vascularization.[15] Management of CoNV due to herpetic keratitis provides an additional contribution to the treatment.[16] In our study, we aimed to evaluate the long-term results of FND therapy in the treatment of CoNV due to herpetic keratitis.

MATERIALS AND METHODS

In this retrospective study, 12 eyes of 12 patients who had CoNV due to herpetic stromal keratitis and underwent FND between 2016 and 2020 were included. Informed consent from the patients and approval from the local ethics committee were obtained. Demographic characteristics of the patients, history of herpetic keratitis, previous treatments, best corrected visual acuity (BCVA) before the FND procedure and BCVA at the last follow-up, the number of FND session, FND related complications, regression, and relapse of CoNV were recorded. Anterior segment photographs of all patients were recorded before and after the procedure to better demonstrate the change in CoNV status. If no regression was observed during the first-month follow-up after the first FND procedure, an additional FND session was planned. In the last follow-up of the patients, the success of the FND procedure was defined as unsuccessful, partially successful, and successful, considering the corneal transparency status and visual improvement.

The FND procedure was started with topical anesthesia (proparacaine HCl 0.5% [Alcaine, Alcon]) using aseptic methods under the operating microscope. The needle of the 10–0 monofilament nylon suture was inserted into the areas with neovascularization at a depth of approximately 500 μm tangentially, 0.5–1 mm from the limbus. By touching the diathermia probe to the needle holder in coagulation mode in a way to affect the neovascular area, the procedure was terminated by observing the occlusion of the vessels with a slight whitening of the cornea in 1 s or less.

After the FND application, moxifloxacin and loteprednol drops were started 4 times a day. Topical moxifloxacin was stopped 1 week after the FND. Loteprednol treatment was gradually tapered and discontinued. Systemic oral acyclovir 800 mg prophylaxis was started before the procedure and used for at least 6 months after the procedure. The patients were examined in the first week and in the first, third, and sixth months after the procedure. After 6 months, patients were followed up every 3 months.

Statistical analysis

PASW Statistics (SPSS) 17 software was used for comparisons. The distribution of the data was evaluated with the Shapiro–Wilk test. The Wilcoxon test was used for comparisons. A statistically significant level was determined as $p<0.05$.

RESULTS

Twelve eyes of 12 patients (10 males, 83.3%; 2 females 16.7%) were included in the study. The mean age of the study group was 56.75±13.24 (range: 39–88) years. The mean follow-up time was 20.58±9.79 (range: 12–42) months. The mean preoperative BCVA was 1.40±0.44 log MAR and it increased to 1.11±0.52 log MAR at the last visit ($p=0.018$). The FND was performed once in 9 patients (75%), two times in 2 patients (16.7%), and three times in 1 patient (8.3%).

In the evaluation of the FND succession, there was no change in 2 patients (16.7%), partial regression was observed in 4 patients (33.3%), and complete regression was observed in 6 patients (50%). While no complications developed in 9 patients (75%), procedure-related complications developed in 3 patients. Subconjunctival hemorrhage developed in 2 patients (16.7%), and intrastromal hemorrhage developed in 1 patient (8.3%). Corneal perforation was observed in 1 patient (8.3%), and it was treated conservatively (bandage soft contact lens used for the treatment of corneal perforation). While recurrence was observed in 2 patients (16.7%) after FND (one session was performed on one of the patients, and two procedures were performed on the other), no recurrence was observed in 10 patients (83.3%). A total of 10 patients (83.3%) had a regression in CoNV with at least one FND session. Eight of them (66.7%) had a regression in CoNV

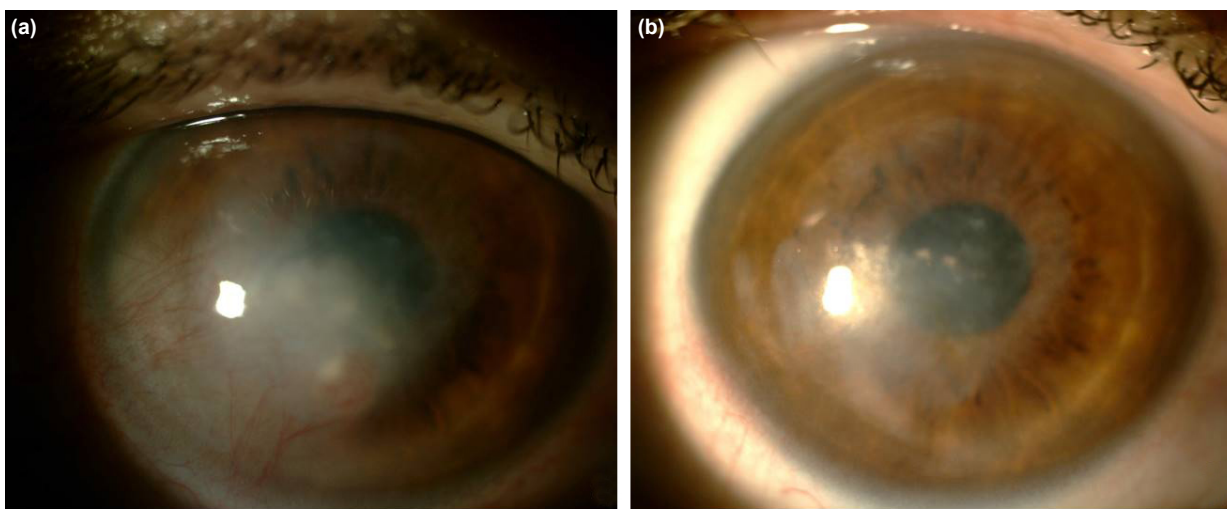

Figure 1. Anterior segment image of a patient with vascularization secondary to herpetic keratitis before **(a)** and 6 months after single-session fine needle diathermy treatment **(b)**.

after one time of FND, one of them (8.3%) had regression with 2 FND sessions, and one of them (8.3%) had regression with 3 FND sessions. The mean time between FND repetitions was 2.2 months. The mean number of FND sessions was 1.33±0.65. During the follow-up period, no CoNV activation was observed after FND treatments. Anterior segment image of a patient with vascularization secondary to herpetic keratitis before and 6 months after single-session FND treatment is shown in Figure 1.

DISCUSSION

Corneal vascularization is necessary for the repair and regeneration of damage to the cornea such as infection, allergic, and toxic conditions. However, permanent vascularization in the cornea may cause some undesirable conditions. The avascular feature of the cornea makes the cornea an immune-privileged region, but factors such as disruption of the tight alignment of collagen lamellae, increase in inflammatory cytokines, and hypoxia due to infectious, inflammatory, degenerative, traumatic, iatrogenic causes induce the development of new vessels in the cornea.[3] As a result, there may be calcium and lipid accumulation in the cornea, which may cause a loss of corneal transparency.[17,18] In this study, we aimed to evaluate the efficacy and safety of the FND procedure in the treatment of CoNV due to herpetic keratitis.

Many methods have been described in the treatment of CoNV. Although topical steroid drops are considered the most commonly used and standard treatment modality in the treatment of CoNV, these drops have risks such as cataracts, glaucoma, and opportunistic infections in long-term use.[19] There are studies reporting that topical non-steroidal anti-inflammatory drugs are used in the treatment of CoNV. However, its clinical use is limited because it causes serious side effects such as corneal ulcers.[20]

There are also treatment methods applied with direct intervention to the neovascularization area in the treatment of CoNV. These include cryotherapy, conjunctival resection, radiotherapy, yellow light laser, and corneal argon laser photocoagulation (CALF) treatments.[6,8,9] However, the effectiveness of these treatment methods other than yellow light laser and CALF is low. Yellow light laser treatment is not preferred because it is expensive and difficult to reach by ophthalmologists.[11] CALF treatment is less preferred in clinical practice because of its low effectiveness in deep and afferent vessels and because it causes complications such as iris atrophy and iatrogenic macular laser burn.[21]

FND treatment has become a more preferred modality compared with other treatment options as the procedure has no learning curve, is easy to access, and can easily occlude afferent or efferent vessels at any corneal depth.[11,12,22] Trikha et al.[12] reported that the success of FND treatment was 89.3% in their study group in which 25 (44.6%) of 56 eyes were treated for CoNV due to HSV keratitis, and they added that they found a statistically significant increase in visual acuity after the FND procedure. Similarly, FND treatment was applied to 12 eyes of 12 patients with CoNV due to HSV keratitis in our study, and the mean BCVA statistically significant, increased from 1.40±0.44 log MAR to 1.11±0.52 log MAR after the FND treatment. In our study group, recurrence was observed only in 2 patients (16.7%) after treatment. However, Trikha et al.[12] observed no recurrence in any eyes in their study groups. The most important cause of permanent vision loss in herpetic keratitis cases is the scar tissue that develops in the vascularized cornea. HSV-1 infection induces a chronic immune-inflammatory response in the cornea, resulting in a scenario that results in corneal scarring, thinning, and neovascularization.[23] The graft survival rate is very low in penetrating keratoplasty cases applied to improve vision in herpetic keratitis cases.[24] In our study, visual acuity improvement was obtained in 83% of the cases with CoNV due to herpetic keratitis. Therefore, FND treatment can be applied as the first-line treatment option in these cases. Although our study included a small number of patients, it is the first study to include the results of FND treatment only in cases with herpetic keratitis.

There are studies on clinical or experimental models of topical or subconjunctival use of anti-VEGF therapies (pegaptanib, bevacizumab, ranibizumab, and aflibercept) in CoNV.[25–27] Stevenson et al.[28] reported that topical ranibizumab treatment was more effective than topical bevacizumab in CoNV. Petsoglou et al.[29] reported that after three injections of subconjunctival bevacizumab, there was a statistically significant decrease in CoNV compared with placebo cases. In a small group study conducted in the pediatric population, it was reported that 88.9% of the cases regressed in CoNV with topical or subconjunctival bevacizumab application with FND treatment combination.[30] However, in studies on the efficacy of anti-VEGFs, it has been reported that if the vessels mature in CoNV, they will acquire a connective tissue wall covered with pericyte, that CoNVs will become independent of VEGF, and that the treatments may be ineffective.[31] The efficacy of anti-VEGFs is limited in deep, nourishing, and mature CoNV. It seems possible to increase success rates with the combination of the FND procedure and anti-VEGF agents.

FND treatment is a relatively easy procedure and without serious complications in CoNV. Intracorneal hemorrhage is the most common complication in the intraoperative and early postoperative period.[32] It most commonly occurs as a result of rupture of intracorneal vessels due to misdirection of the needle tip prior to diathermy application. Generally, intracorneal hemorrhage regresses within 1 or 2 weeks without additional treatment. In our study, intracorneal hemorrhage developed in 1 patient (8.3%) and regressed spontaneously within 1 week. Other complications of FND include whitening at the corneal entry site of the needle, subconjunctival hemorrhage, and localized corneal thinning.[10] However, these complications also regress within 1 or 2 weeks. The most serious complication

of FND is corneal perforation. It is usually caused by high diathermy settings or by applying FND to deeply located CoNVs. In the management of corneal perforation, observation with a bandage contact lens is generally sufficient, but intraoperative corneal repairing may be necessary in cases with intense Seidel positive. In our study, corneal perforation was observed in 1 patient (8.3%) and the patient was treated with a bandage contact lens without further interventions.

In conclusion, the treatment of CoNV with FND is a simple, low-cost, and accessible treatment method. It can also be applied successfully in herpetic keratitis cases without serious complications. As graft survival is low in penetrating keratoplasty applied to improve visual acuity in patients with scarring and neovascularization due to herpetic keratitis, FND treatment can be applied as the first-line treatment option in these cases.

Ethics Committee Approval

This study approved by the Kartal Dr. Lütfi Kırdar City Hospital Clinical Research Ethics Committee (Date: 22.06.2021, Decision No: 2021/514/204/13).

Informed Consent

Retrospective study.

Peer-review

Internally peer-reviewed.

Authorship Contributions

Concept: B.T., N.T.G., E.G.; Design: B.T., B.K., E.G., B.Kan.; Supervision: B.T., H.S.K.; Fundings: B.T., B.Kan.; Materials: B.T., B.K., B.Kan., N.T.G.; Data: B.K., B.T., N.T.G.; Analysis: B.T., B.Kan., N.T.G., H.S.K.; Literature search: B.T., H.S.K., B.K., E.G.; Writing: B.T., E.G., H.S.K.; Critical revision: B.T., B.K., B.Kan., N.T.G., E.G.

Conflict of Interest

None declared.

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Herpetik Stromal Keratite Bağlı Gelişen Korneal Neovaskülarizasyon Tedavisinde İnce İğne Diatermi Tedavisinin Uzun Dönem Sonuçları

Amaç: Herpetik keratite bağlı kornea neovaskülarizasyonunun (KNV) tedavisinde ince iğne diatermi (İİD) tedavisinin uzun dönem sonuçlarını değerlendirmek.

Gereç ve Yöntem: Herpetik keratit nedeniyle KNV gelişen ve İİD uygulanan hastaların verileri geriye dönük olarak incelendi. Demografik veriler, intraoperatif ve ameliyat sonrası komplikasyonlar, ameliyat öncesi ve sonrası en iyi düzeltilmiş görme keskinliği (EİDGK), İİD işlem sayısı kaydedildi.

Bulgular: Herpetik keratite bağlı KNV gelişen 12 hastanın 12 gözü çalışmaya dahil edildi. Hastaların 2'si (%16.6) kadın, 10'u (%83.4) erkekti. Ortalama yaşları 56.75±13.24 (39-88) idi. Ortalama takip süresi 20.58±9.79 (12–42) aydı. Ortalama İİD sayısı 1.33±0.65 idi. Ameliyat öncesi ortalama EİDGK 1.40±0.44 log MAR ve ameliyat sonrası ortalama EİDGK 1.11±0.52 log MAR idi (p=0.018). Herpetik KNV'li tüm gözler, kornea vaskülarizasyonundaki gerileme ve görme keskinliğindeki iyileşmeye göre tam gerileme (n=6, %50), kısmi gerileme (n=4, %33.3) ve değişim olmaması (n=2, %16.7) şeklinde kategorize edildi. İki hastada (%16.7) subkonjonktival kanama gelişti. Bir hastada (%8.3) kornea perforasyonu gelişti ve konservatif olarak tedavi edildi. Takip süresi boyunca hiçbir hastada İİD'den sonra KNV aktivasyonu olmadı.

Sonuç: Herpetik keratite bağlı KNV'de İİD tedavisinin KNV rekürrensini önlemede etkili olduğunu ve İİD tedavisi sonrası kazanılan görme keskinliğinin uzun dönem takipte korunduğunu göstermiştir.

Anahtar Sözcükler: Herpetik keratit; ince iğne diatermi; korneal neovaskülarizasyon.