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Mini Review

Haze-Free Correction of Refractive Errors using Transepithelial Photorefractive Keratectomy: An Alternative to Laser-Assisted in Situ Keratomileusis

Pitra Ariesta Shinta Dewi[1]*, Sophia Pujiastuti[1], Henry Albar Wibowo[1] and Dini Hapsari[1]

[1]*Silc Lasik Center, Eye care center in Central Jakarta, Indonesia*

***Corresponding author:** Pitra Ariesta Shinta Dewi, Silc Lasik Center, Eye care center in Central Jakarta, Indonesia.

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Abstract

Corneal refractive surgeries are increasingly popular worldwide. While they are generally safe and present with high rates of satisfaction, epithelial and stromal damage from the procedure may affect corneal integrity and function. The consequent corneal wound healing process may also result in complications that impact visual outcomes, such as the occurrence of corneal stromal haze. Transepithelial photorefractive keratectomy (tPRK), which utilizes excimer laser rather than mechanical or chemical debridement, could prevent such complication. This review evaluates the potential of tPRK in correcting refractive errors with minimal corneal stromal haze. We found that tPRK and its modified techniques are promising alternatives to other refractive surgery techniques such as LASIK. Further studies should be conducted to further confirm the superiority of tPRK in minimizing postoperative corneal stromal haze compared to other techniques.

Keywords: Haze-free correction; tPRK; LASIK

Introduction

Corneal refractive surgeries are performed worldwide to achieve permanent correction of refractive errors. The number of refractive surgery procedures performed in the last 20 years have also exponentially increased. While refractive surgeries are generally safe with high rates of satisfaction, epithelial and stromal damage from the procedure may affect corneal integrity and function. This damage in turn triggers a regenerative response, namely the corneal wound healing process. Normally, this process ultimately results in restoration of the corneal tissue without the formation of scar or vascularization. However, this process may also result in complications which might impact the visual outcomes of kerato refractive procedures [1,2]. Transepithelial photorefractive keratectomy (tPRK), which utilizes excimer laser rather than mechanical or chemical debridement, could prevent such complications. The tPRK technique averts complications related to debridement such as in conventional PRK and corneal flap such as in laser-assisted in situ keratomileusis (LASIK). As such, this review aims to evaluate the potential of tPRK in correcting refractive errors with minimal corneal stromal haze.

Discussion

Stromal haze as complication of corneal refractive surgeries

There exist several definitions of corneal stromal haze, including (1) a decrease in tissue transparency, (2) a marginal loss of corneal clarity, and (3) a subepithelial stromal opacity. Patients with

corneal haze may be asymptomatic or experience starburst and visual loss. It may even induce stromal reaction with consequent refractive regression, irregular astigmatism, and corneal surface irregularity. Clinically insignificant haze is reported to be present in most eyes following PRK for approximately 1–2 years after surgery. Meanwhile, clinically significant haze is reported in a smaller proportion of eyes, approximately less 0.5–4% of eyes [3]. A grading system of corneal stromal haze was previously described by Fantes, et al. [4] ranging from 0.5 to 4 (Table 1).

Table 1: Staging of corneal stromal haze [3,4].

Stage	Slit Lamp Image Description
0	No haze, cornea completely clear
0.5	Faint haze can be seen with indirect broad tangential illumination
1	Minimal haze difficultly seen with direct and diffuse illumination; does not interfere with fine iris details
2	Mild haze obscuring iris details
3	Moderate-dense haze partially obscuring the iris details
4	Severely dense haze completely obscuring intraocular details

Typically, two types of haze are observed. The first type is the "typical transitory haze" which is more prevalent but rarely associated with clinical symptoms. It usually appears 1–3 months after surgery and disappears or becomes insignificant within 1 year post operation. The other type is the "late haze" wherein the eye is normal initially, but consequent haze formation occurs in 2–5 months post operation. The late haze is less common and may severely affect vision due to decreased corneal transparency and myopic regression. While late haze may resolve over time, it may stay longer and persist for up to 3 years [3].

Corneal stromal haze is the result of a process started by corneal epithelial and stromal injury; in this case the corneal basement membrane is damaged by surgical laser. This is also accompanied by apoptosis and necrosis of the surrounding corneal cells. Consequently, peripheral keratocytes migrate centripetally and will then transform into activated fibroblasts. These fibroblasts lay down the extracellular matrix, transform into myofibroblasts and precipitate stromal edema, ultimately rendering the stromal surface irregular. Cytokines are also implicated in this process. For example, TGF-β stimulates myofibroblast transformation and inhibits IL-1α and IL-1β myofibroblasts apoptosis. The non-orthogonal pattern of the type I and III fibrillary collagen and presence of type IV collagen not normally present in the corneal stroma are thought to cause postoperative subepithelial haze. The presence of myofibrils in the corneal stroma also contributes to decreased transparency due to their lower crystallin production. The highly reflective myofibrils also contribute to haze formation as they scatter light randomly in the photo ablated region [3,5].

The transepithelial photorefractive keratectomy technique

In conventional PRK, the corneal epithelium is removed either manually or with alcohol. Subsequently excimer laser ablation is utilized to correct the refractive error. However, this method is associated with drawbacks such as prolonged epithelial healing (due to basement membrane injury or toxicity from alcohol), pain, and various degrees of corneal haze despite administration of mitomycin C [6]. Mitomycin-C is an alkylating antibiotic which has anti fibroblastic properties and also exhibits inhibitory effects on cell growth. It has been found to be useful in the prevention of corneal stromal haze. However, there are concerns for the cytotoxic effects of mitomycin to the corneal endothelium. Reduction of the application time and dose of mitomycin-c was suggested to counter this issue [7,8].

Introduced in 1990, tPRK is a modification of the conventional PRK technique. Classically, it is a two-step procedure consisting of excimer laser phototherapeutic keratectomy to remove the corneal epithelium followed by stromal laser ablation. A single-step tPRK had also been developed in 2007, wherein ablation of the corneal epithelium and stroma is performed in a single continuous session with shorter duration [7,9] Further modifications to the single-step tPRK technique were later developed, such as the reverse single-step tPRK (ss-tPRK) [10], smart-pulse technology coupled with ss-tPRK [11], and refined ss-tPRK [12].

While associated with diminished wound healing response and hence less corneal haze, stromal haze can still occur after the performance of tPRK. Ellakwa, et al. [9] studied the stromal corneal haze in a study involving 100 myopic eyes. The preoperative and postoperative best corrected visual acuity (BCVA) of the patients was 0.274 ± 0.227 and corrected to 0.92 ± 0.1223 in Snellen and log MAR equivalent. The preoperative spherical and cylinder error was 2.475 ± 2.014 and 1.496 ± 1.224 respectively, which were subsequently corrected to 0.08 ± 0.001 and 0.025 ± 0.000 respectively. The results were statistically significant. Meanwhile, the mean percentage of postoperative corneal haze after 1 week was 1.22 ± 1.19, which then decreased to 0.8 ± 1.05 after 1 month, decreased to 0.325 ± 0.605 after 3 months, and then further decreased to 0.12 ± 0.356 after 6 months. A statistically significant difference between the mean percentage of haze during the first and the last follow up was observed. Linear regression analysis also showed significant correlation between preoperative BCVA, degree of refractive errors, postoperative central corneal thickness, and ablation depth with the incidence of corneal haze.

Aslanides, et al. [11] also reported accelerated epithelial healing and less haze and pain in patients receiving modified

tPRK compared to LASIK, though other clinical outcomes were similar between the two groups. Faldallah et al.[10] compared the performance of tPRK compared with conventional alcohol PRK. The study found that tPRK for mild to moderate myopia with or without astigmatism was associated with significantly less pain and less haze after surgery. While patients treated with tPRK also reported faster healing times, the visual outcomes between the two groups were similar.

Conclusions

The occurrence of corneal stromal haze is a problem in the practice of ophthalmology. tPRK and its modified techniques are alternatives to other refractive surgery techniques such as LASIK. Further studies should be conducted to further confirm the superiority of tPRK in minimizing postoperative corneal stromal haze compared to other techniques.

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None.

Conflict of Interests

None.

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