

Femtosecond Laser Versus Mechanical Microkeratome in Thin-Flap Laser in Situ Keratomileusis (Lasik) for Correction of Refractive Errors

an Evidence-Based Effectiveness and Cost Analysis

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Abstract:

Introduction: To compare the efficacy and cost-effectiveness of Femtosecond laser versus mechanical Microkeratome corneal flap creation in correction of refractive errors.

Methods: In this review, a comprehensive search of Medline, SCOPUS, Cochrane, TRIP database, supplemented by HTA and economic databases was performed. We searched for randomized controlled trials (RCTs) of Femtosecond laser which included mechanical Microkeratome in other arm. The quality of the retrieved studies was appraised by two independent reviewers and appropriate articles were finalized.

Result: A total of 1142 articles were identified, of which, 1059 were excluded after review of the titles and abstracts and 83 articles remained. Systematic reviews and RCTs were evaluated through CASP international worksheet. Eventually, 61 titles were excluded, leaving 22 articles to be reviewed.

Safety: There was no individual evidence to cover all safety components about Femtosecond laser, but in summary, this modality seems a safe method for corneal flap creation.

Effectiveness: No statistically significant difference was shown in visual acuity and refractive errors. The important secondary end point of this review was diffuse Lamellar keratitis in 17% of the Femtosecond group versus 5% in mechanical Microkeratome. Inflammation was low-grade and improved during the first 3 months of follow-up period with a low dose medication without corneal scarring. The two groups was comparable in all clinical outcomes including Uncorrected Visual Acuity (UCVA), Best Special Corrected Visual Acuity (BSCVA), manifest refraction, wave front aberrometry, Schirmer test, and Tear Break up time (TBUT).

Cost Analysis: Results showed that marginal cost incurred due to Femtosecond technology adoption may vary from 27 to 117 €(resulted from sensitivity analysis). It is clear that additional cost may be a small proportion of LASIK procedure total cost.

Conclusion: Although Femtosecond flap creation is a modern method with a good quality of corneal flap, but, there is no high-quality evidence to show superiority of Femtosecond laser in clinical outcomes. Although the efficacy and cost of the systems is almost equal, traditional method still remains as the standard approach.

Keywords: Lasers; Keratomileusis, Laser In Situ; Laser Therapy; Cost Analysis; Evidence-Based Medicine

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Introduction

After introducing Laser in situ keratomileusis (LASIK) in 1990s, it is going to become the most common refractive surgical procedures for correcting myopia, hyperopia, and astigmatism. The LASIK is a two-stage procedure; in the first step, the surgeon should create a flap of corneal tissue. The second step is considered as inner cornea reshaping using an excimer laser to correct the vision of the patient. Despite the good success rates, like many other cosmetic surgeries, LASIK is not without complications and some major complications (e.g. epithelial defects, incomplete flaps, decentered flaps) are linked to the corneal flap creation(1). Since the introduction of LASIK, various mechanical Microkeratomes have been developed to create the corneal flap. However, unpredictable flap thickness may increase the risk of corneal ectasia.

Recently, the Femtosecond laser has been emerged to become an appropriate alternative to mechanical Microkeratomes. This method has been approved by FDA (the Food and Drugs Administration in the United States) and CE (European credit). It is used in United States, Australia, and at least 20 centers in Europe. Femtosecond Laser creates a computer-guided, précised corneal flap, without heating the surrounded tissues. Corneal transplantation and cataract surgery are two recent fields for application of the Femtosecond Laser(2-5). However, due to the low levels of evidences for corneal transplantation and cataract surgery, this study only focused on LASIK. A total of 26% of Iranian population are suffering from myopia. Although wearing glasses or contact lens is satisfactory for most of them, there is a growing interest toward laser surgeries(6). According to the development of LASIK technology in the recent years, there is a dramatically increased request for modern approaches by the patients and ophthalmologists. The aim of this review was to evaluate the safety, efficacy, and cost- effectiveness of Femtosecond in comparison with mechanical Microkerotoms in Iranian health centers.

Methods

Based on the following answerable question (PICO), we searched MEDLINE via Pubmed

(including Clinical Queries) (from January 2005 to June 2010), Cochrane (from 2005 to June 2010), SCOPUS (June 2010), TRIP database (from 2005 to June 2010), NHS Economic Evaluation Database (June 2010) and HTA database (June 2010), NHS Centre for Reviews and Dissemination (CRD; June 2010), Dissertation Abstracts Online (UMI) via ProQuest, and Google Scholar.

PICO: P(patient): Patients with refractive errors/I(Intervention): LASIK with Femtosecond/ C(comparision): LASIK with mechanical microkerotome/ O(outcomes): Refractive, Error correction, morbidity, complication

We searched Pubmed (including Clinical Queries) for both MESH terms and free language keywords including Femtosecond laser, Keratomileusis, Laser In Situ (subject heading), and LASIK. We also limited the search to "Title /abstract" field. In Cochrane Library database, we searched Femtosecond laser and LASIK keywords in "Title, abstract and keyword" fields. We searched Google Scholar for Femtosecond laser, LASIK, and compare in "Medicine, Pharmacology, and Veterinary Science" subject area. In other databases, we searched for Femtosecond laser and LASIK keywords.

Two independent reviewers evaluated the selected randomized controlled trials; non-randomized comparative studies were included in the papers and critical appraisal was done by CASP international tool. For any disagreements, a third party was invited to solve the problem. The studies included in this summary are highlighted in the reference list. One Iranian epidemiological and one big case series were included to evaluate the burden of disease and Femtosecond safety issues. In order to economically evaluate alternatives, the process of surgery, regarding the perspective of the study, was determined through literature review, interview, and observation. Cost elements including personnel cost, consumables, depreciation and utilities were estimated. To cope with the issue of generalizability, the sensitivity analysis was conducted. Prices of the equipments in the market were considered in the analysis.

Results

A total of 1142 articles were identified, of

Table 1. Number of the articles found in various databases

	Total results	Selected results	Final results
Pubmed (including Clinical Queries)	158	21	16
Cochrane			
TRIP database	32	2	-
SCOPUS	64	10	-
Google Scholar	136	30	5
	376	20	1

which, 1059 were excluded on the basis of the titles and abstracts and 83 remained. These articles were evaluated by clinical librarians and expert evaluators; also, systematic reviews and RCTs were evaluated through CASP international worksheet. Eventually, 61 titles were excluded, leaving 22 to be reviewed (Table 1).

Evidence based analysis of safety, effectiveness and cost effectiveness:

Safety

Flap thickness is an essential safety issue in prevention of ectasia following LASIK surgery. Mean flap thickness in Femtosecond Laser was 160 µm compared to 230 µm in mechanical Microkeratomes, which was significantly thinner ($p < 0.001$). In addition, after Femtosecond software update, the mean obtained flap thickness decreased to 60 µm. Overall rate of epithelial defect in mechanical microkeratome, was 7.7% to 9.6%, but no epithelial defect is reported in Femtosecond group ($p = 0.001$). Buttonholes, transacted flaps was not seen in the available evidences. Overall corneal flap-related complication rate was 5% including flap decentration, irregular flap or bad surfaces, flap laceration, epithelial abrasion and buttonholes(7-8). Despite the clinically significant post-operative minor inflammation in Femtosecond laser compared to the mechanical microkeratome, the difference was not statistically significant(7). In the recent report, 2000 surgeries were performed without major events(9). There was no individual evidence to cover all safety components about Femtosecond laser; but in summary, this method seems a safe modality for corneal flap creation.

Efficacy

From 2005 to 2010, four randomized

controlled trials have been conducted worldwide. Unfortunately, the end points of the studies were not similar, and none of the studies covered all important complications. In other words, the evidences suffered from heterogeneity. Due to the information obtained from aberrometry, good corneal flap makes less aberration errors. Tran et al.(10) demonstrated that 10 weeks after LASIK, statistically significant changes in defocus wavefront aberrations were observed in Femtosecond (baseline: 3.5 RMS, 10 weeks post-flap: ~3.2 RMS, $p = 0.008$) and Microkeratome (baseline: 3.5 RMS, 10 weeks post-flap: ~2.7 RMS, $p = 0.004$) flap creation. In the mechanical group, statistically significant interments of higher-order aberrations (Trefoil and quadrafoil Zernicke terms) were noted after flap creation ($p = 0.02$). Conversely, no significant changes in higher-order aberrations were observed in the Femtosecond group(10). In a RCT conducted by Patel et al, backscatter from the middle third of the corneal light scattering in Femtosecond group was 6% more than mechanical ($p=0.007$) but became normal in 3 and 6 months of follow-up. No statistically significant difference was shown in visual acuity and refractive errors(11-12).

In another uncontrolled study(13) on 100 patients (200 eyes), the visual outcome was comparable ($p=0.5$) and Femtosecond made a round and regular shape flap ($p=0.016$). The important secondary end point of this study was that diffuse lamellar keratitis was present in 17% of the Femtosecond versus 5% in mechanical group ($p =0.001$). Inflammation was very low-grade and improved during the first 3 months of follow-up period with a low dose of medication without corneal scaring.

Buzzone et al(14) showed that the postoperative mean uncorrected visual acuity was 8.6 ± 2.3 in the Femtosecond laser group and 9.3 ± 1.6 in the Microkeratome group, whereas the mean best-corrected visual acuity was 9.1 ± 1.1 in the Femtosecond laser group and 9.5 ± 0.9 in the Microkeratome group. In this study, increasing factor (IF: value of the optical aberrations ratio between the preoperative and postoperatively) was calculated. At one year postoperative, the IF for total aberration, spherical-like aberration, and coma like aberration was not statistically significantly different between the two groups(14). In the study conducted by Gil-Cazorla et al(9), the incidence

of postoperative diffuse lamellar keratitis was significantly higher in the Femtosecond laser group (0.5%) compared with the Microkeratome group (0.1%) (P = 0.03). In the recent Chinese report(15) of a non randomized controlled trial, two groups were comparable in all clinical outcomes such as UCVA, BSCVA, manifest refraction, wave front aberrometry, schirmer test, and Tear Break up time (TBUT). Same results were obtained in another pair eyes randomized trial for total high order aberration,spherical aberration, and coma(16).

Other Issues

There is a lack of evidence on the utilization of the Femtosecond laser in corneal transplantation and cataract surgery. It seems that the aim of corneal transplantation is thin donor generation on corneal endothelium. Available studies(3-4) reported that the histology of the Femtosecond laser-formed stromal dissections did not appear substantially better compared to manual deep lamellar endothelial keratoplasty dissections in both recipient and donor tissues. Therefore, additional research is required to examine and fine-tune the potential use of Femtosecond laser in corneal transplantation surgery. However, early indications demonstrate that Femtosecond may have some benefits to penetrating keratoplasty(5,17), while it is supported by some in vitro studies(18-19).

surgical process using two methods showed that all stages including diagnosis, preoperative procedures, operations, and postoperative procedures were similar for both methods. In the new method, Femtosecond laser has been installed on the LASIK set and used for creating of the flap. Therefore, the only difference in the resources used for the two methods was related to the cost of Femtosecond laser. If the Femtosecond laser is used as the preferred method, the health system, the providers and patients would incur the costs of purchasing, installing, running, training and maintenance of this technology. The recent study focuses on this issue to conduct an economic evaluation. The price of is about 350,000 to 400,000 Euros (for different brands) that is added on new costs for current costs(20-22). Since the analysis should be done on the basis of unit cost, the unit cost of services was computed using three scenarios. That is, the unit costs were computed for three number groups of patients (300, 500, and 1000). Sensitivity analysis conducted for exchange rate and the life time period of Femtosecond laser and the results are reported in table 2. This table showed marginal cost incurred due to Femtosecond laser technology, per procedure and sensitivity analysis based on equipment life time, exchange rate, and annual quantity of surgery. According to this sensitivity analysis, the cost had a fare relation with increasing patients' number per year.

Cost effectiveness

The examination of the performing refractive

Discussion

It is almost clear that Femtosecond laser may

Table 2. marginal cost incurred due to Femtosecond laser technology, per procedure and sensitivity analysis based on equipment life time, exchange rate and annual quantity of surgery

	Equipment price (€)	Life time period	Annual Number of surgery	Unit cost (€)	Unit cost (Rials)
Scenario 1	350000	10	300	117	1521000
Scenario 2	350000	10	500	70	910000
Scenario 3	350000	10	1000	35	455000
Scenario 4	350000	15	300	78	1014000
Scenario 5	350000	15	500	47	611000
Scenario 6	350000	15	1000	23	299000
Scenario 7	400000	10	300	134	1742000
Scenario 8	400000	10	500	80	1040000
Scenario 9	400000	10	1000	40	520000
Scenario 10	400000	15	300	88	1140000
Scenario 11	400000	15	500	53	689000
Scenario 12	400000	15	1000	27	351000

Note: 1 Euro equal to 13000 Rail

produce predictable flap thickness, increased post-operative flap stability, and decreased epithelial injury(2,7,10-11). Despite these advantages, the current RCTs were unable to demonstrate its superiority to mechanical Microkeratome. Based on the available evidences, this technology could achieve an acceptable position in ophthalmology. It is clear that both surgical methods cure patients with high effectiveness but the only difference between the two methods was related to postoperative side effects that patients would face. Often, these side effects had no long-term effects on the vision of the patients. They can be sorted out with prescribed medicine and given advice. The potential for utilizing Femtosecond laser in corneal transplantation and cataract surgery is a significant interest. However, the issues identified in the current studies showed that further clinical research is required to confirm the in vitro studies. Meanwhile, this review demonstrates in vitro superiority with a clinical equal safety and effectiveness for Femtosecond versus mechanical Microkeratome. However, clinical evidence for the effectiveness of Femtosecond laser in corneal transplantation remains limited.

Results show that marginal cost incurred due to Femtosecond technology adoption may vary from 27 to 117€(resulted from sensitivity analysis). It is clear that additional cost may be a small proportion of LASIK procedure total cost. Thus, it seems that the incurred cost for patients is small but how do the uncontrolled imports affect the issue? Since the extent of effects will be broad, conducting economic evaluation with cost-effectiveness technique will be useful. It is better to pose our question in this way: do the patients prefer to pay this amount? What are their opinions? How do they prioritize? Considering this fact that LASIK surgery is a luxury, using patients' preferences in accepting or rejecting new methods will be helpful.

Conclusion

In summary, Femtosecond flap creation is a modern method with a good quality of corneal flap. Although the in-vitro studies demonstrated a superb quality flap, there is no high level of evidence to show superiority of Femtosecond laser in clinical outcomes. However, the efficacy and cost for system is almost equal; so, traditional

method still remains as a standard approach and Femtosecond laser is an optional approach which depends on the patient preference.

Number of Studies Included:

Total number of studies 22
 Level II evidence 5
 Level III evidence 13
 Level IV intervention evidence 4

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