Study Protocol and Statistical Analysis Plan

Study title:

Safety and Suitability of Implantable Collamer Lens (ICL) Implantation for Correction of Refractive Errors Without the Use of Dispersive Ophthalmic Viscosurgical Devices (OVDs)

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List of Abbreviations

BSS: Balanced Salts Solution

CV: Coefficient of Variation

ECD: Endothelial cells density

ICL: Implantable Collamer Lens

IOP: Intra-Ocular Pressure

OVD: Ophthalmic Viscosurgical Device

PIOL: Phakic Intra-Ocular Lens

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1 Background

Refractive errors (myopia, hyperopia and astigmatism) are quite prevalent worldwide, they constitute the most common cause of visual impairment with myopia in particular being progressively increasing in its prevalence so that it is predicted that by 2050 nearly half of the world population will be myopic.[1,2] Management modalities include correction with glasses, contact lenses, laser vision correction, intracorneal implants and intraocular refractive procedures such as phakic intraocular lens (PIOL) implantation which involves the use of implantable collamer lens (ICL) in many cases.[3] PIOLs are being extensively used since they preserve the integrity of the cornea and thereby attaining higher quality of vision compared with conventional kerato-refractive procedures. Furthermore; they allow broader range of refractive errors to be corrected.[3,4] The Staar V4c EVO visian ICL (Staar surgical Inc, Lake Forest, CA, USA) has demonstrated effectiveness and an excellent safety profile with more than one million ICL implants had already been performed globally.[4] However, complications such as raised intraocular pressure (IOP), cataract and pupillary block do happen.[4,5] The ICL implantation procedure typically utilizes viscoelastics to facilitate introduction and positioning of the implant. Viscoelastics should be removed thoroughly at the conclusion of the procedure, and failure to do so may induce early postoperative IOP rise.[6,7] It is logical to assume that viscoelastics use during surgery increases operation cost and time due to the extra steps involving the injection and removal of the substance. Increased manipulation during ICL implantation surgery and irrigation required to ensure adequate removal of viscoelastics may encourage cataract formation as well.[5] Few studies investigated the safety and efficacy of ICL implantation without the use of viscoelastics, where they implemented balanced salt solution (BSS) instead as a novel technique[8,9]. In the present study we retrospectively investigated the safety and efficacy of modifying ICL implantation technique by using cohesive OVD only without using dispersive OVDs.

2 Aim(s) / Objective (s)

Is omitting dispersive viscoelastic from the standard surgical technique and utilizing only cohesive OVDs (in what we call it reduced- OVD technique) safe and suitable?

3 Study Design and Methodology

3.1 Study Overview

This is a retrospective cross-sectional comparative study.

Data from private hospital records were accessed and analysed retrospectively.

3.2 Study Setting / Location

The study participants were all from Al-Ferdos private hospital in Baghdad, Iraq.

3.3 Study Population

All refractive surgery candidates attending the above hospital for the purpose of phakic introcular lens implantation were included in the study. However, the initial group allocation occurred before the commencement of the study on the basis of surgeon and patient preference, thereby, randomization was on convenient basis.

3.3.1.1 Eligibility Criteria

To be eligible for enrolment into the study all of the inclusion criteria must be met. A participant will be excluded from the study if any of the exclusion criteria is present.

Inclusion Criteria

Refractive surgery candidates

Aged from 18-55 years

Phakic intraocular lens implantation was performed (ICL type)

Committing to at least one preoperative visit for baseline assessment and multiple postoperative visits (at least 2 visits within a year) for follow-up assessment.

Exclusion Criteria

Patients with incomplete data and no commitment to follow up visits

Presence of the following ocular conditions preoperatively: unstable refraction, severe ocular surface disease, cataract, glaucoma, corneal pathology such as Fuch's dystrophy or corneal scarring, uncontrolled intraocular inflammation, macular scarring or any other retinal issue that may adversely affect vision after surgery.

3.4 Identification and Recruitment of Participants

Potential participants will be identified by screening of all medical records from the above hospital regardless of the time of the surgery.

Study investigators will identify study participants individually after screening of medical records.

Since this study is retrospective, initial surgery consent was considered as the participant consent for the study.

3.5 Study Interventions / Procedures

After enrolment, the record of each participant is examined meticulously for completeness of preoperative and postoperative data pertaining to study including:

Patient age and gender, date of the procedure and its operative notes including laterality and surgical steps.

preoperative and postoperative assessments such as uncorrected and best corrected visual acuity, refractive error quantification both objectively utilizing an autorefractometer autorefractor Nidek ARK 1 (Nidek Inc, Gamagori, Japan) and subjectively as manifest refraction, clinical slit-lamp examination notes, intraocular pressure with air puff tonometers, AC depth assessment by Pentacam Scheimpflug (Oculus Optikgeräte GmbH Inc., Wetzlar, Germany), specular microscopy study of corneal endothelial cells (endothelial cell density (ECD), coefficient of variation (CV) and hexagonality) using Topcon SP-1p Specular Microscope (Topcon Corporation, Tokyo, Japan),

Typically, there is a preoperative visit and multiple postoperative visits extending over the period of 1-2 years after the procedure.

3.6 Data collection and analysis

Data will be collected by study co-investigators with assistance from IT personnel at the respective hospital from patients records that were identified as eligible for the study according to the inclusion criteria above. According to their data, participants will be split into two groups:

1- Traditional OVD group

In this group of patients, the ICL was implanted utilizing both cohesive and dispersive ophthalmic viscosurgical device.

2- Reduced OVD group
In this group of patients, the ICL was implanted with the use of cohesive OVD only.

There is one primary outcome of interest which is the unaided visual acuity after the surgery, and several secondary outcomes including postoperative intraocular pressure, corneal specular microscopy parameters (ECD, CV and hexagonality), and the observed adverse events that can happen during the operation or postoperatively.

Data will then be stored electronically in a sheet format to enable for later statistical analysis.

Data collection was started at the conduct of the study in March 2024, and it is expected to be completed 3-4 months later.

3.7 Handling of Missing Data

Section 3.5 of this protocol defines the data sets that will be collected from patients. Any missing information in this regard would be considered as incomplete data and this will meet an exclusion criterion and thereby a participant would be totally excluded from the study even if all other parameters are present.

4 Statistical Considerations

Biostatisticians had been consulted regarding the statistical analysis of data from this study.

4.1 Sample size and statistical power

This study involves a convenient non-probability sample based on the availability of patients records in the respective center for enrolment and analysis.

4.2 Statistical methods

After collection of data from patients records and its subjection to thorough analysis for incompleteness and exclusion criteria, these data will be stored electronically in sheet formats for later analysis. All statistical test and subsequent analyses will be performed using SPSS version 26 (IBM statistical software). Data will be classified into categorical and numerical. Categorical variables were described using frequencies and percentages and were analysed using Chi-squared test. Numerical variables, described as mean $\pm$ standard deviation, will be subjected to tests of normality to determine the appropriate statistical tests for inter- and intra-group comparisons. Unpaired t test or Mann-Whitney test was used to compare the two groups (traditional and modified OVD) according to fulfilled statistical assumptions. These two groups were compared for statistically significant difference regarding all parameters that were collected as per section 3.5 of this protocol. These statistical comparisons were made both preoperatively to determine baseline characteristics of the study participants and postoperatively to determine any significant difference between the two groups. Within the same group whether traditional or reduced OVD, all of the aforementioned parameters were compared again pre- and postoperatively this time using either one sample paired t test or Wilcoxon signed-rank test according to fulfilled statistical assumptions. Significance was considered at P value less than 0.05.

5 Ethical Considerations

The study merely investigates the records of patients that had already undergone refractive surgeries. It followed the principles of the “Declaration of Helsinki” and local laws and regulations.

The study was approved by the institutional review committee at the respective hospital and a similar committee at the college of medicine of university of Basrah according to the local guidelines and protocols. Written informed consent was obtained from each patient before the surgery.

Patients data are to be stored safely electronically using dedicated computers for the task. Patients privacy and confidentiality was taken into account.

6 Study Impact and Significance

Traditionally dispersive OVDs has been used extensively during loading and implantation steps of ICL surgery. Reducing both the amount and the types of viscoelastics used (cohesive only) might potentially reduce cost and time of the procedure and might provide a substitute for safety studies regarding omitting or further reduction of cohesive OVDs and utilizing BSS only which carries lower risk of raised IOP and lower cost of the procedure.

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