Bilateral diffuse lamellar keratitis following bilateral simultaneous versus sequential laser in situ keratomileusis

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**SCIENTIFIC REPORT**

**Aim:** To determine the difference in the incidence of bilateral diffuse lamellar keratitis (DLK) in patients undergoing simultaneous versus sequential laser in situ keratomileusis (LASIK) as an indication of intrinsic risk for inflammation.

**Methods:** A retrospective non-comparative case series of 1632 eyes that had undergone bilateral, simultaneous or sequential LASIK between April 1998 and February 2001 at a university based refractive centre by three surgeons. All cases that developed clinically evident DLK were identified and reviewed. In order to identify isolated cases and exclude those caused by environmental factors, when more than one patient in a given session developed DLK, the session was excluded. The main outcome measure was the incidence of unilateral and bilateral isolated, non-epidemic DLK.

**Results:** Of 1632 eyes, 126 eyes (7.7%) of 107 patients developed at least grade 1 DLK. In six operating sessions, DLK was observed in more than one patient per session, and on this basis 13 patients were excluded. Of the 94 remaining patients developed DLK in both eyes (17.0%). Six of 41 patients (14.6%) in the simultaneous group, versus 10 of 53 patients (18.9%) in the sequential group developed bilateral DLK (p >0.5).

**Conclusion:** In isolated, non-epidemic bilateral DLK, a similar incidence was observed regardless of whether the surgery was simultaneous or sequential, suggesting an underlying intrinsic cause for DLK.

Diffuse lamellar keratitis (DLK) is a condition described by a non-infectious aggregation of inflammatory cells in the interlamellar interface that accumulates within the first week after laser in situ keratomileusis (LASIK). This pattern of cellular infiltration along the lamellar interface has been noted not only after primary LASIK procedures, but after re-treatments or associated with epithelial defects, both traumatic and spontaneous.

Since the initial descriptions of cases of DLK, multiple aetiologies have been hypothesised. However, it is unlikely that a single causative agent might explain all cases, as it most likely represents a non-specific inflammatory response. A potential plane that persists indefinitely is created by the microkeratome, allowing inflammatory cells to migrate along this interlamellar space in response to an inflammatory event. Potential stimuli may include debris deposited by surgical instruments including the microkeratome, powder from gloves, intralamellar haemoglobin, particles from the drape, endotoxins, meibomian gland secretions, epithelial defects, and povidone-iodine solution.

It was our opinion that DLK seemed to represent a non-specific response to a wide variety of potential insults. As it has been emphasised in previous descriptions and studies, clustered epidemic cases can often be attributed to identifiable environmental causes such as endotoxins released from steric.

**METHODS**

We retrospectively reviewed the available clinical charts of all refractive surgery clinic patients who underwent bilateral, simultaneous or sequential LASIK between April 1998 and February 2001 at a university based refractive centre. Cases performed as part of an FDA study protocol were excluded, owing to variable accessibility of those records. All the surgeries were performed by three highly experienced surgeons. In order to minimise the probability of including cases in which inflammation was the result of external environmental factors, and to identify isolated cases, we excluded all patients in any operating session if more that one patient developed DLK.

Sequential surgery was defined as surgery performed on each eye on two consecutive days, while simultaneous surgery was defined as surgery performed on both eyes on the same day. In simultaneous surgery, the second eye was draped separately after completing the treatment of the first eye, and a second microkeratome and new blade used for the second eye. Before surgery, the eyelids were prepared with Betadine 5% (Purdue Frederick, Norwalk, CT, USA). The eyelashes and eyelids were isolated with a drape. A lid speculum was placed. Preoperative medication included oxybuprocaine (proparacaine) 0.5% and ofloxacin 0.3%. The surgeons and assistants wore powder-free gloves during the instrument set up and surgery. The automated corneal shaper (ACS) (Bausch and Lomb, Irvine, CA, USA) or the Moria Carriazo-Barraquer (Microtech, Doylestown, PA, USA) were used to make corneal flaps. All patients were prescribed a topical fluoroquinolone, ofloxacin 0.3% (Allergan, Irvine, CA, USA) four times a day and fluoromethalone 0.1% (FML, Allergan, Irvine, CA, USA) four times a day starting immediately postoperatively. For surgery performed sequentially, if DLK was noted in the first eye, for the second eye the frequency of topical corticosteroid application following surgery was prophylactically increased to every hour while awake until the degree of inflammation could be assessed on the first day after surgery.

For each eye in which DLK developed, we recorded the date of surgery, the grade of inflammation and whether the patient had simultaneous or sequential surgery. A $\chi^2$ test to compare proportions in each group was performed using STATA.
RESULTS
Of 1632 eyes that underwent bilateral surgery, 126 eyes (7.7%) of 107 patients developed DLK; 119 (94%) of these were categorised as grade 1 or 2 (mild DLK). In one surgical session, three patients developed grade 1 DLK (both eyes of a simultaneous case, and in one eye of two sequential cases). In five other surgical sessions, grade 1 DLK developed in two different patients (five simultaneous and five sequential). Since DLK appeared in more than one patient in these sessions, these patients were excluded from the analysis (13 patients). In all other cases, DLK appeared in only one patient of all patients undergoing surgery in that session (94 patients).

Of these 94 patients, 41 (43.6%) underwent simultaneous surgery and 53 (56.4%) underwent sequential surgery. Six of 41 patients (14.6%) in the simultaneous group, versus 10 of 53 patients (18.9%) in the sequential group developed bilateral DLK (p >0.5).

DISCUSSION
We identified isolated, non-epidemic cases of DLK, and found that some degree of inflammation appeared in both eyes in a similar proportion of cases, whether or not surgery was performed on the same day or one day apart. This observation is consistent with the hypothesis that in a certain proportion of cases, DLK can be attributed to intrinsic rather than environmental causes. It might be expected that observed DLK in one eye might lead to more careful attention to potential causes of DLK in the second eye and, as noted, patients were advised to use topical corticosteroids more frequently on the contralateral eye when surgery was applied to the contralateral eye when surgery was performed in a sequential fashion. If more aggressive corticosteroid treatment does indeed limit the severity of the DLK that is more likely to occur in the second eye if seen in the first, then there would indeed be an advantage to sequential rather than simultaneous surgery.

In summary, there was no difference in the incidence of non-epidemic, isolated bilateral DLK in simultaneous and sequential LASIK, suggesting an underlying intrinsic cause for isolated DLK. Further study is required to better define specific risk factors for the development of DLK following LASIK, and the effectiveness of various treatment strategies.

REFERENCES
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Br J Ophthalmol 2003 87: 1086-1087
doi: 10.1136/bjo.87.9.1086