ORIGINAL ARTICLE

Hyperactivity of the Inferior Oblique Muscle in the Human Eye: Histopathological Study

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Abstract

Background: Awareness of the impact of the various surgical treatments requires an awareness of a slightly different architecture of the inferior oblique (IO) muscle in comparison to the other extraocular muscles. The IO muscle's anatomy has been linked to particular clinical diagnoses in a number of investigations. **Aims of Study:** To establish a correlation between the various levels of clinical overaction and the histological alternations of the IO muscle. **Materials and Methods:** Once the clinical severity of the muscle over-action was established, 10 samples from the IO muscles were obtained during the strabismus surgery. As a control, one muscle biopsy was obtained during enucleation surgery. A light microscope was used to examine each biopsy. **Results:** Grade II and grade III IO overaction revealed numerous histological abnormalities under light microscopy, including fibro-fatty infiltrations, nerve bundle enlargement, muscle fiber degeneration, and varied muscle fiber size. Fatty infiltration, mononuclear infiltration, and perimysium and endomysium fibrosis were observed in grade III IO overaction. **Conclusion:** The clinical stages of muscle overaction are correlated with histopathological alterations in the IO muscle.

Key words: Extraocular muscle, histopathology, inferior oblique, light microscope, overaction

INTRODUCTION

Due to the anatomical differences between the inferior oblique (IO) muscle and other extraocular muscles (EOM), numerous researchers have attempted to determine the relationship between alterations in the muscle's ultrastructure and the clinical impact on its function[1]. The muscle originates in the anterior region of the orbital floor close to the edge and inserts between the inferior and lateral rectus muscles in the inferolateral quadrant of the sclera posterior to the equator[2]. The structural differences between extraocular and skeletal muscle are not surprising given the fundamental differences in function, specifically the constancy of activity (even while sleeping) and the rapidity and fine gradation of contraction of EOM required to fixate subjects of interest on the fovea. Both sets of six muscles must be extremely coordinated and operate simultaneously because both eyes must move in unison[3]. Muscle fibers, which are long, cylindrical, multinucleated cells with sizes ranging from 10 to 100 μm, make up EOM[4]. The IO overaction makes the eye elevated in adduction, both horizontally and in upgaze[5]. A typical feature of new and recurrent cases of strabismus is the overaction of the IO muscle[1]. According to a prior study, the prevalence of overreaction was over

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72% in people with infantile esotropia and above 30% in people with acquired esotropia or exotropia[6]. The basic form of IO overaction is bilateral and of unknown cause. It often causes infantile esotropia to occur after the 1st year of life, while some children also have intermittent exotropia or accommodative esotropia[7]. The secondary type, in contrast, is unilateral and is caused by paresis or paralysis of the superior oblique muscle[8]. Clinically, IO overaction can be ranked I through III. The only indication of minor overaction in grade I is the intense "up-in" gaze. The "adducted" stare is a sign of moderate overreaction in grade II. Grade III shows severe overaction, as seen in the primary gaze[9]. This study is concerned with exploring a relationship between different clinical grades of inferior oblique over-action and the structural changes in the muscle in these grades. A good knowledge of the pathological change causing the disease can help manage the condition.

MATERIALS AND METHODS

The current study included one control (one normal IO muscle) and six patients (10 diseased IO muscles) divided into three groups. Patients with grade II or grade III IO muscle over-action, diagnosed clinically and documented by the ophthalmology consultant, were included in the study. Cases with primary and secondary IO muscle over-action were also included. Patients with IO muscle weakening due to other pathologies were excluded. The patient was also excluded from the study if he had any interventions that affected the structure of the IO muscle, either accidentally or iatrogenically. The muscle sample obtained from patients who underwent enucleation eye surgery due to other pathology not related to the IO muscle was considered the control group. The second group was called Grade II IO muscle over-action. This group included four patients with six muscles; patient one participated by two muscles, patient two participated by two muscles, patient three participated by one muscle, and patient four participated by one muscle. All patients in this group had an elevation of the eye in adduction. The last group is Grade III IO muscles over-action. This group included two patients with four muscles, two from each one. All patients in this group had an elevation of the eye in the primary gaze (hypertropia).

All muscle samples were obtained from patients who were scheduled for surgery in Alex I Care ophthalmology center after clinical evaluation to determine the patient's group. The study was reviewed by the PSA University board and did not require the patient's prior acceptance, as the used muscle samples were the waste of the operation. All specimens were collected by myectomy. The degree of muscle overaction, as determined by clinical diagnosis, determined the length of the removed segment. This was always done in accordance with the surgical results of the muscle's vascularity and thickness.

Since the IO muscular belly's thickness varies, we remove the portion from the thickest region – typically the center part of the belly – during a myectomy. The removed portion

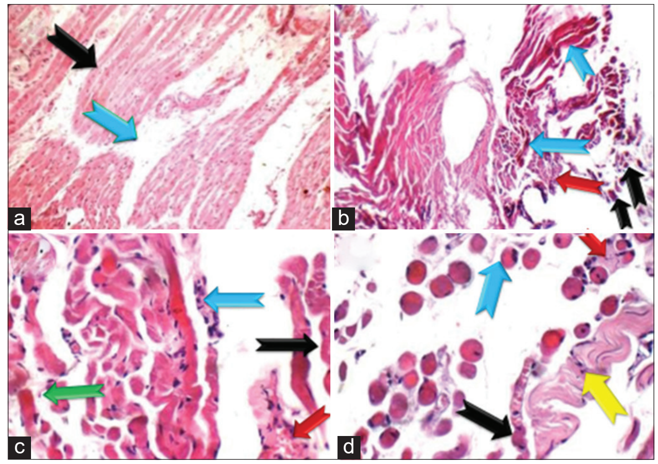

Figure 1: Different images of inferior oblique muscle stained with Hematoxylin and Eosin (a) Control group shows average fascicles of muscle fibers (black arrow) with average loose connective tissue (blue arrow) (×235). (b) Group II shows mild variability of muscle fiber size (black arrow) with scattered hyper-contracted fibers (blue arrow) and moderate perimysial fibrosis (red arrow) (×200). (c) Group II shows moderate numbers of hyper-contracted (black arrow) and fibrotic muscle fibers (blue arrow) with scattered mononuclear cellular infiltrate (green arrow) and congested blood vessels (red arrow) (×400). (d) Group III shows hyper-contracted and fibrotic muscle fibers (black arrow) with scattered regenerating fibers with vesicular nuclei (blue arrow) and marked perimysial (yellow arrow) and mild endomysial fibrosis (red arrow) (×400)

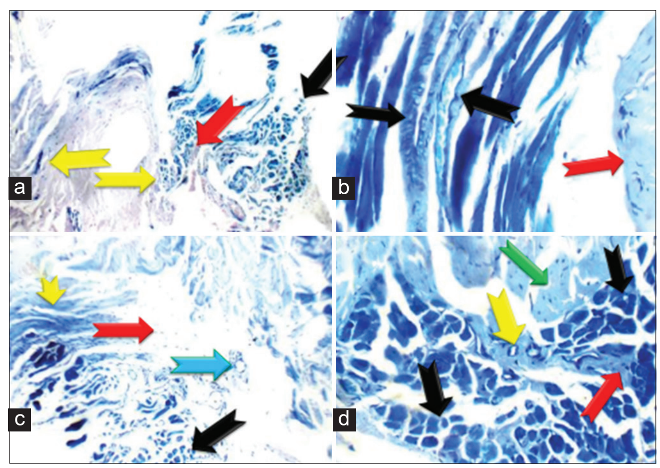

Figure 2: Different images of inferior oblique muscle stained with Toluidine blue. (a) Group II shows mild variability of muscle fiber size (black arrow) with moderate perimysial (yellow arrow) and endomysial fibrosis (red arrow) (×200). (b) Group II shows some hyper-contracted and fibrotic muscle fibers (black arrow) and moderate perimysial fibrosis (red arrow) (×400). (c) Group III demonstrates moderate variability of muscle fiber size (black arrow) with moderate perimysial fibrosis (yellow arrow), mildly dilated blood vessels (blue arrow) with mild inflammatory cellular infiltrate (red arrow) (×200). (d) Group III showing many hyper-contracted muscle fibers (black arrow) with scattered cytoplasmic vacuoles (yellow arrow), marked perimysial (green arrow), and endomysial fibrosis (red arrow) (×400)

was consistently the same during operation, ranging from 5 to 8 mm based on the clinical stage. Therefore, the excised muscle section from Group III patients were found to be 7-8 mm thick, while that from group II 5-6 mm thick, relatively thinner than group III.

All biopsy specimens were prepared and examined histopathologically. After being taken right away, the muscle samples were preserved for 24 h in 10% neutral formaldehyde. After being cut, the samples were dehydrated in increasing alcohol grades, and xylol was added as a cleaning agent. Light microscopic examination was done using both hematoxylin and Eosin and Toluidine blue stains.

RESULTS

The current study included three groups, the first one is the control group, the second one is grade two IO over-action (Grade II), and the third one is grade three IO over-action (Grade III). IO control group obtained from a case of enucleation – removing the whole eye – due to another pathology, not related to IO muscle to ensure that there were no pathological findings related to other diseases. This group showed average muscle fibers with cross striations and peripheral nuclei. The control group also demonstrated average fascicles of muscle fibers with average loose connective tissue.

This group was compared with the pathological findings in the other two groups.

This study includes 10 muscle biopsies taken from six individuals, two of whom had unilateral muscle affection and four of whom had bilateral muscle affection. Six out of 10 biopsies (60%) had grade II IO overaction, whereas four out of 10 (40%) had grade III IO overaction.

The grade II group included four patients and six muscle samples. The ages of this group (Grade II IO over-action) range from 3 to 12 years old, with a mean age of 6.5 ± 4 years and an interquartile range of 6 years. Grade III included two patients and four muscle samples. The mean age of this group is 7.5 ± 3.5 years old. The mean age of all cases (both grade II and grade III) is 6.8 ± 3.2 years old.

During histopathological examination by light microscope variations in the muscle fibers were noticed in both right and left IO muscles with mild-to-moderate percent. There were degenerated muscle fibers moderately scattered in both the right and left IO muscle samples. In addition, we found degenerated hyper-contracted muscle fibers moderately scattered in the right eye IO muscle. Control Group I shows mild variability of muscle fiber size with moderate perimysial and endomysial fibrosis in ×200 magnification [Figure 1a] Group II shows some hyper-contracted and fibrotic muscle fibers and moderate perimysial fibrosis in ×400 magnification [Figure 1b and c, Figure 2a and b]. Group III demonstrates moderate variability of muscle fiber size with moderate perimysial fibrosis, mildly dilated blood vessels (blue arrow) with mild inflammatory cellular infiltrate in ×200 magnification [Figure 2c]. Group III also shows many hyper-contracted muscle fibers with scattered cytoplasmic vacuoles (yellow arrow), marked perimysial, and endomysial fibrosis in ×400) magnification [Figure 1d and 2d]. A summary of the histopathological results is shown in Table 1.

Table 1: Percentage of histopathological findings in grade II inferior oblique overaction in comparison with grade III

Histopathological findings	Grade II percentage	Grade III percentage
Variability in the size of muscle fibers	66.6	75
Hypercontracted muscle fibers	50	75
Split muscle fibers	66.6	100
Regenerating muscle fibers	33.3	25
Degenerated and fibrotic muscle fibers	100	100
Perimysial fibrosis	66.6	100
Endomysial fibrosis	66.6	75
Congested blood vessels	50	75
Cytoplasmic vacuoles	50	50
Cytoplasmic inclusion bodies	0	10
Mononuclear cellular infiltration	33.3	25
Pyknotic nuclei	33.3	75
Vesicular nuclei	33.3	30
Hypertrophied nerve bundles	17	75
Areas of hemorrhage	0	10

DISCUSSION

This study contained 10 muscle biopsies, all of which displayed structural alterations when seen under a light microscope. Variability of the muscle fiber size was found in all the IO muscle samples either grade II or grade III over-action.[10] Similar findings were reported by a previous histopathological study for different grades of IO muscle over-actio.[10] It was noticed that the variability in the muscle fiber size was mostly mild-to-moderate in grade II whereas in grade III it was of moderate to marked degree. This was agreed with what other studies found in their study of morphological differences in the IO muscles from subjects with over-elevation in adduction.[11] They asserted that histological analysis of muscle cross-sections from people with IO muscle over-action and control revealed both qualitative and quantitative variations. Hyper-contracted and split muscle fibers came to be the second most common finding in the current study, and this is an expected finding as the majority of the muscle fibers were degenerated. Congested blood vessels represented around 60% of the total muscle samples of the current study, and this is due to muscle hypertrophy which is associated with its over-action as reported by an earlier study[11]. Taking into consideration the presence of congested blood vessels, this can explain the presence of areas of hemorrhage, which represented around 10% in the current study. Mononuclear cellular infiltration was found in around 60% of total muscle samples, both grades II and III, and this is mostly due to inflammatory response following necrosis of some fibers. Bahn reports a similar explanation in another work[12]. Cytoplasmic inclusion bodies were detected only in grade III IO over-action in the current study and this is because the degeneration process is more in grade III than in grade II. It is expected to have some pathological changes in the muscle iatrogenically induced during sample resection and preparation, although it is not so common as the biopsy can be easily taken from the IO muscle without causing any undesirable results during myectomy. This is agreed with previous research that reported the same thing in their study[13].

CONCLUSION

By discussing the results with the previous work on the same point, it was concluded that there is a relationship between the histopathological changes in the IO muscle and the clinical grades of its over-action. It is recommended to study medical ways that can stop the progression of these changes in the muscle.

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AVAILABILITY OF DATA AND MATERIALS

The data are available upon request from the authors.

ETHICS APPROVAL

All series of steps that were implemented in this study that included animal models complied with the Ethics Committee of Prince Sattam bin Abdulaziz University Institutional Review Board (SCBR-300/2024).

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