**Incidence, risk factors and management of intractable diplopia**

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Synopsis/Precis:

The incidence of intractable diplopia was 53 cases per year. The most common causes were strabismus surgery (32%), spontaneous presentation (25%), severe head trauma (8%) and cataract surgery (6%). Treatment was only successful in 54% of cases.

**ABSTRACT**

**Aims**

There is a paucity of literature concerning intractable diplopia. The aims of this study were to determine the incidence of intractable diplopia in the UK, identify the causes and any associated risk factors, establish how cases are managed and if the treatment is successful and tolerated.

**Methods**

A one year prospective observational study was undertaken via the British Ophthalmological Surveillance Unit (BOSU). This involved implementation of a reporting mechanism, which then triggered distribution of an incident questionnaire to explore clinical details concerning each case and a follow up questionnaire six months later to explore how the case had been managed.

**Results**

The incidence of intractable diplopia was between 53 and 63 cases per year. The most common preceding events were strabismus surgery (32%), none known i.e. spontaneous (25%), severe head trauma (8%), cataract surgery (6%) and vitrectomy (6%). In the at-risk age group of 7yrs and above, the incidence of intractable diplopia following strabismus surgery is 1 in 494 (95% CI; 1 in 296-790) cases. A total of 9 different treatments were used in the management, with many patients receiving between two and four different methods. The overall success rate was poor, but most effective were opaque IOL’s (86%) and opaque contact lenses (50%).

**Conclusion**

Intractable diplopia is a relatively rare, but important condition. The main risk factor is a pre-existing strabismus and careful counselling is needed when planning surgical correction in patients with no demonstrable binocular function. Treatment success of intractable diplopia is high when using opaque IOL’s, albeit with additional risk, but is often disappointing via other methods where it can be difficult to eradicate the diplopia successfully.

**INTRODUCTION**

Intractable diplopia is a condition where binocular diplopia can only be eliminated via a means of occluding one eye. It can occur in patients with strabismus where binocular vision is absent and the ability to suppress is lost, either due to a change in alignment following botulinum toxin or surgery1,2 or via reduction in the density of suppression following amblyopia treatment.3 Intractable diplopia can also present following cataract surgery where once the vision is restored, diplopia is perceived due to inability to fuse the images.4,5 Other potential causes are loss of fusion following severe head trauma and brain lesions or due to incompatibility of images after refractive surgery. The very nature of intractable diplopia means that it cannot be eliminated by surgical realignment of the eyes or correcting the angle with prisms and therefore presents important quality of life issues for the individuals affected. Elimination of the diplopic image can only be achieved by occluding one of the eyes. A variety of methods have been employed such as using occlusive contact lenses, Bangerter filters, opaque tape applied to glasses, induction of ptosis via botulinum toxin, corneal tattooing and opaque intraocular lenses.1,6-9 These methods are often poorly tolerated, may cause irritation and headaches, can be cosmetically poor or lead to corneal epitheliopathy or ulcers. At best the diplopia is resolved, but by virtue of the treatment the patient is effectively left with only one functioning eye.

Whilst it is clear that intractable diplopia would be a serious debilitating condition10,11 for those affected, little is known regarding the incidence or presentation. It is reported to be a rare occurrence, but to date there has been no prospective study of intractable diplopia. Previous studies have either reported case reports, or retrospectively provided estimates of intractable diplopia resulting from the individual treatments of adult strabismus surgery (0.8%),2 cataract surgery (accounting for 4.6% of patients who reported post-op diplopia)4 or amblyopia treatment (estimated 5 cases per year in the UK).3 Knowledge of the incidence and presentation of intractable diplopia will provide a valuable base on which strategies to prevent its occurrence can be established. Additional information about how the patients with intractable diplopia are managed and how the different treatments are tolerated will provide guidance on the most effective method to manage this condition. The aims of this study therefore were to determine the incidence of intractable diplopia in the UK, identify the causes and any associated risk factors, establish how cases are managed and if the treatment is successful and tolerated.

**METHODS**

In line with research governance in the UK, NHS R&D and institution approval was obtained prior to commencement of the study. Ethical approval was not required for this study as the research only involved the use of previously collected, non-identifiable information. A one year prospective observational study was undertaken via the British Ophthalmological Surveillance Unit (BOSU). Details of the procedures of a BOSU study have been documented previously.12 However, in summary, all consultant and associate specialist ophthalmologists in the UK are surveyed by the BOSU via a reporting card containing up to 10 rare eye conditions. When a condition is observed within that month the clinician reports the incidence of the case to BOSU, which informs the principal investigator (PI). To be eligible for reporting a case in this study, specific conditions needed to be met as defined by the authors (Table 1).

Table 1 Case Definition

|  |
| --- |
| The following needed to be met in order to be identified as a case of intractable diplopia |
| Constant binocular diplopia present in all positions of gaze |
| Absence of both fusion and suppression |
| Diplopia cannot be eliminated by surgical realignment or prisms and can only be relieved by some means of occluding either eye |
| A minimum of 3 months has occurred since the onset of the diplopia and the diplopia continues to persist |
| Diplopia resulting from acquired nerve palsies is excluded |

When notified of a new case by BOSU, the PI (DN) sent out an incident questionnaire to the clinician to ascertain if the case met the parameters of the case definition and was a new presentation, details of the event that preceded the intractable diplopia from a predetermined list with the option to add ‘other’ if necessary and non-identifying patient details to identify duplicate reporting. Respondents were also asked if there was a pre-existing manifest strabismus present prior to the onset of the diplopia. A follow up questionnaire was sent out 6 months later to enquire whether treatment had been given, if it was successful and if any complications occurred. Details of information requested via both questionnaires is given in Table 2.

Table 2

Information requested about preceding events via the incident questionnaire and information sought relating to the treatment via the follow up questionnaire

|  |
| --- |
| **Incident questionnaire** |
| **Preceding event** | **Details asked specific to each event** |
| Cataract surgery | Type (traumatic, age-related, other)How long presentAfter removal, the refractive error was corrected by IOL, contact lenses or spectaclesDetails of anisometropia after cataract removalIf a manifest strabismus occurred after the cataract removal |
| Refractive surgery | Type of surgery performedIf aim was to create monovisionDetails of anisometropia after surgery |
| Strabismus surgery | Was treatment received for primary/secondary/consecutive eso/exotropia, vertical strabismus or otherWas the risk of diplopia assessed |
| Botulinum toxin |
| Occlusion therapy for amblyopia | Was the risk of diplopia assessed and if so using the Sbisa/Bagolini filter bar, Neutral density filter bar or other |
| Atropine treatment for amblyopia |
| Severe head trauma | No further questions were asked |
| Total loss of fusion following a brain lesion |
| No known preceding event |
| Other | Asked to specify |
| **Follow up questionnaire** |
| **Information requested** | **Additional specific questions** |
| Did the patient receive treatment for the intractable diplopia | If answered no, was this because the patient did not want treatment, a decision had not yet been made or other |
| The diplopia was treated by, opaque tape/occlusion, Bangerter filters, occlusive contact lens, botulinum toxin to induce ptosis, corneal tattoo, opaque IOL, other | If more than one treatment was used indicate the order in which treatments were givenBangerter filters - strength usedIOL – type used |
| Acuity immediately prior/after the treatment | Test used |
| Was diplopia eliminated following the final treatment or just sufficient to ignore | None |

To calculate the risk of diplopia resulting from strabismus surgery, the total number of strabismus operations performed annually in those over 7 years (representing the age group at risk of intractable diplopia) was obtained from the Hospital Episode Statistics database13 of the Information Centre for Health and Social Care. Using estimates to account for the discrepancy between procedures performed in England alone versus the UK, as described previously in another BOSU study14 gave a figure of 8400 strabismus procedures undertaken annually in the UK.

**RESULTS**

**Incidence and cause**

A total of 70 cases of intractable diplopia were reported to BOSU in the one year study period. Of these 7 were misdiagnoses and 10 did not respond to the questionnaire despite further requests and attempts to obtain the data. The confirmed incidence of intractable diplopia was therefore 53 cases per year. The cases comprised of 25 males and 28 females. The mean±sd age at diagnosis was 41.1±19.8 years, range from 12 to 79 years. A pre-existing strabismus was present in 33 cases (62%). The preceding event that caused the intractable diplopia is summarised in Table 3.

Table 3 Event preceding the intractable diplopia (n=53)

|  |  |
| --- | --- |
| Event | N (%) |
| Ocular realignment  | Strabismus surgery | 17 (32.1) |
| Botulinum toxin to EOM’s | 1 (1.9) |
| Ocular surgery/ treatment | Cataract surgery | 3 (5.7) |
| Refractive surgery | 0 (0) |
| Vitrectomy | 3 (5.7) |
| Retinal detachment surgery | 1 (1.9) |
| Bilateral panretinal photocoagulation for diabetic retinopathy | 1 (1.9) |
| Amblyopia treatment | Occlusion | 0 (0) |
| Atropine | 0 (0) |
| CNS events | Severe head trauma | 4 (7.5) |
| Multiple sclerosis | 1 (1.9) |
| Subarachnoid haemorrhage secondary to PCA aneurysm | 1 (1.9) |
| Phosphomannoisomerase deficient with seizures and cerebellar ataxia | 1 (1.9) |
| Ocular disorders | Ocular trauma | 1 (1.9) |
| Corneal ulcer | 1 (1.9) |
| Optic neuropathy  | 1 (1.9) |
| Prolonged misalignment in thyroid eye disease with loss of fusion | 1 (1.9) |
| Not known (spontaneous) | 13 (24.5) |
| Other | Maxillo-facial surgery | 1 (1.9) |
| Sinus surgery and damage to EOM’s | 1 (1.9) |
| Neck injury | 1 (1.9) |

Details of those conditions where further questions were asked are given below.

**Intractable diplopia following strabismus surgery or botulinum toxin to the EOM’s (n=18)**

The procedures were to treat primary esotropia (n=12, 66%), primary exotropia (n=3, 17%) and consecutive exotropia (n=3, 17%). There were no cases of secondary strabismus or vertical strabismus. The risk of diplopia was assessed pre-operatively in 7 (39%) not assessed in 5 (28%), not known in 1 (5%) and 5 (28%) did not provide a response. An estimated 8400 surgical procedures per year for strabismus in the UK (in the at-risk age group of 7yrs and above), indicates that intractable diplopia occurs post-operatively in 1 in 494 (95% CI; 1 in 296-790) cases.

**Intractable diplopia following cataract surgery (n=3)**

The type of cataract was age-related, traumatic and secondary to retinal surgery. The refractive error following cataract removal was corrected by IOL’s (n=1) and contact lenses (n=2), with one of the latter reporting significant anisometropia of 12DS. A manifest strabismus was reported to occur in two of the three cases following cataract removal.

**Treatment of intractable diplopia**

Follow-up data was obtained for 36 cases. Of these, 24 had treatment (67%), 7 (19%) did not want treatment, 3 (8%) were yet to decide or seeking a second opinion and 2 (6%) were reported as not treatable. A total of 9 different treatments were employed, the frequency of their use and success is indicated in Table 4.

Table 4 Frequency of treatments used and success

|  |  |  |  |
| --- | --- | --- | --- |
| Treatment | Frequency used n (%) | Frequency used as first line treatment n (%) | Diplopia eliminated or ignored n (% for each treatment) |
| Yes | No | Can ignore |
| BT to EOM | 11 (23) | 7 (29) | 0 (0) | 9 (82) | 2 (18) |
| Occlusive CL | 10 (21) | 4 (17) | 5 (50) | 4 (40) | 1 (10) |
| Opaque IOL | 7 (15) | 3 (13) | 6 (86) | 0 (0) | 1 (14) |
| Strabismus surgery | 5 (11) | 3 (13) | 0 (0) | 5 (100) | 0 (0) |
| Prisms | 5 (11) | 3 (13) | 2 (40) | 3 (60) | 0 (0) |
| Opaque tape/occlusion | 4 (9) | 0 (0) | 0 (0) | 3 (75) | 1 (25) |
| Bangerter filter | 3 (6) | 3 (13) | 1 (33) | 2 (67) | 0 (0) |
| BT to induce ptosis | 1 (2) | 1 (4) | 0 (0) | 1 (100) | 0 (0) |
| High powered lens | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 1 (100) |

Many patients received more than one treatment in order to achieve success or find a treatment that could be tolerated, hence the number of treatment types and frequency used far exceeds the number of patients that received treatment. The number of different treatments that patients received ranged from one to four, with those willing to try multiple options achieving greater success (Table 5).

Table 5 Number of treatments received and success

|  |  |  |
| --- | --- | --- |
| Number of treatments | Cases n (%) | Diplopia resolved n (%) |
| Yes  | No  | Can ignore |
| One | 10 (42) | 3 (30) | 4 (40) | 3 (30) |
| Two | 8 (33) | 4 (50) | 2 (25) | 2 (25) |
| Three | 5 (21) | 5 (100) | 0 (0) | 0 (0) |
| Four | 1 (4) | 1 (100) | 0 (0) | 0 (0) |

Overall of the 24 patients that received treatment it was successful in 13 (54%), failed in 6 (25%) and diplopia still present but could ignore in 5 (21%). Complications were reported in 5 (21%) patients: 3 following opaque IOL’S (1 needed surgical repositioning as the claw detached from the iris, 2 had post-op uveitis), 1 following opaque contact lens had difficulty tolerating in summer with hay fever and 1 following BT to the EOM’s, but the nature of the complication was not provided.

**DISCUSSION**

To our knowledge this is the first prospective multicentre study of the incidence and management of multicausal intractable diplopia. We found an incidence of 53 cases of intractable diplopia per year in the UK with a range of preceding events, most commonly ocular realignment, ocular surgery/treatment, CNS events and spontaneous presentation with no known cause. The diplopia was managed via a variety of methods, which often required multiple techniques to eradicate the diplopia. The study had some limitations due to missing data resulting in an unknown diagnosis in 10 (14%) of the 70 cases reported and there is no known data available to provide a denominator for the incidence following cataract surgery or severe head trauma. However, this study provides data via nationwide case ascertainment, using a robust and well-established methodology ensuring validity of the data obtained. Previous studies in this field have either used case reports1,15 or retrospective reviews of intractable diplopia that has occurred following a single specific treatment.2-5

Our study found that the most common event preceding the onset of intractable diplopia was strabismus surgery, accounting for almost a third of cases. This is reflected in the albeit, sparse literature with six out of the eight cases reported by Gruzensky and Palmer occurring following strabismus surgery.1 These were selected cases though and therefore does not provide a reliable indication of incidence. The only other study exploring intractable diplopia after strabismus surgery, reported an occurrence of 3 cases from 424 patient records (0.8%).2 This is greater than our finding (0.2%, 1 in 494), but is difficult to compare given the estimate was derived from retrospective medical records of a single surgeon. Of the 424 patients in their study, 143 experienced diplopia when corrected using prisms in the post-operative diplopia test (PODT). After surgery, 40 had temporary diplopia with only 3 suffering from intractable diplopia. Estimating the risk pre-operatively therefore can be unreliable and may explain why this assessment was only undertaken in 39% of cases in our study. It should be noted however, that whilst this study demonstrated the PODT had a lower than desirable specificity (68%), the sensitivity was actually 100%.

Other causes found were as a result of head trauma, which has been reported previously in isolated cases,16 vitrectomy of which we are not aware of previous cases and following cataract removal. The diplopia following cataract removal appeared to be as a result of an induced strabismus or anisometropia (and subsequent aniseikonia). Strabismus (25% of cases) and anisometropia (8.5%) has also been reported to be the cause of intractable diplopia following cataract removal in a recent retrospective review.4 We did not find any cases following amblyopia treatment which is surprising given our previous reports estimating an occurrence of 24 cases in a five-year period in the UK.3 There may be several reasons to explain the absence of this cause in our study. In 25% of cases the intractable diplopia occurred spontaneously without any obvious preceding event. However, all of these cases had a history of a pre-existing strabismus. Given that they had no fusion, it is likely that the onset was early within the critical period and most likely had received amblyopia treatment as a child, though this is unknown. The risk of amblyopia treatment as a cause of intractable diplopia may therefore only present later in life. Identification of cases was undertaken by senior ophthalmologists using the BOSU reporting system. It is possible that cases due to amblyopia treatment were missed as they may have been seen solely by orthoptists in orthoptic-led clinics. Another reason may be that the effective vision screening procedures in the UK results in far fewer children receiving treatment at an older age. This may of course change given recent reports indicating greater plasticity of the visual cortex17 and treatment being considered to remove suppression in adults.18

A variety of methods were employed to try to successfully manage the intractable diplopia. The success in adequately eliminating diplopia via a means that could be tolerated was disappointing. Of the nine methods employed, only opaque IOL’s were successful in the majority of patients, though this method also had the highest rate of complications. Finding a method of eliminating the diplopia is therefore difficult and over half of the patients received multiple different methods to try to find an approach that was successful and acceptable. It is surprising that some methods used such as prisms, strabismus surgery and botulinum toxin to the EOM’s were attempted given our definition that generally some form of occlusion is the only way to eradicate intractable diplopia. It is possible that these methods were used prior to the diagnosis of intractable diplopia being made but we consider this is unlikely for two reasons. Firstly, the questionnaire clearly asked for the methods that were used to try to treat the intractable diplopia and secondly, some of these methods have been reported to be used in other studies.7 Our findings are comparable to others, where patients have tried strabismus surgery, occlusion, opaque contact lenses, induced ptosis via botulinum toxin and found all methods to be either ineffective or unacceptable.7 We found opaque IOL’s to be by far the most successful method (diplopia eliminated in 86%) and is reasonably comparable to a survey of ophthalmologists, that reported 67% of patients were asymptomatic on discharge following this procedure.9 Satisfaction with this treatment has also been documented via the Visual Function Index (VF-14),19 where 12 patients unresponsive to Blenderm/Bangerter filters, Fresnel prisms, occlusive contact lenses, botulinum toxin and strabismus surgery, received opaque IOL’s and had a mean post-operative VF-14 score of 91 out of 100.6

Intractable diplopia is a relatively rare condition, but if it occurs has substantial QoL implications for individuals,10,11 either via the condition itself or via the treatment which generally involves rendering the patient monocular and it is difficult to achieve patient satisfaction. A careful pre-operative examination may help to reduce the risk though its onset can also be unpredictable.2 Though no cases of intractable diplopia were identified in this study to be directly attributable following amblyopia treatment, cases have been reported in the literature and future management using emerging treatments to actively remove suppression may need careful patient selection to avoid the risk of inducing intractable diplopia. Management of intractable diplopia can give disappointing results, many options fail to yield satisfaction though opaque IOL’s seem to be the most reliable and favoured by patients.

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