

Strabismus and Amblyopia: Recent Advances.

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Abstract: *Strabismus is a challenging field of ophthalmology. A good amount of progress has been made in understanding the pathogenesis of various types of strabismus and surgical techniques are being continuously modified to incorporate the new information. All efforts are directed to the attainment of the ultimate goal of binocularity and stereopsis. Recognition of the importance of early correction of infantile esotropias, the interaction of genes and environment, measuring distant stereo-acuity in intermittent divergent squints to check for deterioration of control, are recent applications. Topical anaesthesia is increasingly being used to allow early titration of adjustable sutures. Newer kinds of bioadhesives are being tried out and computer simulation models help improve surgical outcome. Different kinds of weakening procedures on the inferior and superior oblique muscle are now known to give desired results. The congenital cranial disinnervation disorders (CCDDs) is a group of disorders resulting from aberrant innervation of the ocular and facial musculature, including Duane syndrome, congenital fibrosis of the extraocular muscles (CFEOM), Möbius syndrome etc. Surgical management in Duane's has now progressed beyond limiting cocontraction, to improving abduction, by transposition of vertical recti as is true for Abducens nerve palsies. Oculomotor nerve palsies are being tackled with periosteal anchoring of the globe and lateral rectus. An improved, but still inadequate understanding of nystagmus, helps improve head posture in most cases. Mention is also made of some ongoing studies designed to address issues of public health importance in the context of strabismus and amblyopia.*

INTRODUCTION

Our understanding of the physiological processes concerning vision and ocular alignment are constantly being revised in the light of newer information. This paper reviews the current concepts of etiopathogenesis of abnormalities of the motor, sensory and cortical mechanisms, and the modalities available to correct them with special emphasis on the commonly performed surgical procedures. Mention is also made of some ongoing studies designed to address issues of public health importance in the context of strabismus and amblyopia.

ETIOLOGY

An increased risk of early onset strabismus, especially infantile esotropia, accommodative esotropia, and exotropia, both intermittent and constant, has been related to prematurity, family history, refractive error, poor neurodevelopmental error or ROP. Structural anomalies may also be a factor. However, their relative importance is not settled. Sensory deprivation of congenital origin tends to cause esotropia, whereas acquired sensory deficits more commonly result in exotropia. Infantile esotropia has been blamed on a defect in cortical fusional mechanism and overzealous convergence mechanism, and a theory combining the two has been proposed. While twin studies have highlighted the role of genetics, studies showing discordance in monozygotic twins with only one of the twin having features of infantile esotropia emphasize the role of environmental factors¹. Siblings of children with accommodative esotropia have a high prevalence of amblyogenic risk factors. The characterization of nystagmus has improved, but the comprehension of the underlying oculomotor control process still remains elusive. Binocular coordination of saccades has been shown to improve after strabismus surgery in children. Amblyopia is known to mainly affect the parvocellular pathways, but controversy exists regarding, among others, the best modality of treatment, and the upper age limit for it. Newer information on the anatomy of the inferior oblique, changes in rectus extraocular muscle pulleys following surgery and pathophysiology of superior oblique muscle myokymia has become available.

The Congenital cranial disinnervation disorders (CCDDs) is a group of disorders resulting from aberrant innervation of the ocular and facial musculature. They generally arise from abnormal development of individual or multiple cranial nerve nuclei or their axonal connections.

Although the majority are either proven or suspected to have a genetic etiology, phenocopies occur. The CCDDs include Duane syndrome, congenital fibrosis of the extraocular muscles (CFEOM), Möbius' syndrome, Horizontal Gaze Palsy with Progressive Scoliosis (HGPPS), the Bosley-Salih Alorainy/Athabaskan Brain-stem Dysgenesis Syndromes (BSAS), and an expanding list that may include congenital third and fourth nerve palsies, Marcus Gunn jaw winking ptosis, and others².

ESOTROPIA

It is known that stereopsis develops at 3-5 months of age. Early surgery for congenital esotropia, definitely results in improved binocular vision if performed before 2 years of age, but whether the same benefit accrues if surgery is performed before 1 year of age has not been resolved. The factors that are thought to determine binocularity are the duration of misalignment, the age of alignment, postoperative microtropia, and associated motility disorders. The duration of misalignment being less than one year is definitely correlated with better binocular outcome. This implies that it is not just enough to operate early but to ensure proper alignment early. The optimum result is the monofixation syndrome within 8 prism diopters of orthotropia with or without binocularity. In acquired esotropia of adult onset, delayed surgery does not result in adverse outcome with respect to binocular status as compared to early surgery.

Residual dynamic stereopsis in the peripheral visual field has been reported in esotropes and exotropes who lacked central static stereopsis, and this improved in 56% of the patients after strabismus surgery, either through a significant gain of stereoactive fields or through a decrease in threshold values.

EXOTROPIA

In intermittent exotropes, middle and distance stereoacuity are affected more than near stereoacuity. Superior surgical results have been reported with timely surgery, the criteria being intermittency, duration of less than 5 years, and alignment before the age of 7 years. Postoperative adjustment of innervations may be an important factor. Improvement in distance stereoacuity measured with both the FD2 and the Distance Randot stereotests in patients who underwent surgery for intermittent exotropia has been found. The FD2 and Distance Randot may be useful outcome measures in future clinical trials of interventions for intermittent exotropia³.

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Consecutive exotropia occurs more commonly in the presence of deep amblyopia, and long term follow up is required. It may or may not require surgery, the determining factor being the sensory status. The likelihood of postoperative diplopia, if such did not exist preoperatively, is rare, and could be assessed in some patients with prism test, but its management can be difficult.

TREATMENT OF STRABISMUS

That there are definite positive psychosocial outcomes of correction of strabismus and amblyopia has been emphasized in recent publications, and the term 'cosmetic' in the context of strabismus surgery is no longer tenable⁴. A more appropriate term, 'reconstructive surgery' has been suggested, since the process involves re-establishing the natural alignment and not just changing cosmesis. An interesting study done in children, shows that they can discriminate strabismus even in dolls that they play with, and actually become abusive against such dolls as early as 5 years of age. This highlights the negative influences that an uncorrected strabismus has on their psyche.

Our current knowledge suggests that amblyopia is best treated with full time occlusion therapy, although certain drawbacks are known. It has been suggested that all forms of amblyopia need not be treated fully before surgical correction, provided amblyopia therapy is continued post operatively. But such study should not change our concept of correcting the amblyopia, if treatable, before surgery as experience has taught us. The role of levodopa-carbidopa has been reported as a facilitator of amblyopia therapy. A recent study emphasizes that it does not have a significant incremental effect on occlusion alone, but it does seem to increase the risk of occlusion amblyopia, so caution needs to be exercised.⁵ Dissociated vertical deviation occurs in almost all patients with surgically treated congenital esotropia, and its development was found not to be related to the timing of surgical intervention during the first 24 months of life. In intermittent exotropia, overcorrection following both combined recession-resection and bilateral lateral rectus recession on postoperative day 1 resulted in better alignment at 1 year. For convergence insufficiency exotropia, medial rectus resection with adjustable suture with post operative overcorrection is effective in avoiding long term undercorrection. Reports are available on long term (upto 15 years) outcome of surgery for the near angle in patients with accommodative esotropia and a high accommodative convergence to accommodation ratio, but the advisability of surgery for this condition is controversial.

ROLE OF ANESTHESIA

Recent interest has focused on the role of topical anesthesia for surgery, and also post operative suture adjustment, even for pediatric patients. In a pilot study, Ropivacaine was reported to reduce the pain of postoperative suture adjustment, without affecting the ease of adjustment itself or the final outcome. Post operative adjustment of sutures has also been performed immediately at completion of surgery with co-maintenance of anesthesia using propofol and midazolam. Lidocaine jelly in combination with intravenous nalbuphine is an effective topical anesthesia strategy that provides for the patient's comfort and the surgeon's ability to fine-tune ocular alignment on the operating table⁶. Deep topical fornx nerve block versus peribulbar block in one-step adjustable-suture horizontal strabismus surgery. In one study, retroequatorial myopexy (Faden) was associated with more post operative vomiting in children.

SURGICAL TECHNIQUE

The techniques for exposure have been described elsewhere. The dose-response curves/tables commonly referred to are retrospective, and are to be used as a guide only. The surgeon's learning effect is an important factor. The surgical procedure needs to be decided on an individual basis, and should be aimed at symmetrizing the perceived defect. The considerations for surgery in children are different from those in the elderly, and the same has been highlighted.

Several studies have reaffirmed our time tested beliefs. The effect of surgery is greater in infants and adults, for recessions than resections, for larger deviations, and in the presence of restrictions. Results are unpredictable in strabismus with amblyopia, especially if the deviation is of long duration. In the presence of both horizontal and vertical deviations, the greater deviation is to be corrected first. A combined recession-resection procedure in one eye gives added effect, with a minimum procedure giving 20-25 pd of correction, and a maximal procedure giving 40-60pd. A bilateral recession can correct from 15-20pd upto 50 pd of deviation. As a general rule, both recession and resection on the vertical recti are more effective and more predictable than those on the horizontal recti. Medial rectus recession is more effective than lateral rectus recession, and the range for it is 3-8mm. However, our preference for the upper limit is 5.5 mm for infants and 6mm for adults, and we reserve the larger amounts for special situations only. Lateral rectus recessions are performed from 5-12 mm. But again our upper limits are 7.5 and 9 mm, respectively, for infants and adults. Resections that are recommended are 4-8mm for medial rectus, 4-10mm for lateral rectus, and 2-5 mm for the vertical recti, with or without advancement. A hang back technique is particularly useful in children and in the presence of smaller globes, myopia and collagen vascular disease. A common example is two muscle surgeries for congenital esotropia, comprising either a recession of the medial recti of 3-7 mm, or a hang back recession. The upper limits of both recession and resection for vertical recti are 5mm. Guidelines for intraoperative measurements in relation to horizontal extraocular muscle surgery, and the factors influencing the outcome, have been published.

Additional procedures that can be performed along with are slanting, differential slanting of two halves of the muscle, retroequatorial myopexy with or without an adjustable, and vessel sparing procedures to minimize the risk of anterior segment ischemia. Further refinements in techniques, such as the use of augmented rectus muscle transposition surgeries, wherein 75% of the muscle is transposed with or without a posterior fixation suture, for complex strabismus have also been described.

ADJUSTABLE SUTURES

A reappraisal on adjustable sutures, including a technique named the ripcord, commented on its usefulness for concomitant deviations, whose anatomical substrate is unpredictable, with the final position being determined by applying both subjective and objective tests at the time of adjustment. In general, the best results are obtained when the tunnels are shorter, perpendicular to the insertion, and in the plane of muscle action. The use of larger needles and hyaluronate may facilitate the procedure. The adjustment may be done immediately at the completion of surgery, and upto 24 hours, as no significant difference was observed between adjustments done 6 hours or 24 hours postoperatively. The risk of vasovagal attack at the time of suture readjustment has been found to correlate with an intraoperative fall in heart rate by 10%. The strongest criticism of the adjustable technique is that no long term prospective studies are available. The indications, effectiveness and results of the inverse Knapp procedure have also been reviewed.

OBLIQUE MUSCLE SURGERY

An inferior oblique weakening viz, myectomy can correct 11.5 prism diopters (pd) of hyperdeviation, and reduce excyclotorsion. Disinsertion of the inferior oblique for superior oblique palsy is also effective. But it is the graded inferior oblique recessions that are more commonly performed, and includes recessions of 6-10mm, with or without anterior positioning at stations +2 through 0 to -2. Efficacy of inferior oblique anterior transposition placement grading for dissociated vertical deviation has been reported. Variants of this technique are true and pure anterior positioning, determined primarily by whether a torsion or vertical deviation is the greater abnormality. A combined procedure on the inferior and superior oblique is required to correct vertical deviations that exceed 25pd. Weakening all four oblique eye muscles for dissociated vertical deviation has been recently suggested.

It is important to bear in mind, however, that the practical limits for tolerance of torsion is limited to about 4 degrees, and that for cyclofusion about 11 degrees only, and therefore surgery should be performed in a manner such that the torsional deviations are not unduly changed.

A new procedure for absent superior oblique following a partially successful recession of the antagonist inferior oblique has been described. The inferior oblique was detached and transposed to a new insertion in the inferior nasal quadrant that effectively converted it from an extorter and elevator of the globe to an intorter and depressor. Inferior oblique strengthening in general is not effective and not recommended. Graded recessions of the superior oblique muscle, including asymmetric hang back, superior oblique tendon elongation with silicone band, autogenous fascia lata⁷ have been analyzed of their effects upon its vertical, torsional and horizontal force components.

Posterior tenectomy of the superior oblique selectively affects the functions of the superior oblique muscle and weakens the depression and abduction action while sparing the torsion, except possibly in down gaze and is ideal for patients with mild to moderate superior oblique over action with minimal torsion⁸.

Among the suture materials, Vicryl is the least slippery and is the one used most often, but Biosorb -C and Dexon-S are also in use. Some authors have advocated the use of nonabsorbable sutures to reduce the incidence of scar remodeling, which has been seen at re-exploration and is thought to contribute to variability of results of strabismus surgery. The factors responsible for resurgeries are manifold, and their management has been reviewed.

Strabismus is a common accompaniment of craniofacial dysostosis, and tends to be of a complex nature. V-patterns and oblique dysfunction are common, and do not respond satisfactorily to surgery.

PARALYTIC STRABISMUS

The problems of surgical management of paralytic strabismus have been highlighted. In sixth nerve palsy, the modified transposition procedure that joins lateral strips of the vertical recti and sutures this junction to the lateral rectus muscle, compared favorably to the classic technique of Hummelsheim. An improvisation is an augmented vertical muscle transposition that avoids scleral stitches, which is less time consuming, and carries less operative risk and trauma. An augmented Hummelsheim procedure, with or without adjustable sutures, has the advantages of less tissue damage and vessel sparing. Success has also been reported with the split rectus muscle modified Foster procedure, whereby posterior fixation sutures are applied 8mm behind the insertion.

Congenital third nerve palsy is as much a challenge for surgical correction as it is for amblyopia. A simplified procedure of superior oblique transposition and superior oblique fixation to the nasal periosteum for third nerve palsy, and an anterior translocation of the superior oblique tendon have been found to be safe and effective. The use of a nonabsorbable polyester suture to anchor the globe to the nasal periosteum is an additional technique that holds promise to align the eyes in the primary gaze⁹.

Lateral rectus muscle disinsertion and reattachment to the orbital wall to absorb its force and thus remove abduction torque is another surgical procedure for restoring ocular alignment patients with third cranial nerve paralysis and Duane syndrome with severe exotropia. Additional surgery to bring the eye to the midline included medial rectus resection, medial transposition of the vertical recti, and passive suturing of the eye to the medial orbit wall¹⁰.

The augmented Knapp procedure with superior posterior fixation suture is the preferred surgical treatment for patients with DEP¹¹.

RESTRICTIVE STRABISMUS

In Duane's syndrome with esotropia, transposition of both vertical rectus muscles to the lateral rectus muscle with a posterior lateral augmentation (Foster) suture placed in each transposed muscle obtained improved head

position and better alignment in primary position and had a reduction in the incidence of reoperation for undercorrection. A modified method of augmentation has been described by the use of a single lateral fixation suture of 5-0 polyester that incorporates the muscle bellies of both vertical muscles. The lateral rectus muscle can be disinserted and attached to the lateral orbital wall¹². The subject of resection has been addressed but it remains controversial.

Management of vertical deviations after vertical rectus transposition surgery in patients undergoing VRT for esotropic Duane syndrome involves recession of one of the transposed muscles¹³.

Superior oblique tendon elongation, using a silicon tendon expander, has been shown to be effective for Brown's syndrome.

In a comparative evaluation it was seen that while both silicon expander and translational recession effectively weaken the superior oblique and collapse the A-pattern strabismus, the latter is more effective and has a much more significant torsional effect.

The surgical management of strabismus in Graves' ophthalmopathy and following retinal detachment surgery has been reported to be successful. Enhancing procedures such as recession of the conjunctiva and Tenon's capsule are especially useful in these cases. The relaxed muscle technique provides excellent ocular alignment and relief from diplopia in a majority of patients with Thyroid Related Ophthalmopathy (TRO) associated strabismus¹⁴.

NYSTAGMUS

The role of auditory biofeedback has been found to be useful in management of nystagmus. The surgical management of congenital nystagmus continues to evolve. Kestenbaum's surgery gives a correction of approximately 1.5 deg/mm, and a dosage of 2/3rd of the horizontal head turn (HT) in each eye has been recommended. The Modified Anderson procedure for correcting abnormal mixed head position, artificial divergence surgery, and shifts of the horizontal recti for correcting a torsional component have also been reportedly successful.

Periodic alternating nystagmus is a condition which responds to retro-equatorial recessions of all four horizontal recti as seen in a case of post-traumatic acquired PAN which did not respond to Baclofen therapy.

Simple tenotomy of all four horizontal recti with reattachment at the original insertion in patients with infantile nystagmus syndrome does lead to some improvement in foveation over a broadened visual field¹⁵. Less commonly encountered conditions are strabismus surso-adductorius, which is managed with graded inferior oblique recession, with low incidence of undercorrection, chronic progressive external ophthalmoplegia, which may require adjustable sutures for a successful outcome, and convergent strabismus fixus, which usually requires bilateral recession-resection surgery. A snapped inferior rectus muscle, such as during detachment surgery, may be managed with a total anterior transposition of the inferior oblique muscle.

OTHER DEVELOPMENTS

The role of corneal laser surgery in patients with strabismus is not defined at the moment, although preliminary reports suggest that it may be a viable option, at least in the short run. Two other entities that have found emphasis recently are diplopia after cataract surgery, and sensory aberrations following macular translocation surgery. Diplopia may result from myotoxic effects of local anesthetics, muscle injury caused by a bridle suture, alteration in binocular vision (amblyopia, previous strabismus or long sensory deprivation), refractive alterations and previous disease. This can be difficult to treat. Sensory problems concerning subjective cyclorotation and vertical deviation resulting in diplopia have been reported following macular translocation in the treatment of age related macular degeneration. Surgery for cyclotropia may be useful as a secondary procedure. But in either case, the role of strabismus surgery is still

undefined. Strabismus surgery has been performed in conjunction with phacoemulsification also. The role of antibiotics, steroids and NSAIDs in the perioperative period has been studied, and it has been found that NSAIDs have an efficacy which is comparable to that of steroids.

ADJUVANTS

The newer surgical adjuvants include ADAL-1, fibrin glue and an experimental agent, ADCON-L. ADAL-1 bioadhesive is said to be equivalent to Dexon 6/0 suture group in terms of resistance to traction force between muscle and sclera one week after surgery. It is being evaluated as an alternative to sutures in strabismus surgery, since it gives a rapid and efficient adhesion between muscles and sclera and is well tolerated by the ocular tissues. Experimental use of a gel consisting of a polyglycan ester in a gelatin matrix (ADCON-L) prevents adhesions and allows post operative suture adjustment. The other materials that have been used to reduce post operative adhesions are sheets of silicon and PTFE. These are inserted between muscle and sclera. Other materials include viscoelastics like hyaluronate, and antiproliferative agents like Mitomycin C and Daunorubicin. Fibrin glue has been reported to be as effective as vicryl for conjunctival closure.

Botulinum toxin, with or without prisms, has been found to be of benefit for the management of sixth nerve palsy, diplopia, and may even obviate the need for surgery. It has been used with success in infantile esotropia upto 7 months of age, but since general anesthesia is required the supposed benefits are marginal. Free mucosa transplant in the correction of extreme deviations of exotropia has also been described.

A pilot trial of bupivacaine injection into the lateral rectus as a method of enlarging and strengthening the muscles to treat comitant esotropia, showed improved eye alignment¹⁶.

COMPLICATIONS

The complications that have been emphasized recently are endophthalmitis after pediatric strabismus surgery, which is usually caused by virulent organisms and has a poor prognosis, and globe perforation. The latter has been related to limbal traction sutures, use of scissors, operations on previously operated eyes, and operations by trainees. The use of spatulated needles has been found to be a safe and effective remedy. Slipped and lost extraocular muscles can be difficult to retrieve, but it has been made easier with the use of imaging and combined approach with an ENT surgeon, using image guided technology and transnasal endoscopy. The effect of strabismus surgery on the corneal endothelium has been studied retrospectively, but and no long term studies are available. Anterior segment ischemia and retinal detachment has been noted after vertical muscle surgery with lateral fixation sutures. Scleral dellen cans also form.

NEWER ADVANCES

A report on virtual eye muscle surgery based upon the *integration of biomechanical muscle data into a computer model* has been shown to be useful for the virtual reality training for the surgery of human eye muscles. This applies specially for models of children aged 1 to 3 and may be helpful for evaluation of the quality of specific techniques for eye motility surgery, like optimized transposition surgery of the superior oblique muscle. Feasibility of electrically stimulating the lateral rectus muscle to recover its physiologic abduction ability in cases of complete sixth cranial (abducens) nerve palsy has been recently proven in the feline lateral rectus muscle model¹⁷.

Evaluation of the *ultrasound biomicroscope* and the *laser-solder repair* technique for possible application in strabismus surgeries are being evaluated.

The *50-MHz UBM* can accurately measure the horizontal EOM insertion distances from the limbus for muscles in patients that had previous surgery¹⁸.

Experimental studies show that vascular microdissection that spare the

anterior ciliary arteries, even when 3 to 4 recti are operated simultaneously, result in less anterior segment ischaemia. However, hemodynamic changes on the color doppler imaging have been seen in the ophthalmic artery after operation on two or more horizontal recti of the same eye.

Several systems are in use for the assessment and management of squint and amblyopia. Their drawback is the lack of standardization and rationalizing, especially when used to screen infants and children for amblyopia and strabismus. Recent studies include 'The vision in preschoolers study (VIP STUDY)', and the 'Screening for studies on nystagmus and strabismus', and the Amblyopia treatment trials.

The Amblyopia Treatment Studies compared the gold standard of prescribed full-time patching to several less intense prescribed patching regimens and to the use of atropine penalization. The Amblyopia Treatment Study 1 reported that 6 or more hours of daily prescribed patching was equivalent to daily atropine penalization in the treatment of moderate amblyopia. The Amblyopia Treatment Study 2 indicates that fewer hours of prescribed patching may be as effective as full-time occlusion. Furthermore, atropine penalization seemed to lead to similar success compared to moderate patching regimens. In some cases, even older children aged 7 to 18 years who presented with amblyopia responded to therapy¹⁹. Weekend atropine may be another alternative and can improve visual acuity in children 3 to 12 years of age with severe amblyopia¹⁹. The Vision in Pre-schoolers Study found that when the best screening tests were used by highly skilled personnel (optometrists and ophthalmologists experienced in working with young children), approximately two thirds of children with one or more VIP targeted disorders and 90% of those children with the most important conditions were identified. Specially trained pediatric nurse and lay screeners performed effectively when using selected vision screening tests to identify preschool-aged children in need of a comprehensive eye examination²⁰. Visual screening at the time of vaccination has been found to be a viable strategy, and may be especially relevant in the Indian scenario.

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