"PREVALENCE OF OCULAR SIDE EFFECTS OF DEFLAZACORT TREATMENT IN DUCHENNE MUSCULAR DYSTROPHY, A ONE YEAR HOSPITAL BASED CROSS-SECTIONAL STUDY"

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This is to certify that the dissertation entitled **"Prevalence Of Ocular Side Effects Of Deflazacort Treatment In Duchenne Muscular Dystrophy, A One Year Hospital Based Cross-Sectional Study"** is a bonafide research work done by **REG NO: (BK0115002).**

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LIST OF ABREVIATIONS

AC	-	Anterior Chamber
ACG	-	Angle Closure Glaucoma
CACG	-	Chronic Angle Closure Glaucoma
DMD	-	Dunchenne Muscular Dystrophy
DFZ	-	Deflazacort
IOP	-	Intra Ocular Pressure
LE	-	Left Eye
Mm hg	-	Millimeters Of Mercury
Min.	-	Minutes
NCT	-	Non-contact Tonometer
NO.	-	Number
PCIOL	-	Posterior Chamber Intra Ocular Lens
PI	-	Peripheral Iridectomy
POAG	-	Primary Open Angle Glaucoma
Post-op	-	Post-Operative
RE	-	Right Eye
VA	-	Visual Acuity
Vn	-	Vision

ABSTRACT

Background & Objectives – Duchenne muscular dystrophy (DMD) is the most common hereditary neuromuscular disease with an incidence of 1 in 3,600 live born infant boys. Corticosteriods form the mainstay in the medical management of this disease , initially prednisolone was used but due to a large number of systemic and ocular side effects Deflazacort treatment was initialted. Deflazacort is a third generation of corticosteriod and not much is researched from ophthalmic point of view. The prevalence and association of ocular side effects in these patients was the mainstay of the study

Methods - Cross sectional one year study was conducted in JNMC, Belagavi. 50 diagnosed patients with Duchenne muscular dystrophy were taken up for the study using 0.9 mg/kg of Deflazacort on daily basis and a complete ocular examination was performed along with intraocular pressure. The different findings were associated with the age and duration of treatment with Deflazacort using SPSS software for its statistical analysis.

Results –A a total of 50 patients were tabulated, The mean age of the patients were 8.78 years & the mean age of diagnosis of DMD is 7 years . Thirty two percent (16/50) had cataract (Posterior subcapsular cataract) in both eyes. One – ten months on treatment 16 (32%) patients , 11- 20 months is 15 patients (30%) and beyond 21 months is 19 patients (32.21%) had Posterior subcapsular cataract. The average intraocular pressure in both eyes is 13.2 and 14.01 mm of mercury respectively.

Conclusion :- Evaluating the ocular side effects of Deflazacort in patients diagnosed with Duchenne muscular dystrophy (DMD) and we found very strong association of

the incidence of cataract (PSC) with the consumption of this drug . Deflazacort keeps the patients intraocular pressure within normal limits and reduces the incidence of glaucoma induced by corticosteroids as compared to Prednisolone. The presence of cataract causes visual debilitation in the patients. Hence there is a need for surgical intervention to restore the vision. In the future the patients will progressively lose vision and will need more vigilant ophthalmic follow ups.

Keyword duchenne muscular dystrophy, steriod catarct , Posterior subcapsular catarct.

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INTRODUCTION

Duchenne muscular dystrophy is an X linked disease affecting 1 in 3600-6000 live male births making is a rare disease[1]. Affected individuals have mildly delayed motor milestones and most are unable to jump and run due to proximal muscle weakness and this results in the use of Growers manoeuvre when raising themselves from the floor. Most patients are diagnosed with the same at 5 years of age, when their motor milestones are delayed from the rest of their peers. If this disease goes untreated the muscular strength will reduce and the children will take up to the wheelchair before the second decade of life[2]. Mean age of death is around 19 years of age and its mostly due to respiratory, orthopedic, cardiac complications. DMD occurs due to mainly deletion in the Dystrophin gene (DMD; locus Xp21.2)[3-4]. Mutations lead to a defect or absence in muscle Dystrophin and this leads to rapid muscle degenerations causing loss of independent ambulation by the age of 13 years[1]. Milder allelic forms also exist known as Becker dystrophy where ambulation is lost at a much later phase of life that is after the age of 19 years[5-6]. After many animal models of therapeutic strategies human trails have been started leading to the hope of finding a definitive treatment for this incurable disease. Although the definitive treatment has not been reached the diagnosis is rather become swift and interventions targeting the complications and manifestations have led to improvement in the overall quality of life health and longevity with life expectancy reaching the 4th decade of life. There are various treatment modules that have been practiced with corticosteroids such as prednisolone with preserves muscle function in DMD but its mechanism of action is not known and the side effects make it a less favorable choice when it comes in array of the other corticosteroids that can be used such as Deflazacort.

Since Deflazacort, Methyloxazoline derivative of prednisolone, Deflazacort (DFZ), is a third generation corticosteroid it still has most of the side-effects shown by steroid which is known to cause ocular side effects such as cataract and glaucoma[7].

With the prolonged life long use of deflazacort for an improved quality of living , the incidence of posterior subcapsular catarct would be there and hence its important to review these cases regularly to ensure good vision

Some children may be steroid responders may show a rise in the intraocular pressure and hence are at a higher risk of developing glaucoma

Deflazacort like other steroids would make the vision a compromising factor in a life which has no mobility.

The need for the study stems from not enough research done on its ocular side effects in its various modules of treatment in India or in international arena.

OBJECTIVES

PRIMARY OBJECTIVE

To find the prevalence of ocular side effects of Deflazacort

.SECONDARY OBJECTIVE

To find the correlation of Deflazacort's ocular side effects to dosage and duration of therapy in regard to

- Visual acuity
- Changes in the lens
- Changes in the intra ocular pressure
- Changes in the posterior segment

REVIEW OF LITERATURE

The term neuromuscular disease defines disorders of the motor unit and excludes influences on muscular function from the brain, such as spasticity. The motor unit is made up of 1) motor neuron in the brainstem or ventral horn of the spinal cord 2)its axon, which together with other axons forms the peripheral nerve 3)the neuromuscular junction; and all muscle fibers innervated by a single motor neuron[8]. Motor unit sizes varies from muscles to muscle and with the precision of muscular function required. Upper motor neuron controls alter the muscle tone, precision of movement, reciprocal inhibition of antagonistic muscles during movement, and sequence the muscle contractions to achieve smooth, coordinated movements. Supra-segmental impulses increase or inhibit the monosynaptic stretch reflex ; the corticospinal tract is inhibitory upon this reflex[5].

Diseases of the motor unit are common in children. These neuromuscular diseases may be genetical, congenital or acquired, acute or chronic, and progressive or static[1]. Because specific therapy is available for many diseases and because of genetic and prognostic implications, precise diagnosis is important; laboratory confirmation is required for most diseases because of overlapping clinical manifestations.

Duchenne muscular dystrophy (DMD) is the most common hereditary neuromuscular disease affecting all races and ethnic groups. Its characteristic clinical features are progressive weakness, intellectual impairment, hypertrophy of the calves, and proliferation of connective tissue in muscle. The incidence is 1 in 3,600 live born infant boys[2]. This disease is inherited as an X-linked recessive trait. The abnormal gene is at the Xp21 locus and is one of the largest genes. Becker muscular dystrophy

(BMD) is a disease that is fundamentally similar to DMD, with a genetic defect at the same locus, but clinically it follows a milder and more protracted course.

Infant boys are non symptomatic at birth, although some are mildly hypotonic. Early milestones such as gross motor skills, such as rolling over, sitting, and standing, are not delayed or mildly delayed . Poor head control in infancy may be the first sign of weakness. Distinctive facial weakness is a late even, a "transverse" or horizontal smile may be seen. Walking is often accomplished at the normal age of approximately 12 months [5], but hip girdle weakness may be seen in subtle form as early as the 2nd year. An early Gowers sign is often evident by age 3 year and is fully expressed by age 5 or 6 year. A Trendelenburg gait, or hip waddle, appears at this time[9]. Common presentations in toddlers include delayed walking, falling, toe walking, and trouble running or walking upstairs, developmental delay, and, less often, malignant hyperthermia after anesthesia. The length of time a patient remains ambulatory varies greatly. Some patients are confined to a wheelchair by 7 year of age; most patients continue to walk with increasing difficulty until age 10 year without orthopedic intervention. With orthotic bracing, physiotherapy, and sometimes minor surgery (Achilles tendon lengthening), most are able to walk until age 12 yr[9]. Ambulation is important not only for postponing the depression that accompanies the loss of an aspect of personal independence but also because scoliosis usually does not become a major complication as long as a patient remains ambulatory, even for as little as 1 hour per day[2-5]; scoliosis often becomes rapidly progressive after confinement to a wheelchair.

The lens is a vital refractive element of the human eye. In 2002, the World Health Organization estimated that lens pathology (cataract) was the most common

cause of blindness worldwide, affecting over 17 million people[10]. Not surprisingly, cataract surgery is the most common procedure performed in the developed world. An understanding of the basic science of the lens provides valuable insight into the various pathologies involving the lens and their treatment.

Lens is a transparent crystalline structure with functions of maintaining its own clarity, refracting light, accommodation[11]. The lens has no blood supply or innervation after fetal development, depends entirely on aqueous to meets its metabolic demands.

Lens lies behind the iris and in front of the vitreous body suspended in position with the zonules of Zinn. Over all the lens consists of capsule , cortex and nucleus.

In a non accommodative state the lens contributes to about 15- 20 dioptre of 60D of the refractive power the rest is made up by the cornea and air interface[12].

The lens continues to grow through out life since birth measuring at 9 mm equatorially , 5 mm antero-posteriorly and weighing in at 255 mg at adult life. Relative thickness increases with age nut refractive power of the lens decreases due to presence of stagnated proteins thus the eye becomes progressively myopic or hyperopic[10-12]

The lens complex is made up of

1. Lens capsule
2. Zonular fibrils
3. Lens epithelium
4. Nucleus and cortex

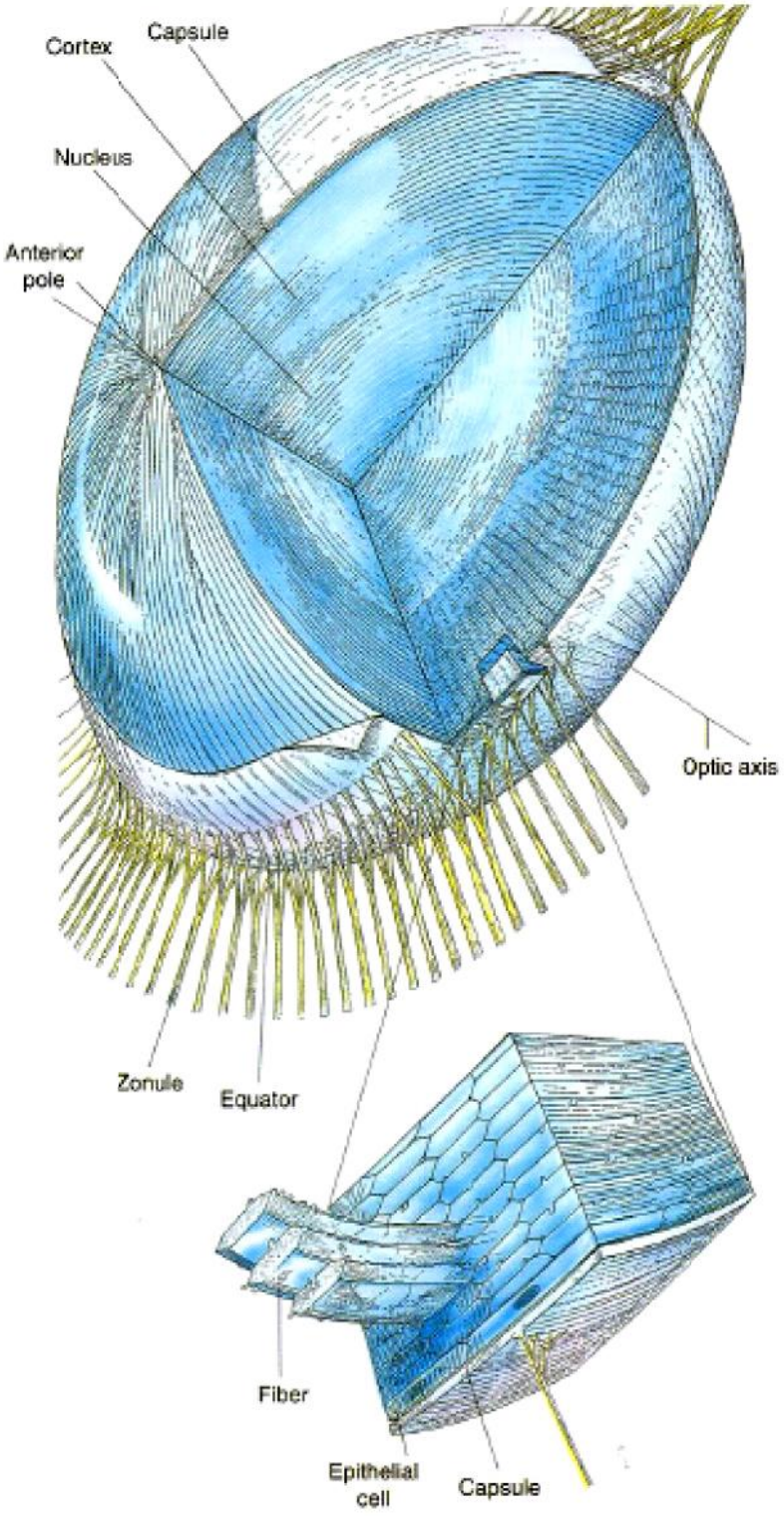


Figure 1 :- Lens anatomy and cross section

Lens Capsule

Transparent elastic basement membrane composed of type IV collagen secreted by lens epithelium capable of moulding leading to accommodation.

Outer later of the lens capsule serves for attachment of zonular fibrils anterior lens capsule is thicker than the posterior capsule and keeps on thickening through out life.[13-15]

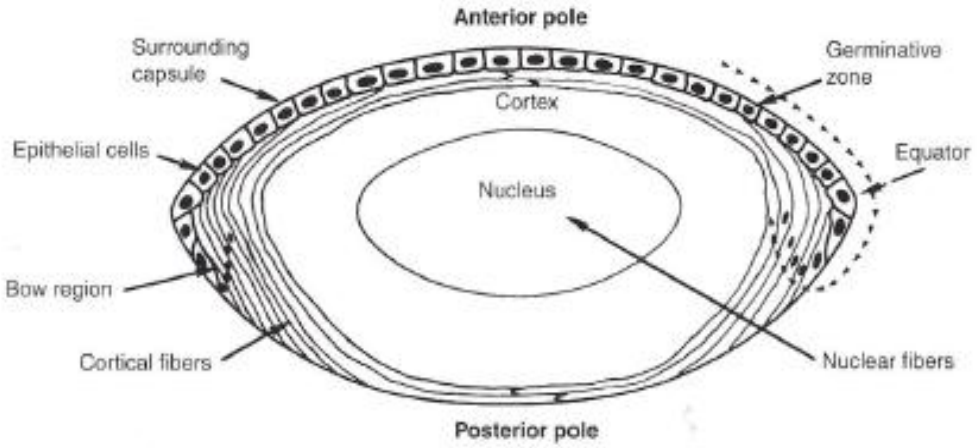


Figure 2 :- Lens Capsule

Zonular Fibres

The lens is supported by zonular fibers that originate from basal laminae of the non-pigmented epithelium of the pars plana and pars plicata of the ciliary body. These zonular fibers insert, in a continuous fashion, on the lens capsule in the equatorial region, anteriorly 1.5 mm onto the anterior lens capsule and posteriorly 1.25 mm onto the posterior lens capsule[16]. With age, the equatorial zonular fibers regress, leaving separate anterior and posterior layers that appear in a triangular shape on cross section of the zonular ring. The fibers are 5- 30 microns in diameter; light microscopy shows them to be eosinophilic structures that have a positive periodic

acid-Schiff (PAS) reaction[17-20]. Ultra-structurally, the fibers are composed of strands, or fibrils, 8-10 nm in diameter with 12- 14 nm of banding[13].

Lens Epithelium

Immediately behind the anterior lens capsule is a Single layer of epithelial cells. These cells are metabolically active and carry out all normal cell activities, including the biosynthesis of DNA, RNA, protein, and lipid; they also generate adenosine triphosphate to meet the energy demands of the lens. The epithelial cells are mitotic, with the greatest activity of pre-mitotic (replicative, or S-phase) occurring in a ring around the anterior lens known as the germinative zone[21]. These newly formed cells migrate toward the equator, where they differentiate into fibers. As the epithelial cells migrate toward the bow region of the lens, they begin the process of terminal differentiation into lens fibers. Perhaps the most dramatic morphologic change occurs when the epithelial cells elongate to form lens fiber cells. This change is associated with a tremendous increase in the mass of cellular proteins in the membranes of each fiber cell[19]. At the same time, the cells lose organelles, including cell nuclei, mitochondria, and ribosomes. The loss of these organelles is optically advantageous because light passing through the lens is no longer absorbed or scattered by these structures. However, because these new lens fiber cells lack the metabolic functions previously carried out by the organelles, they are now dependent on glycolysis for energy production.[13]

Nucleus and Cortex

No cells are lost from the lens; as new fibers are laid down, they crowd and compact the previously formed fibers, with the oldest layers being the most central.

The oldest of these, the embryonic and fetal lens nuclei, were produced in embryonic life and persist in the center of the lens .The outermost fibers are the most recently formed and make up the cortex of the lens. Lens sutures are formed by the arrangement of inter-digitations of apical cell processes (anterior sutures) and basal cell processes (posterior sutures)[22]. In addition to the Y-sutures located with in the lens nucleus, multiple optical zones are visible by slit-lamp bio-microscopy.

These zones of demarcation occur because strata of epithelial cells with different optical densities are laid down throughout life. There is no morphologic distinction between the cortex and the nucleus; rather, the transition between these regions is gradual. Although some surgical texts make distinctions among the nucleus, epi-nucleus, and cortex, these terms relate only to potential differences in the behavior and appearance of the material during surgical procedures[23-25].

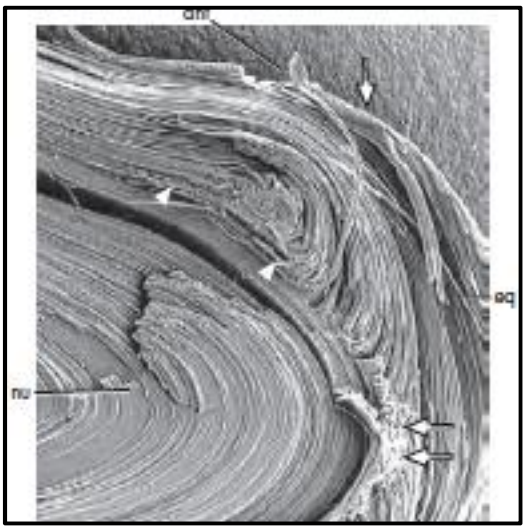


Figure 3:- Electron Microscope Showing Arrangement Of Lens Fibers

Mechanisms of Corticosteroid-Induced Cataract Formation

It appears that a number of factors are operative in eliciting the pathologic consequences of corticoids on the lens. Many investigators have made important contributions in this area and have there by shed light, not only on the characteristic changes induced by corticosteroids, but also on the similarities these opacities share with other types of cataracts. Ono and associates[26], in a study of how corticoids are absorbed and inactivated in the lens, found that hypophysectomy, adrenalectomy, daily intra-peritoneal dexamethasone and severe liver impairment all decreased cortisol binding capacity in the lens. The injection of a riboflavin derivative tended to counteract the response.

Corticosteroid-Inhibition Of The Na+- K+ Atp'ase Pump Mechanism

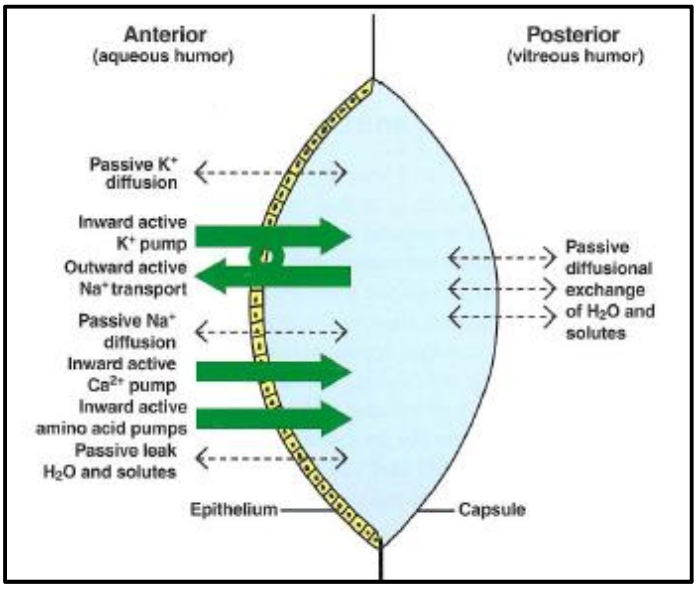


Figure 4 :- Electrolyte Pump Leak Theory

The position of the cataract under the posterior capsule may be related to the "pump-leak" mechanism of the lens, as the epithelium, located anteriorly, acts as an active transport system, while the acellular posterior capsule serves for passive

diffusion[27]. Corticosteroids have been shown to affect water transport and increase the permeability of the lens to cations[28], phenomena which have also been observed in cataracts of either genetic, or chemical origin.

Kinsey[27], Kinoshita[29] and others, in studying various types of cataract formation, have stressed the importance of cation fluxes across the lens and their relation to the cation pump mechanism in maintaining the viability and normal transparency of the lens.

Mayman and associates have reported that the decrease in potassium, the increase in sodium and the concomitant increase in hydration of the lens attending the in vitro incubation of lenses with dexamethasone results from inhibition of the Nat-K+ ATP'ase pump mechanism[30].

In the relative sparing of the lens epithelium in the germinative zone, the PSC secondary to corticosteroids closely resembles that produced by galactose. In this light, it may be that the action of corticosteroids shares similarities with that of galactose, which has been purported to cause cataracts as the consequence of excess water transfer into the lens cell made hypertonic by accumulation within itself of poorly permeable dulcitol[31].

Clinically, hydration of the lens is manifested either as a generalized intumescence, or a localized accumulation of fluid of different refractive index from the surrounding medium, which is responsible, in part, for the dispersion of light and the consequent decrease in its transmission by the lens[28].

Binding Of Corticosteroids To Lens Proteins And The Subsequent Formation Of Lysine-Keto-steroid Adducts.

Previous reports have suggested that corticosteroid- induced lens opacities are associated with the development of covalent glucocorticoid-lens protein adducts.‘ The reaction between glucocorticoids and proteins occurs non-enzymatically via Schiff base formation between a protein amino group and the C-20 carbonyl of the corticosteroid[32].”

A Heyns rearrangement which involves the adjacent C-21hydroxyl group can then take place to produce the stable product (Fig. 1). Earlier studies have implicated the non-enzymatic alteration of lens proteins by low-molecular weight substrates in the cataractogenic effects of glucose and cyanate. crystallins, which allows disullide cross-linking and the formation of high-molecular weight light-scattering aggregates to ensue.

Secondary Oxidation Of -Sh Protein Groups In Lysine-Ketosteroid Adducts Leads To Aggregation Of Crystallins

In vitro, prednisolone has been shown to non-enzymatically react with the amino group of lysine residues in lens crystallins. This modification apparently induces a conformational change, which results in either the exposure of protein sullhydralgroups or in an increased susceptibility to oxidation. With time, disulfide cross-linking occurs to generate complexes which refract light.

Gel analysis of proteins acquired from a human corticosteroid-induced cataract demonstrated that in vivo, prednisolone -lens protein adducts are also present in high-molecular weight, sullhydralcomplexes[33].

Apparently, the mechanism which leads to light-scattering in vitro also occurs in viva. This theory is supported by several studies which have emphasized the role of

both a decrease in free sulfhydra1groups and sullhydral oxidation with the appearance of insoluble lens protein and cataract formation in vitro and in vivo

The evolution of visible, light-scattering complexes is associated with an average molar incorporation of 1 prednisolone molecule per 77 lens protein subunits.

'This is 10 to 50 times the amount of incorporation found in either experimental or human steroid cataracts. In both instances, the extent of modification is quite low and thus serves to highlight the sensitivity of the crystallin's conformation to the presence of the prednisolone[34].

Incubated prednisolone-lens protein solutions examined by gel filtration chromatography have revealed a decrease in the amount of B, this implies that the higher molecular weight light-scattering species are complexes of B and presumably some crystallins[28].

Disulfide bond formation would need to involve only a small number of molecules in order to generate aggregates of this magnitude. The addition of dithiotreitol, a reducing agent, is found to rapidly reverse much of the opalescence associated with the in vitro and in vivo corticosteroid-lens protein light-scattering aggregates, while glutathione, another reducing agent, has only a minimal effect.[35-37]„

This is seemingly the result of the inability of the glutathione tripeptide to pervade extensively aggregated proteins and thereby reduce the disulfide cross links. Similar results, which under score the dissimilarity in the reducing potential of dithiotreitol and glutathione, have been observed for glucose-induced lens protein aggregation in vitro and in vivo. These observations support the concept that an intracellular reducing environment is requisite for the prevention of crystallin

aggregation and resultant cataract formation[37].

Thus, glucocorticoids apparently cause cataract formation by gaining entry to the lens fiber cells and reacting with specific amino groups of the lens crystallins.

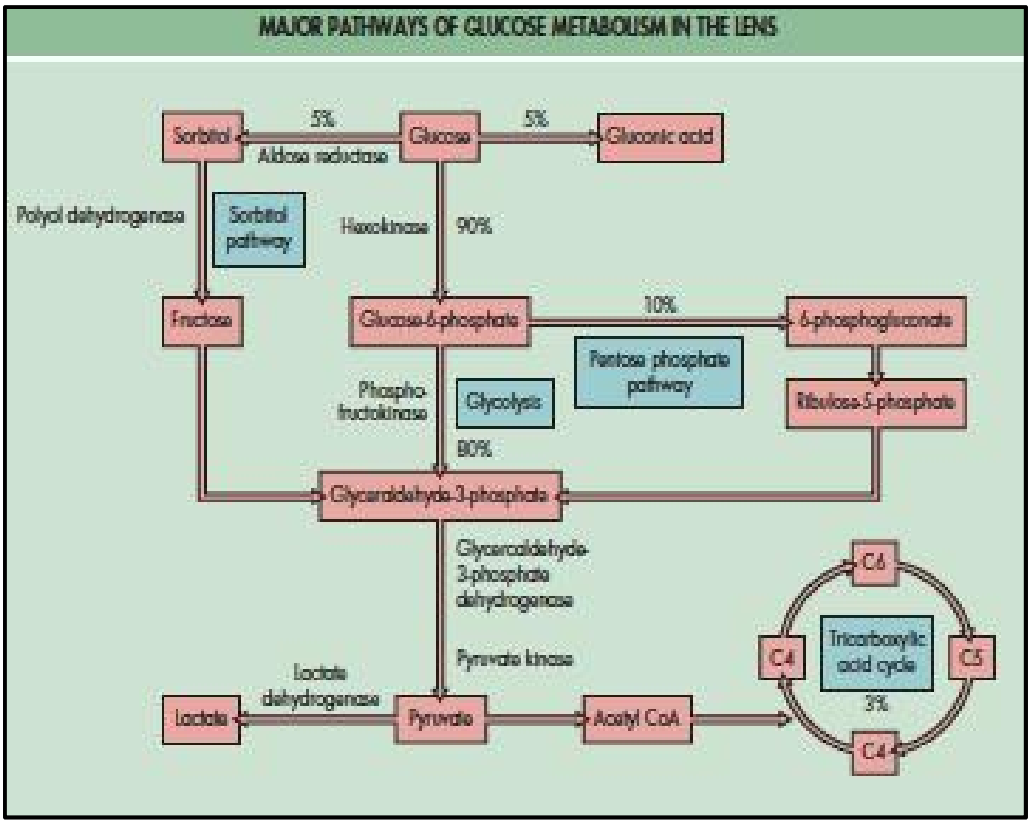


Figure 5 :- Major Metabolic Pathways In Lens Physiology

The history of the meaning of the word Glaucoma:

The discovery of the disease called glaucoma dates back to the 17th century.

Initial comprehension of its pathogenesis and treatment belong to the 20th century.

The word glaucoma came from ancient Greek, meaning clouded or blue-green hue, most likely describing a person with a swollen cornea or who was rapidly

developing a cataract, both of which may be caused by chronic elevated pressure inside the eye.

The definition of glaucoma has changed drastically since its introduction around the time of Hippocrates in approximately 400 BC. The first recognition of a disease associated with a rise in intraocular pressure and thus corresponding to what is now known as glaucoma occurs in the Arabian writings, "Book of Hippocratic treatment"(10^{th}century).

In European writings, Dr Richard Bannister (1622), an English oculist and author of the first book of ophthalmology in English, who makes the first original and clear recognition of a disease with a tetrad (four) of features: eye tension, long duration of the disease, the absence of perception of light and the presence of a fixed pupil.

All through the 18th century the term glaucoma was merely a label applied to an inflamed eye wherein the pupil appeared greenish-blue and the visual prognosis was bad, but the tension of the eye was not stressed.

It was not until the beginning of the 19^{th} century that the first excellent description of glaucoma with raised ocular tension is given by the French Dr Antoine-Pierre Demours (1818). Thereafter the central concept of a rise in the intraocular pressure became fully established. In London, Dr G.J. Guthrie (1823) recognized hardness of the eye as characteristic of a disease which he called GLAUCOMA.

Finally, the essential feature of raised eye tension was fully established by the great Dr William McKenzie, Scottish clinician (1835) who, in the second edition of his classical and widely read textbook, ascribed the raised tension in both chronic and

acute glaucoma. The final clinical observation in this epoch was the unifying concept of Dr Donders (1862) where he described an incapacitating increased eye tension occurring without any inflammatory symptoms as Simple Glaucoma. The concept of glaucoma has been further refined, particularly over the last 100 years.

Dr Drance (1973) provided for the first time the definition of glaucoma as a disease of the optic nerve (an optic neuropathy) caused by numerous factors, called risk factors.

Currently, glaucoma refers to a group of eye conditions which cause characteristic damage to the optic nerve, the "cable" that transmits the visual message from the eye to the brain, and characteristic damage to the visual field. This damage is progressive, leads to loss of vision if untreated and often is caused by "higher pressure inside the eye" than the optic nerve can tolerate.

Aqueous humor outflow system Overview:

Aqueous humor is formed by the ciliary processes, passes from the posterior chamber to the anterior chamber through the pupil, and exits the eye at the anterior chamber angle. Aqueous returns to the venous system primarily by means of the conventional or canalicular pathway (83–96% of flow).

The pathway is through the trabecular meshwork into Schlemm's canal (hence the canalicular pathway). The Schlemm's canal lumen communicates directly with the episcleral veins, completing the circulatory pathway for aqueousreturn to the heart.

Aqueous humor also returns to the heart by a secondary pathway known as the uveoscleral or unconventional route. The uveoscleral route accounts for from 5 to 15% of flow, an amount that decreases with age.

Functions of the conventional aqueous outflow system:[38]

1. It's a circulatory path for aqueous humor return to the vascular system
2. Permits bulk aqueous flow of aqueous out of the anterior chamber but prevents blood reflux into the anterior chamber.
3. Maintenance of a relatively stable intraocular pressure (IOP)
4. A fourth function is filtration of foreign material and debris.

Anatomy of the conventional outflow system:

Schwalbe's line:[39]

Schwalbe's line (composed of collagen and elastic tissue) is an irregular elevation 50–150 micron wide that runs circumferentially around the globe.This line or zone marks the transition from trabecular to corneal endothelium, the termination of Descemet's membrane, and the insertion of the trabecular meshwork into the corneal stroma.

Scleral spur:[39]

The scleral spur is a fibrous ring that appears as a wedge projecting from the inner aspect of the anterior sclera .

The spur is attached anteriorly to the trabecular meshwork and posteriorly to the sclera and the longitudinal portion of the ciliary muscle.

When the ciliary muscle contracts, it pulls the scleral spur posteriorly . The largest trabecular lamellae near the anterior chamber are attached to the scleral spur and accordingly are rotated inward and posteriorly by ciliary muscle contraction.

Rotation alters the position not only of the large lamellae, but also moves the entire attached meshwork further inward and posteriorly. Inward movement of the trabecular meshwork results in an enlargement of intertrabecular spaces and an increase in the size of Schlemm's canal, reducing the tendency of the canal lumen to narrow or collapse.

Trabecular meshwork tissues:[39-40]

In meridional section, the trabecular meshwork has a triangular shape, with its apex at Schwalbe's line and its base at the scleral spur.

The inner layers of the trabecular meshwork border the anterior chamber and are referred to as the uveal meshwork. The next more superficial layer is the corneoscleral meshwork.

The juxtacanalicular space is the next layer, which is between the corneoscleral meshwork and Schlemm's canal inner wall endothelium.

Juxtacanalicular space and cells:[41]

The juxtacanalicular space is 2–20 µm thick in non pressurized eyes. The space separates the outer layers of the corneoscleral meshwork from the inner wall of Schlemm's canal

It has been called by a variety of names like cribriform space, pericanalicular space, and endothelial meshwork.

Juxtacanalicular, subendothelial, and cribriform cells are star shaped. Juxtacanalicular cell cytoplasmic processes attach to processes arising from Schlemm's canal inner wall endothelium.

By distributing IOP-induced stresses across the entire trabecular lamellae system that supports the inner wall endothelium of Schlemm's canal, the stresses are tensionally integrated, which is essential in cellular response mechanisms.

Schlemm's canal[42]:

Schlemm's canal is a vascular sinus with a lumen that communicates around the entire globe.

Collector channels, aqueous veins and episcleral veins:

Schlemm's canal is drained by a series of collector channels that in turn drain into a complex system of intrascleral, episcleral, and subconjunctival venous plexus.

The collector channels arise from the outer wall of Schlemm's canal at irregular intervals. A few (4–6) direct collector channels proceed directly from Schlemm's canal through the sclera thus communicating directly with aqueous veins on the surface of the eye.

Aqueous veins empty into episcleral and conjunctival veins. Where aqueous and episcleral veins join, characteristic laminar flow of aqueous humor and blood is seen on slit-lamp examination at the limbus.

Aqueous outflow physiology

The aqueous outflow system as a passive filter[43]:

The traditional model of aqueous flow is that of a passive, non energy-dependent bulk fluid movement down a pressure gradient with aqueous leaving the eye primarily by the canalicular route.

The model is recognized as being somewhat oversimplified because of a component of uveoscleral flow. In the model, aqueous is forced through a syncytium of extracellular matrix material in the juxta-canalicular space that acts as a passive resistance unit controlling pressure and flow. Evidence favouring the model is the finding of similar aqueous flow rates in living and enucleated eyes.

The aqueous outflow system as a dynamic mechanical pump:

In this model, elastic and contractile tissues of the trabecular meshwork and valves within Schlemm's canal stretch in response to transient pressure increases.

The energy stored during distention is released when the pressure transients decay, causing the tissues to recoil to their prior configuration. The pressure transients thus enable energy-dependent pulsatile fluid movement through the outflow system.

Uveoscleral flow[44]:

A lesser amount of the aqueous humor exits the eye by an alternate route through the ciliary muscle, the iris, the sclera, and other structures of the anterior segment . This alternate pathway is known by a number of terms, including *uveoscleral*, *unconventional*, *extracanalicular*, and *uveovortex flow*.

Aqueous humor enters the ciliary muscle through the uveal trabecular meshwork, the ciliary body face, and the iris root.

The fluid passes posteriorly between the bundles of the ciliary muscle until it reaches the supraciliary and suprachoroidal spaces.

Aqueous humor leaves the eye through the spaces around the penetrating nerves and blood vessels and through the sclera.

The net fluid flow into the uveal vascular system is quite low for a number of reasons: 1) the iris capillaries have thick walls that restrict movement of water and ions.129 2) pressure in the uveal capillaries is higher than IOP. This pressure difference partially offsets the difference in oncotic pressure between the plasma and the tissue fluid of the uveal tract. Thus there is little driving force for fluid to cross the capillary walls.

In human eyes, the unconventional pathway is estimated to carry 5–25% of the total aqueous outflow. uveoscleral outflow increases up to four-fold when the anterior segment is inflammed.

Corticosteroids induce IOP elevation in susceptible patients by reducing trabecular outflow facility through changes to the mechanical structure of the trabecular meshwork, extracellular matrix trabecular deposits and reduction of trabecular endothelial functional and phagocytic activity.4

It is possible with topical, other local (dermal or inhalational), depot (subconjunctival, sub-Tenon's, intravitreal), or systemic corticosteroids. Following 4−6 weeks of topical corticosteroids, in about 5% of patients IOP will rise by more than 16 mmHg and 30%, by 6−15 mmHg.5,6

In a minority, the IOP rise can be faster and greater; risk factors for this include primary open-angle glaucoma (POAG), family history of glaucoma, very young and older ages, diabetes, connective tissue disease, and myopia.7 Ninety-two percent of POAG patients are high steroid responders; among their children, 19%.6 Intravitreal triamcinolone acetonide (IVTA) can increase IOP for months. A 20 mg dose increased IOP above 21 mmHg in 40% of people for up to 9 months: 1% required trabeculectomy.8 More than 50% of children less than 10 years old respond to dexamethasone.9 Within two years of implanting the intravitreal Retisert implant (0.59 mg fluocinoloneacetonide; Bausch & Lomb), which acts for more than 30 months, 60% required IOP-lowering medications and 32% needed filtering surgery.

Topical corticosteroids vary in their IOP elevation effect (from the strongest effect to the least: dexamethasone 0.1%, prednisolone 1%, fluorometholone 0.1%, medrysone 1%);7 to reduce steroid response, minimize the strength, frequency and duration of corticosteroids. If possible, elucidate an individual's IOP steroid response before using depot corticosteroids. Monitoring IOP is essential in all patients receiving corticosteroids. Once topical corticosteroids have ceased, IOP almost always returns to baseline within 4 weeks.10

A study done in 2010 on management of DMD shows 3 modules of treatment[1]

1. Alternate day 2mg/kg every other day. This therapy is less effective but used when daily therapy causes a lot of side effects

2. Daily 0.9 mg/kg causes good muscle preservation but cannot be tolerated by everyone hence the other modules need to be followed

3. Intermittent 0.6 mg/kg give for the 1-20 days and nothing for the rest of the month and repetition of the same. This therapy is least effective but best tolerated altogether.

Maintenance of a daily schedule is appropriate when the child's motor function is stable or in decline and if any glucocorticoid side-effects are manageable and tolerable. If a daily-dosing schedule generates unmanageable and/or intolerable side-effects that are not nullified by a reduction in dose at least once, then it is appropriate to change to alternative regimen. If, however, any glucocorticoid side-effects are unmanageable and/or not tolerable, then an increase in glucocorticoid dose for growth or declining function is inappropriate, and in fact, a decrease in dose is necessary, whether motor function is stable or in decline. This applies to all dosing regimens.

Considering the above modules the DMD patient is going to take Deflazacort for almost all years after diagnosis and only two studies have been done to show the ocular side effects of the same.[1]

In 2001, Holland Bloorview kids rehabilitation hospital, did a study on Deflazacort treatment for male patients with DMD in which 54 male patients who met the inclusion criteria were included[2]. Out of which 30 were treated with Deflazacort and the other 24 were not treated. All 54 were walking at the age of 7.Initial dose of Deflazacort given to the 30 boys was 0.9mg/kg/day along with oral supplements of vitamin D 1000I.U. and calcium 750mg. for over a period of one year.[2]

Cataracts developed in 10 of the 30 male patients treated with Deflazacort. In 9 of the 10 male patients the cataracts were bilateral. The earliest cataracts were

noted 4 months after Deflazacort was begun; the latest was 5.8 years. No correlation was found between the presence of cataracts and their age at the start of Deflazacort, the dose per kilogram taken, or the total amount of Deflazacort taken before the cataracts were noted. Other side effects were not more prevalent in these 10 male patients. That is, they were not the shortest or with the most weight gain. The cataracts were asymptomatic in all 10.

Intraocular pressures and visual acuity remained normal. None of the male patients in the non Deflazacort group had cataracts

In the ocular side effects of the drug out of 40 patients 22 male patients developed bilateral cataract. Cataracts were noted as early as 4 months and as later as 10 years. No other ocular side effects were noted in the 22 patients, cataracts were asymptomatic in all patients. Intraocular pressure and visual acuity also remained normal. None of the male patients not treated with deflazacort developed cataract.[2]

Another study done in 2004 on deflazacort in Duchenne muscular dystrophy: a comparison between different protocols of treatment

1. Protocol –N :- in which 56 male patients(4-8years) met the inclusion criteria and were started on 0.6 mg/kg od deflazacort as a single dose administered for first 20 days of the months and rest of the month went drug free along with month long treatment with calcium (1000 mg) and vitamin D (880ui). All male patients underwent physiotherapy

2. Protocol-T:- 32 male patients(6-9years) were treated with 0.9 mg/kg of deflazacort daily and alterations were made as and when the male patients grew in weight and side effects took over with a mean dose of (0.76mg/kg at

the age of 10 years) and (0.5 mg/ kg at the age of 15 years) along with month long treatment with calcium (1000 mg) and vitamin D (880ui). All boys underwent physiotherapy

The ocular side effect results were 30% of the male patients treated with deflazacort on protocol-T developed asymptomatic cataracts. Cataracts were noted as early as 4 months and as late as 6 years after starting deflazacort. There was no correlation between the presence of cataracts and their age at starting deflazacort, the dose per kilogram taken or the total amount of deflazacort taken before the cataracts were noted. Other side effects were not more prevalent in the boys with cataracts. That is, they were not the shortestor with the most weight gain for example. The cataracts were bilateral and asymptomatic in all male patients.Intraocular pressures and visual acuity remained normal. None of the male patients on protocol-N or the controls developed cataract[3]

Asymptomatic cataracts were documented in 30% of the boys on protocol-T. Most were documented within3–4 years of starting deflazacort. None of the male patients have required cataract surgery. The reported incidence of cataracts in male patients with DMD treated with steroids varies.Ten of 87 male patientson prednisone (0.75 mg/kg per day)observed for only 2 years, developed cataracts[4]

These were mild, asymptomatic and did not progress. A double-blind study from 14 German centres , compared prednisone (0.75 mg/kg per day) with deflazacort (0.9 mg/kg per day) in 100 boys with DMD[5]

16 of 50 male patients treated with deflazacort, but only one of 50 in the prednisone treated group developed cataracts. Of interest was the finding that

cataracts were not reported in male patients treated for 2 years with alternate-day deflazacort (2 mg/kg)and boys reported here on protocol-N. Other side-effects were described as mild [6]

Another study done in 2006 by W.D Biggar at Billorview kids rehab on long term benefits of deflazacort for male patients with DMD in their second decade[7]. Out of 74 male patients(10-18 years) in which 40 were treated with deflazacort and 34 were not, deflazacort was given at 0.9mg/kg/day was given at breakfast and there were the findings recorded to the ocular side effects

Twenty-two of the 40 male patients treated with deflazacort developed bilateral cataracts. Cataracts were noted as early as 4 months after starting deflazacort and as late as 10 years. Other side effects were not more prevalent in these 22 male patients.That is, they were not the shortest boys or the boys with the most weight gain. The cataracts were asymptomatic in all 22 male patients. Intraocular pressures and visual acuity remained normal. None of the male patients not treated has developed cataract[7]

In 2016 , a retrospective study to evaluate clinical outcomes and steroid side effects of 97 patients with DMD aged 10 to < 16 years treated with daily glucocorticoid , prednisone (starting dose 0.75 mg/kg/day) or deflazacort (0.9 mg/kg/day) (89% on deflazacort) for a mean of 8.5 years, had around 18.6% (18 out of 97patients) of the patients landing up with asymptomatic PSC.[45]

In1987, DeSilva did an Open study of 16 DMD patients ranging from 3 to 10 years of age with Prednisone 2 mg/ kg/day for 3 months, then two thirds dose on

alternate days with a treatment period of 1 to 11 months and found an incidence of 2 cases having cataract.[46]

In 1991, Fenichel did an Open study of 92 DMD patients ranging 5 to 15 years of age on Prednisone 0. 75 mg/kg/day for 2 years noting Cataracts in 10 patients[47].

Biggarin 2001 did an Open study of 30 DMD patients ranging 7 to 15 years of age with DFZ 0.9 mg/ kg/day for 5 years and noted 30 % patients had cataract and slight amount of weight gain.[48].

Silversides in 2003 did Retrospective cohort study with patients refusing treatment that formed control group of 33 (21treated) for 8.4 years with DFZ Starting at 0.9 mg/kg/day(gradual decrease in dose with age) till 18 years dosed at 0.59 +/-0. 15 mg/kg/day with a cumulative analysis showing 50% of the treated patient having cataracts[49]

Resende in 2001 did an Open study of 36 DMD patients with DFZ 1mg/kg/ day treated for 12 to 43 months and found that 2 patients had cataract[50].

Biggarin 2006 did an Open cohort study with patients declining treatment forming comparison (control) group in which 40 DMD were treated while 34 not treated ranging from 10 to 18 years of age with DFZ 0.9 mg/kg/day for a mean of 5.5 years and concluded that 22 out of the 40 treated boys had asymptomatic cataract[51].

Biggar in 2004 did a Descriptive and comparative study of 2 cohorts in 2 DFZ protocols, in 2 different centres:

1. Naples protocol (retrospective);
2. Toronto protocol (Biggar 2001 cohort)

It incuded 2 Groups

1. 56 boys 4-8 years
2. 30 boys 6 - 8 years

Were started on

1. DFZ 0.6 mg/ kg/day for 1st 20 days every month, Vitamin D 880 i.u & Calcium 1000 mg daily
2. DFZ 0.9 mg/ kg/day, Vitamin D 1000 i.u & Calcium 750 mg daily

For a mean period of 4 years and found that in the Naples no patients had any cataract where as in the Toronto cohort 30% of the patients had cataract[51].

Alman in 2004 did Prospective cohort study(same cohort as Biggar 2001) with a sample size of 54 DMD patients ranging from 7 to 10 years of age with DFZ, Starting with 0. 9 mg/kg/day (gradual decrease in dose with age) for a period of 7.3 (5 to 8) years found that 33% of the patients inspite of a decreasing dose had developed asymptomatic cataract [52].

Houde in 2008 did a Retrospective cohort study in which patients declining to take corticosteroid or used for less than 6months formed the control group, with 37 treated 42 untreated with mean age being 13.1 years in the treated group and 9.5 years in the non treated group with DFZ started at 0.9 mg/kg Adjusted according to evolution or side effects (max 1 mg/kg) for a period of 66 months noted that 49% of the patients in the treated group had cataract[53].

METHODOLOGY

This study was conducted in the Department of Ophthalmology at KLE'S Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi.

Study Design: Cross Sectional Study

Study period: One year-1st January 2016 to 31st December 2016.

Sample:

Universal sampling

Hospital based study: 50 patients visiting the out patient department with documented Duchenne muscular dystrophy and patients previously registered in the child development clinic register are included in the study.

Selection Criteria

***Inclusion Criteria*:**

- All Duchenne muscular dystrophy patients
- All patients on Deflazacort on daily therapy with 0.9 mg/kg body weight
- Onset of weakness prior to 5 years of age
- Male patient

***Exclusion criteria**:*

1. Boys suffering from development cataract and buphophthalmos
2. Boys using topical cortocisteroids
3. Boys having other forms of muscular dystrophies such as Becker muscular dystrophy
4. Boys using all forms of medication that could raise intraocular pressure as well as cause cataractous changes in the lens
5. Any pateint with previous ocular surgery for cataract and/or glaucoma

Study Participant Selection:

A cross-sectional study, all patients who satisfy the inclusion criteria are invited to participate in the study without the involvement of a sampling process. Participation will be voluntary and participants may exercise their right to pull out of the study at any stage. Written and informed consent have been obtained from all participants before enrollment in the study.

Procedure:

The patients were evaluated as follows:

1) Detailed systemic and ocular history
    - Including the age of appearance of symptoms
    - Age at which diagnosis was made
    - Duration of using deflazacort
    - Dosage of deflazacort
    - Ambulatory status defined using gross motor function classification

Grading	
Grade I	Walk run and climb stairs
Grade II	Walk but climbs stairs using railing
Grade III	Walks using hand-held mobility device
Grade IV	Walks with devices that require physical assistance
Grade V	Uses wheelchair

2) Detailed general examination
3) Visual acuity without/with glasses
4) Refraction
5) Slit lamp examination
6) Fundus examination
7) IOP measurement
8) Fundus photos
9) Anterior segment photos

The protocol of ophthalmic examination will be as follows

1. Visual acuity using lea symbol chart or Snellens chart

- Patient is classified as to having perfect vision of 20/20
- If patient does not have vision of 20/20 refraction is carried out to see the best corrected visual acuity

2. Anterior segment examination on slit lamp bio-microscopy

- Eyelid and adnexa
- Conjunctiva
- Cornea
- Anterior chamber
- Iris
- Lens
- Anterior vitreous phase

Lens changes are seen on LOCS III Posterior sub capsular cataract classification

Grade I	1mm-2mm
Grade II	3mm
Grade III	More than 3 mm

3. Intra ocular pressure using non contact tonometer

4. Dilatation of the eyes using mydriatic eye drops

5. Evaluation of the lens using slit lamp bio-microcopy and using distant direct ophthalmoscope for media opacities

6. Indirect ophthalmoscopy for evaluation of the posterior segment

- Glow
- Media
- Disc
- Cup:disc

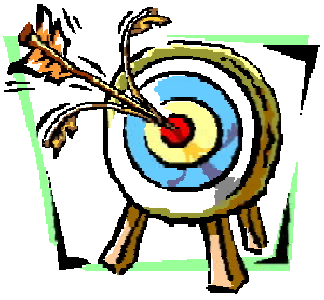
- Blood vessels
- Background
- Macula

7. All abnormalities will be captured on anterior segment camera and fundus camera

Statistical analysis

The data will be tabulated and co-relation between the dosages and durations with the status of the ocular side effects shall be established indicating the significance of the side effects found in the study

Introduction



Objectives

Review of Literature

Methodology

Results

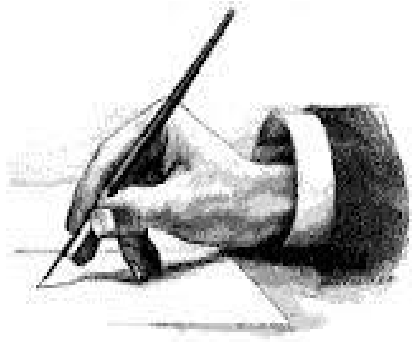
Discussion

Limitations Of The Study

Conclusion

Summary

Bibliography



Annexure-I

Annexure-II

Annexure-III

Annexure-IV

Annexure-V

RESULT

A total of 50 patients were included in the study

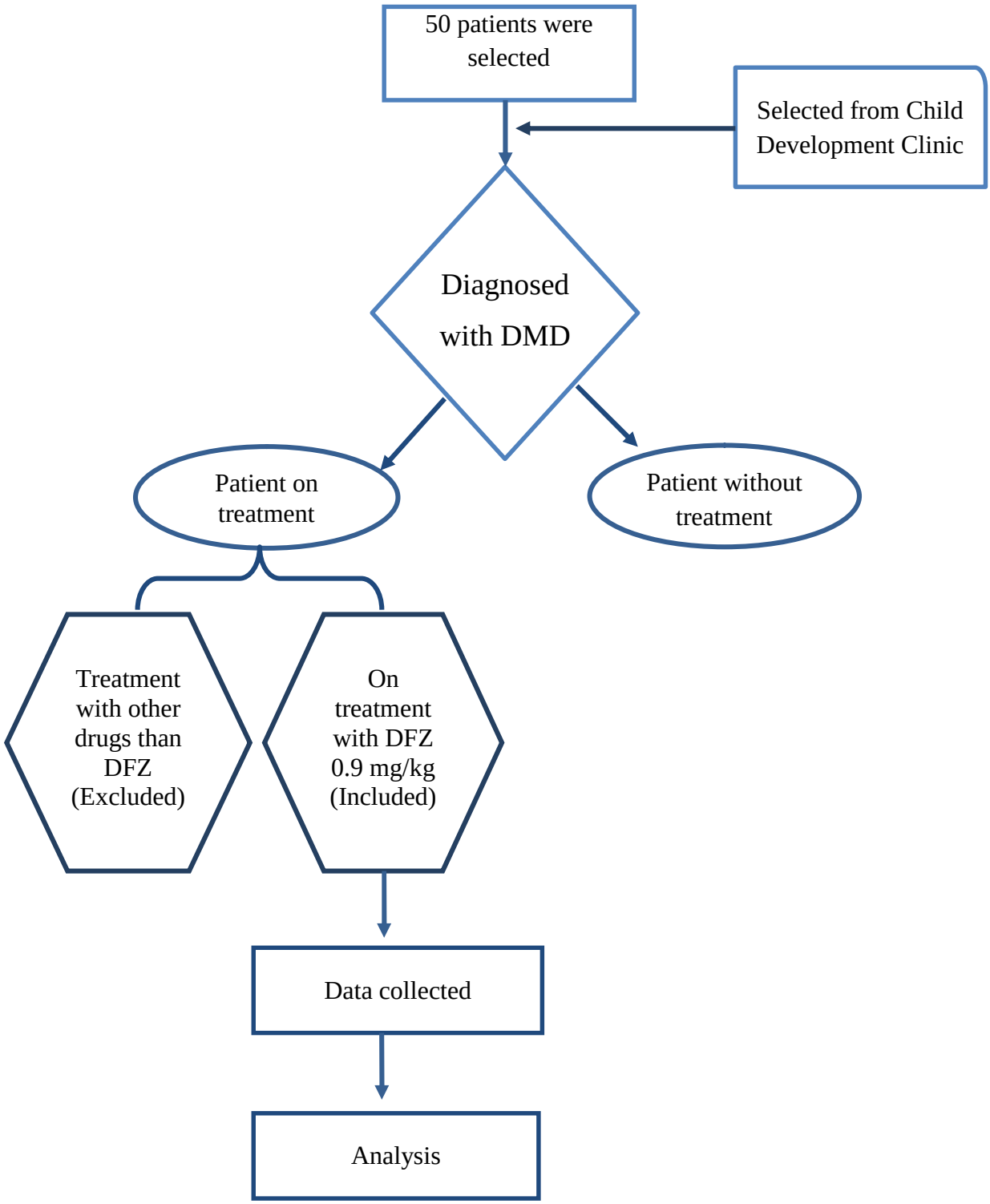


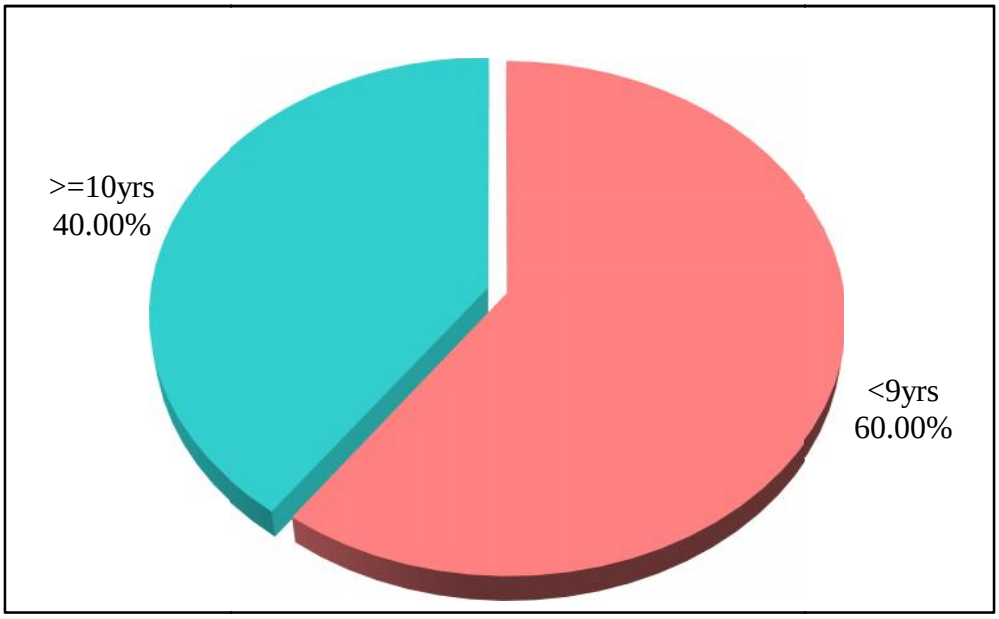
Table 1: Distribution of patients by age groups, Age of diagnosis and Months since on rx.

Factors	Number	Percentage	Mean	SD
Age groups				
<9yrs	30	60.00	6.97	1.27
>=10yrs	20	40.00	11.50	1.64
Total	50	100.00	8.78	2.65
Age of diagnosis				
<5yrs	14	28.00	4.29	0.47
>=5yrs	36	72.00	8.17	2.16
Total	50	100.00	7.08	2.55
Months since on rx				
1-10months	16	32.00	3.81	2.20
11-20months	15	30.00	12.60	1.84
>=21months	19	38.00	32.21	12.04
Total	50	100.00	17.24	14.42

In Table 1 :- there are 50 patients with a mean age of 8.78 years with a mean age of diagnosis of 7.08 years and a mean duration of treatment of 17.24 months falling just short of one and half years

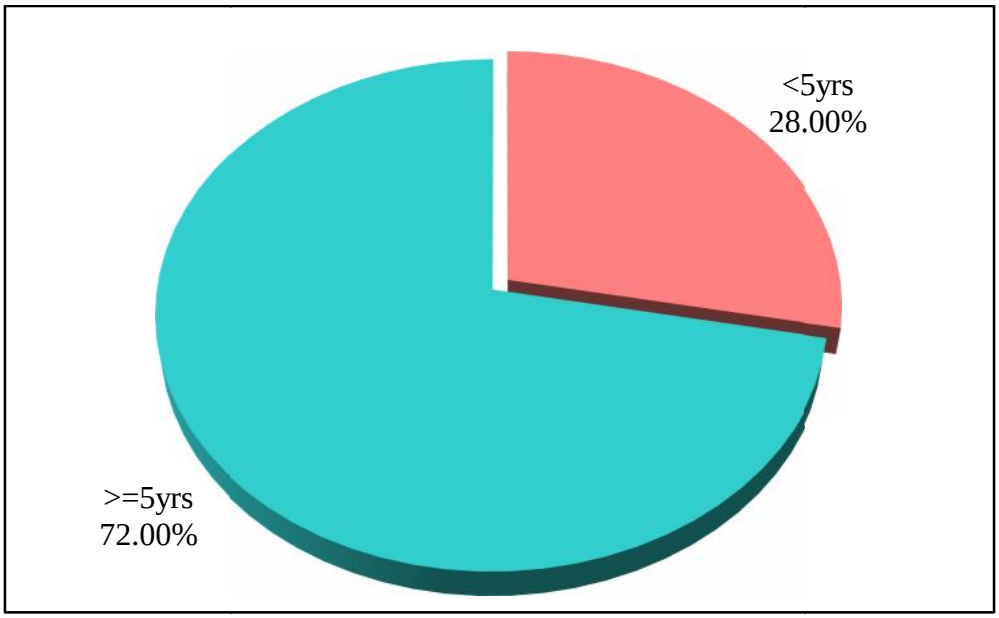
The Graphical analysis of each of the variable is shown in figures 6 to 8

Figure 6 : Age groups wise distribution



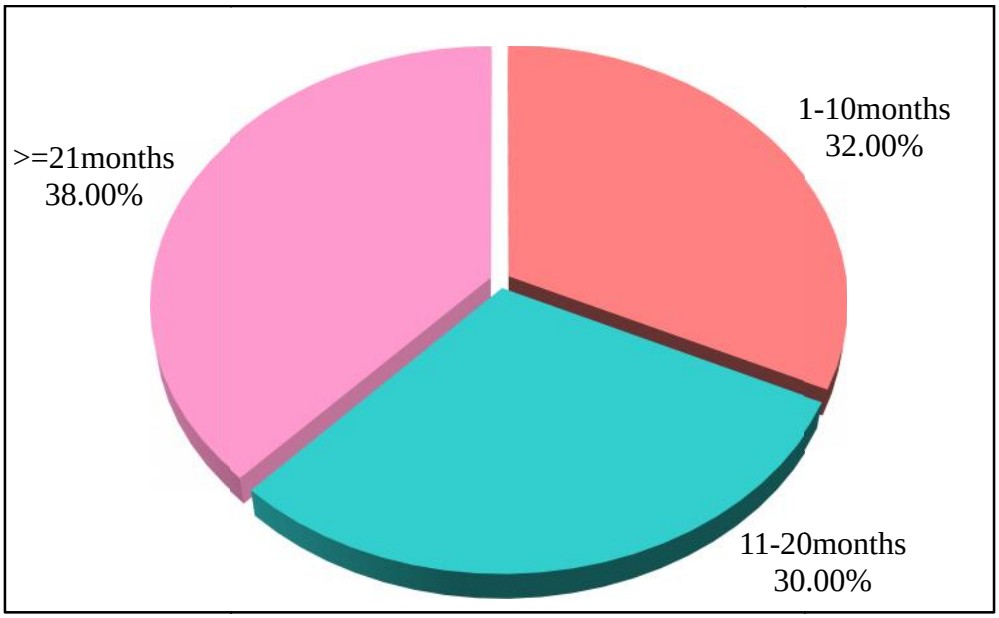
Above pie chart shows the 30 out of 50 patients 60% of the sample size belonged to below 9 years of age where as the rest of them were 10 years and above

Figure 7: Age of diagnosis wise distribution



The above pie chart shows that 36(72 %) of the patients were above 5 years of age of diagnosis , with only 14(28 %) being below five years of age

Figure 8: Months since on Rx wise distribution



The above pie chart shows the duration of treatment with DFZ was16 (32%) in 1 to ten months , 15(30%) in 11 to 20 months , and 19(38 %) in more than 21 months .

Figure 9: Distribution of patients by age groups, Age of diagnosis and Months since on Rx

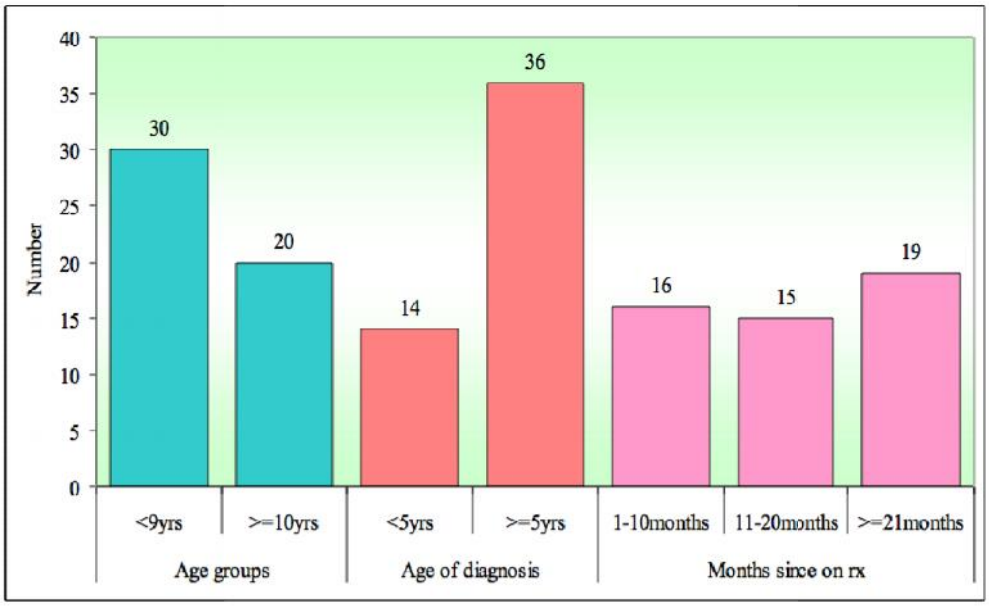
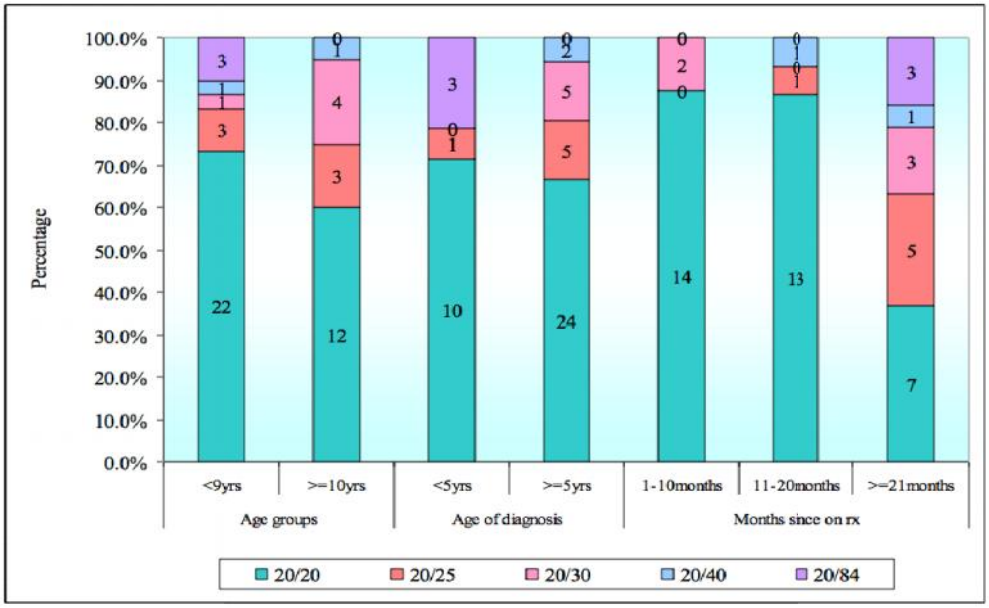


Table 2: Association between different factors with Visual acuity in right eye

Factors	20/20	%	20/25	%	20/30	%	20/40	%	20/84	%	Total
Age groups											
<9yrs	22	73.3	3	10.0	1	3.3	1	3.3	3	10.0	30
>=10yrs	12	60.0	3	15.0	4	20.0	1	5.0	0	0.0	20
Chi-square=5.9804 p=0.2006											
Age of diagnosis											
<5yrs	10	71.4	1	7.1	0	0.0	0	0.0	3	21.4	14
>=5yrs	24	66.7	5	13.9	5	13.9	2	5.6	0	0.0	36
Chi-square=10.8524 p=0.0282*											
Months since on Rx											
1-10months	14	87.5	0	0.0	2	12.5	0	0.0	0	0.0	16
11-20months	13	86.7	1	6.7	0	0.0	1	6.7	0	0.0	15
>=21months	7	36.8	5	26.3	3	15.8	1	5.3	3	15.8	19
Chi-square=18.0108 p=0.0211*											
Total	34	68.0	6	12.0	5	10.0	2	4.0	3	6.0	50

*p<0.05

Figure 10: Association between different factors with Visual acuity in right eye



In Table no 2 and Figure no 10 (Right Eye)

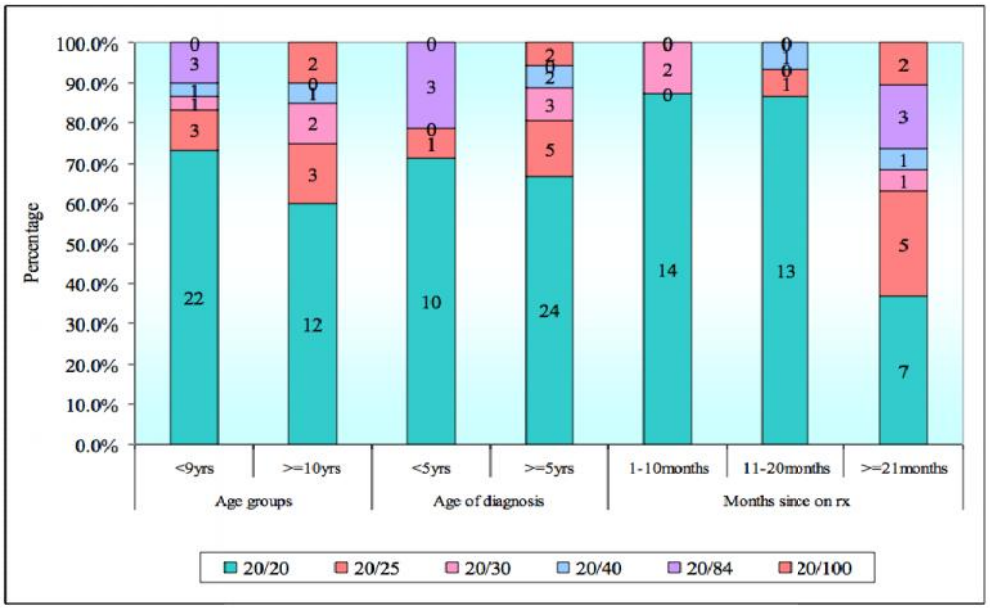
1. There is no association of the age of the patient to the visual acuity as the p value is 0.2006
2. There is a strong association of age of diagnosis with the visual acuity with p value 0.0282
3. There is a strong association of the duration of treatment in months with the visual acuity with p value of 0.0211

Table 3: Association between different factors with Visual acuity in left eye

Factors	20/20	%	20/25	%	20/30	%	20/40	%	20/84	%	20/100	%	Total
Age groups													
<9yrs	22	73.3	3	10.0	1	3.3	1	3.3	3	10.0	0	0.0	30
>=10yrs	12	60.0	3	15.0	2	10.0	1	5.0	0	0.0	2	10.0	20
Chi-square= 6.5365 p=0.2575													
Age of diagnosis													
<5yrs	10	71.4	1	7.1	0	0.0	0	0.0	3	21.4	0	0.0	14
>=5yrs	24	66.7	5	13.9	3	8.3	2	5.6	0	0.0	2	5.6	36
Chi-square= 12.6945 p=0.0264*													
Months since on rx													
1-10months	14	87.5	0	0.0	2	12.5	0	0.0	0	0.0	0	0.0	16
11-20months	13	86.7	1	6.7	0	0.0	1	6.7	0	0.0	0	0.0	15
>=21months	7	36.8	5	26.3	1	5.3	1	5.3	3	15.8	2	10.5	19
Chi-square= 21.0811 p=0.0205*													
Total	34	68.0	6	12.0	3	6.0	2	4.0	3	6.0	2	4.0	50

*p<0.05

Figure 11: Association between different factors with Visual acuity in left eye.



In Table no 3 and Figure no 11 (left Eye)

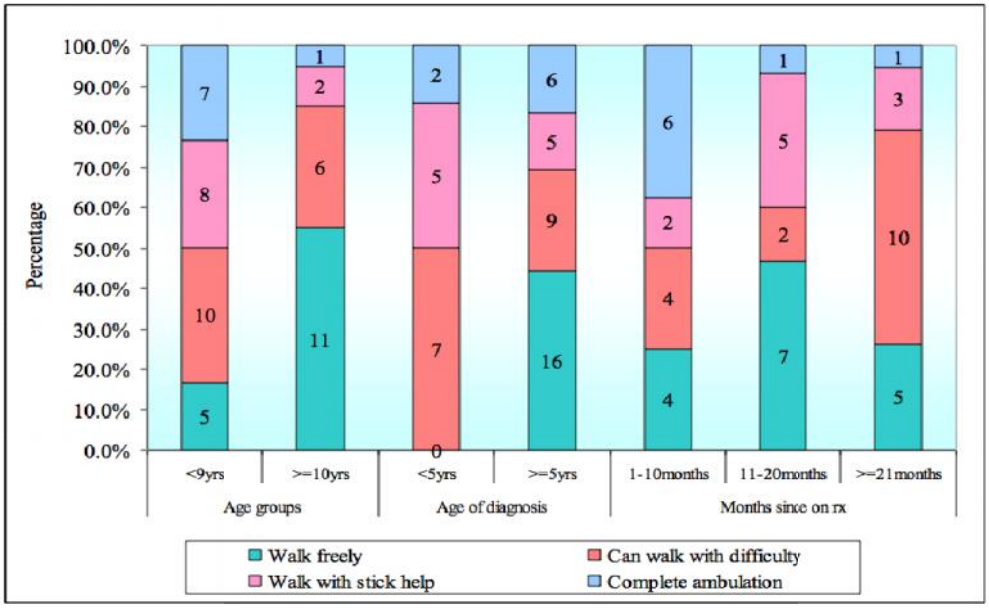
1. There is no association of the age of the patient to the visual acuity as the p value is 0.2575
2. There is a strong association of age of diagnosis with the visual acuity with p value 0.0264
3. There is a strong association of the duration of treatment in months with the visual acuity with p value of 0.0205

Table 4: Association between different factors with Ambulatory status

Factors	Complete ambulation	%	Can walk with stick	%	Walk with difficulty	%	Walk freely	%	Total
Age groups									
<9yrs	5	16.7	10	33.3	8	26.7	7	23.3	30
>=10yrs	11	55.0	6	30.0	2	10.0	1	5.0	20
Chi-square=9.7403 p=0.0209*									
Age of diagnosis									
<5yrs	0	0.0	7	50.0	5	35.7	2	14.3	14
>=5yrs	16	44.4	9	25.0	5	13.9	6	16.7	36
Chi-square=10.6273 p=0.0139*									
Months since on Rx									
1-10months	4	25.0	4	25.0	2	12.5	6	37.5	16
11-20months	7	46.7	2	13.3	5	33.3	1	6.7	15
>=21months	5	26.3	10	52.6	3	15.8	1	5.3	19
Chi-square=14.6116 p=0.0235*									
Total	16	32.0	16	32.0	10	20.0	8	16.0	50

*p<0.05

Figure 12: Association between different factors with Ambulatory status



In Table no 4 and Figure no 12

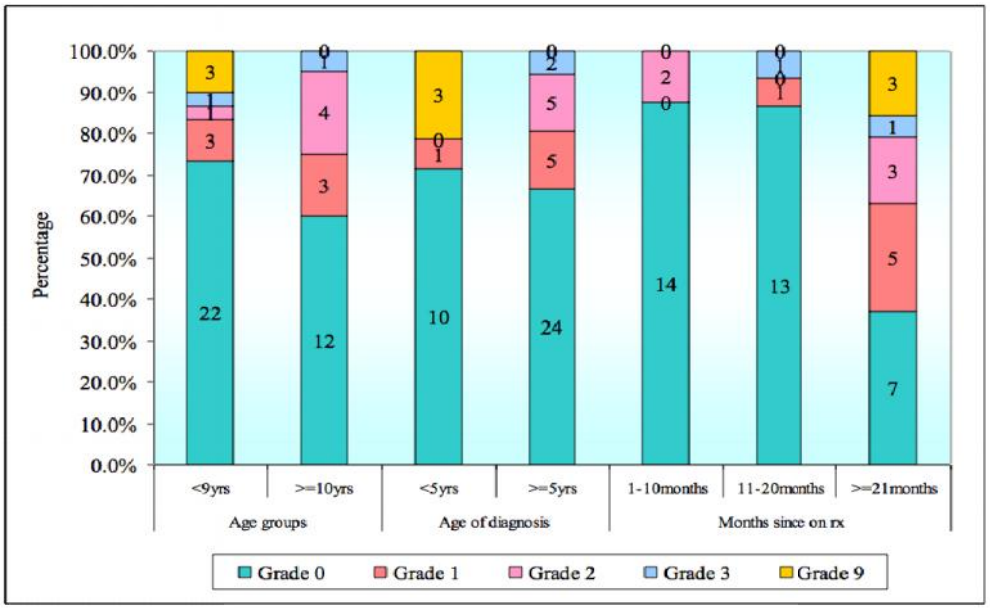
There is a strong association of age of the patient , age of diagnosis and the months on treatment with the ambulatory status with a p value less than 0.05

Table 5: Association between different factors with grades of cataract right eye

Factors	Grade 0	%	Grade 1	%	Grade 2	%	Grade 3	%	Grade 9	%	Total
Age groups											
<9yrs	22	73.3	3	10.0	1	3.3	1	3.3	3	10.0	30
>=10yrs	12	60.0	3	15.0	4	20.0	1	5.0	0	0.0	20
Chi-square=5.2134 p=0.2661											
Age of diagnosis											
<5yrs	10	71.4	1	7.1	0	0.0	0	0.0	3	21.4	14
>=5yrs	24	66.7	5	13.9	5	13.9	2	5.6	0	0.0	36
Chi-square=4.9144 p=0.2962											
Months since on Rx											
1-10months	14	87.5	0	0.0	2	12.5	0	0.0	0	0.0	16
11-20months	13	86.7	1	6.7	0	0.0	1	6.7	0	0.0	15
>=21months	7	36.8	5	26.3	3	15.8	1	5.3	3	15.8	19
Chi-square=19.9228 p=0.0106*											
Total	34	68.0	6	12.0	5	10.0	2	4.0	3	6.0	50

*p<0.05

Figure 13: Association between different factors with grades of cataract right eye



In Table no 5 and Figure no13 (Right Eye)

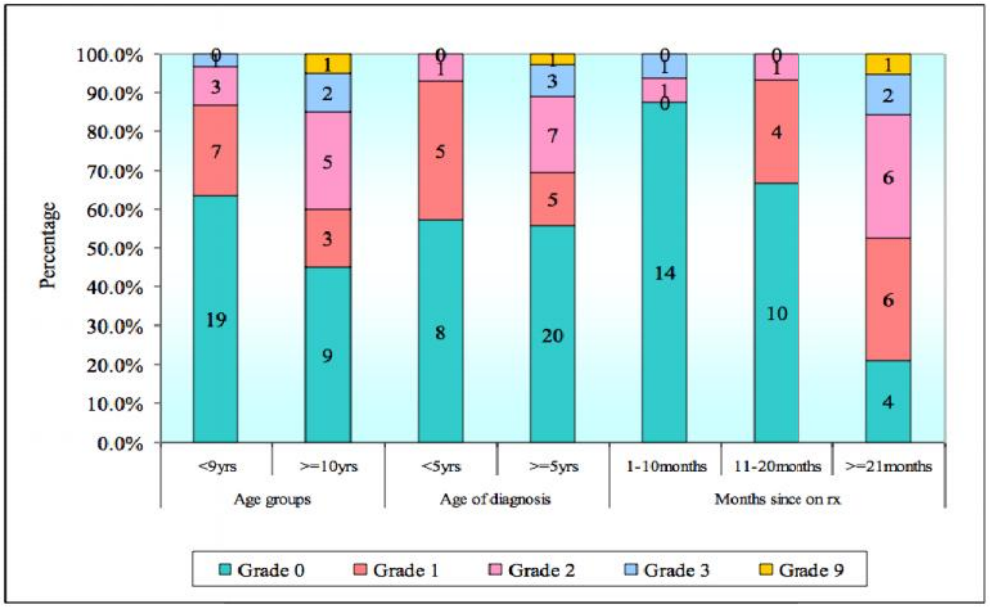
1. in age groups less than 9 years of age 8 patients out of 30 had cataract and above 10 years of age 8 patients out of 20 had cataract i.e 32 percent (16/50) had cataract over all and there is no association of the age of the patient with the grade of cataract
2. Four patients out of 14 had cataract when diagnosed below five years of age and 12 out of 36 patients had cataract when diagnosed after five years of age with no association with the grading of cataract
3. Up till 10 months of treatment with DFZ, 2 patients out of 16 had grade 2 PSC; from 11-20 months, 2 patients had cataract out of 15 and beyond 21 months , 12 out of 19 patients had cataract . There is strong association with p value 0.0106

Table 6: Association between different factors with grades of cataract left eye

Factors	Grade 0	%	Grade 1	%	Grade 2	%	Grade 3	%	Grade 9	%	Total
Age groups											
<9yrs	19	63.3	7	23.3	3	10.0	1	3.3	0	0.0	30
>=10yrs	9	45.0	3	15.0	5	25.0	2	10.0	1	5.0	20
Chi-square=5.2134 p=0.2661											
Age of diagnosis											
<5yrs	8	57.1	5	35.7	1	7.1	0	0.0	0	0.0	14
>=5yrs	20	55.6	5	13.9	7	19.4	3	8.3	1	2.8	36
Chi-square=4.9144 p=0.2962											
Months since on Rx											
1-10months	14	87.5	0	0.0	1	6.3	1	6.3	0	0.0	16
11-20months	10	66.7	4	26.7	1	6.7	0	0.0	0	0.0	15
>=21months	4	21.1	6	31.6	6	31.6	2	10.5	1	5.3	19
Chi-square=19.9228 p=0.0106*											
Total	28	56.0	10	20.0	8	16.0	3	6.0	1	2.0	50

*p<0.05

Figure 14: Association between different factors with grades of cataract left eye



In Table no 6 and Figure no14 (Left Eye)

1. In age groups less than 9 years of age, 11 patients out of 30 had cataract and above 10 years of age, 11 patients out of 20 had cataract i.e 44 percent (22/50) had cataract over all and there is no association of the age of the patient with the grade of cataract
2. Six patients out of 14 had cataract when diagnosed below five years of age and 16 out of 36 patients had cataract when diagnosed after five years of age with no association with the grading of cataract
3. Up till 10 months of treatment with DFZ, 2 patients out of 16 had grade 2 PSC; from 11-20 months, 5 patients had cataract out of 15 and beyond 21 months , 15 out of 19 patients had cataract . There is strong association with p value 0.0106

Table 7: Comparison of different factors with Visual acuity in right eye

Factors	Categories	Mean	SD	SE	Statistic	p-value
Age groups	<9yrs	13.69	2.46	0.45	t=1.8278	0.0738
	>=10yrs	12.54	1.70	0.38		
Age of diagnosis	<5yrs	14.06	2.05	0.55	t=1.6759	0.1003
	>=5yrs	12.90	2.25	0.38		
Months since on Rx	1-10months	12.01*	1.38	0.35	F=7.1656	0.0019*
	11-20months	14.72	2.73	0.70		
	>=21months	13.07	1.76	0.40		
	Total	13.23	2.24	0.32		

*p<0.05, t→ t test, F→ is one way ANOVA applied

Figure 15: Comparison of different factors with Visual acuity in right eye

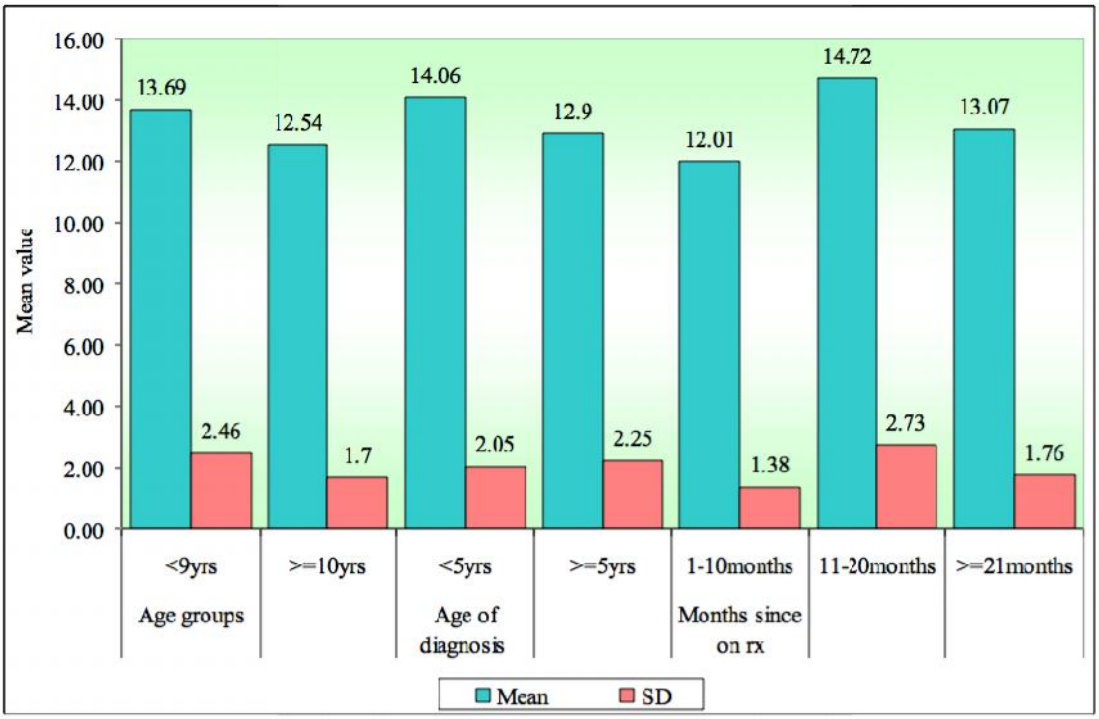


Table8: Comparison of different factors with Visual acuity in left eye

Factors	Categories	Mean	SD	SE	Statistic	p-value
Age groups	<9yrs	13.90	2.08	0.38	t=-0.4847	0.6301
	>=10yrs	14.18	1.96	0.44		
Age of diagnosis	<5yrs	14.34	1.50	0.40	t=0.6984	0.4883
	>=5yrs	13.89	2.20	0.37		
Months since on Rx	1-10months	13.64	2.48	0.62	F=0.4051	0.6692
	11-20months	14.27	2.24	0.58		
	>=21months	14.13	1.37	0.31		
	Total	14.01	2.02	0.29		

t→ t test, F→ is one way ANOVA applied

Figure16: Comparison of different factors with Visual acuity in left eye

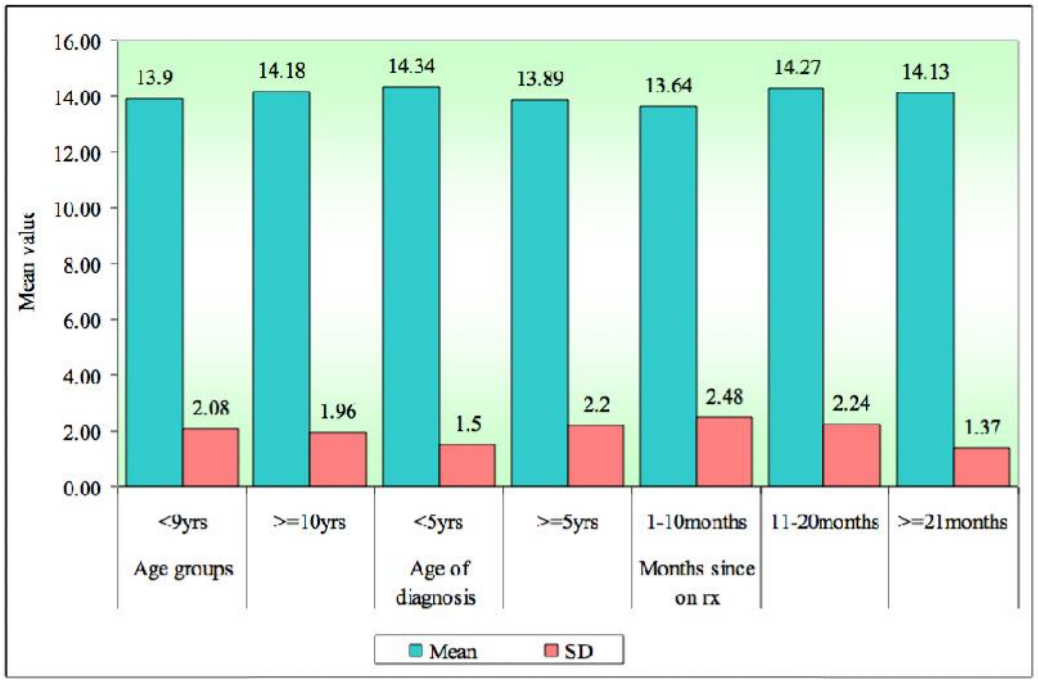


Table9: Correlation between age, age of diagnosis and months since on Rx with IOP, ambulatory status, Grades of cataract right eye and Grades of cataract left eye by Spearman's rank correlation

	Variables	N	Spearman R	t-value	p-level
IOP rt Eye	Age	50	-0.1138	-0.7933	0.4315
	Age of diagnosis	50	-0.2710	-1.9604	0.0500*
	Months since on rx	50	0.2569	1.8416	0.0717
IOP lt Eye	Age	50	0.1023	0.7126	0.4796
	Age of diagnosis	50	0.0590	0.4094	0.6840
	Months since on Rx	50	0.1610	1.1303	0.2640
Ambulatory status	Age	50	-0.5149	-4.1614	0.0001*
	Age of diagnosis	50	-0.3663	-2.7271	0.0089*
	Months since on Rx	50	-0.2534	-1.8150	0.0758
Grades of cataract re	Age	50	0.3200	2.3402	0.0235*
	Age of diagnosis	50	0.0546	0.3790	0.7063
	Months since on Rx	50	0.5759	4.8802	0.0001*
Grades of cataract le	Age	50	0.3200	2.3402	0.0235*
	Age of diagnosis	50	0.0546	0.3790	0.7063
	Months since on Rx	50	0.5759	4.8802	0.0001*

*$p<0.05$

DISCUSSION

Duchenne muscular dystrophy (DMD) is the most common hereditary neuromuscular disease affecting all races and ethnic groups. Its characteristic clinical features are progressive weakness, intellectual impairment, hypertrophy of the calves, and proliferation of connective tissue in muscle. The incidence is 1 in 3,600 live born infant boys[2]. In our study we had a sample size of 50 diagnosed DMD patients who were on treatment with DFZ 0.75 mg per kg of body weight daily since the day of diagnosis.

Our study is a pioneer study in the field of an elaborated ocular diagnosis with classification of the pathology and the visual prognosis in DMD patients. The national and international studies done on the side effects of DFZ are very limited and have only done a superficial analysis as to the incidence of the cataract and have kept the ocular prognosis over a period of time out of the scope of their study

The mean age of the patients were 8.78 years with a standard deviation +/- 2.65 years.

The mean age of diagnosis of DMD was 7 years with a standard deviation of 2.55 years from the above statistics it can be commented that the age of diagnosis of the patient population is fairly young and all the patients were directly started on DFZ and were not earlier on any alternate therapy such as prednisolone or dexamethasone , hence most of the bias caused with multiple module regimes are avoided .

The duration of the treatment was taken in months and was classified into three groups i.e 1- 10 months on R_x had 16 (32%) patients , 11- 20 months is 15

patients (30%) and beyond 21 months is 19 patients (32.21%) , which is an equal distribution of the sample of the time the drug was taken for , and give a more satisfying statistical analysis.

Thirty four patients had perfect vision of 20/20 in the right eye where as 3 patients had a vision of 20/84 and these patients did not correct on refraction showing either a media opacity , retinal involvement or amblyopia .

There is a strong association of the age of diagnosis with the visual acuity in the right eye with a p value of 0.028 which is statistically significant of the fact that the patients with an earlier age of diagnosis had a poor visual acuity which is supported by the association of the duration on DFZ treatment with the visual acuity in right eye with a p value of 0.0211 which can be seen with the reduction in the visual acuity with the increase in the duration of treatment i.e. from 1- 10 months on R_x of VA (20/20) 14 out of 16 (87.5 %) patient fell to 7 out of 9(36.5%) patients that were beyond 21 months on therapy.

34 patients had perfect vision of 20/20 in the left eye where as 3 patients had a vision of 20/84 , 2 patients had a VA of 20/100 & these patients did not correct on refraction showing either a media opacity , retinal involvement or amblyopia .

There is a strong association of the age of diagnosis with the visual acuity in the left eye with a p value of 0.0264 which is statistically significant of the fact that the patients with an earlier age of diagnosis had a poor visual acuity which is supported by the association of the duration on DFZ treatment with the visual acuity in left with a p value of 0.0205 which can be seen with the reduction in the visual acuity with the increase in the duration of treatment i.e. from 1- 10 months on R_x of

VA (20/20) 14 out of 16(87.5 %) patient fell to 7 out of 9 (36.8%) patients that were beyond 21 months on therapy.

Hence from the above it can be made out that both the eyes were statistically significant with the association of the age of diagnosis and duration of therapy with the visual acuity.

Ambulatory status was classified according to the motor component that is patient can walk freely , walk with difficulty , requires a stick or a walker and last resorts to complete ambulation and moves around with the help of a wheelchair.

The association of age with the ambulatory status that patients below 9 years of age 7 out of 30 patients (23.3 %) could walk freely compared to 1 out of 20 patients (5%) above 10 years of age, complete ambulation was found in 5 out of 30 (16.7%) below 9 years compared to 11 out of 30(55 %) in above 10 years.

With a p value of 0.0209 there is a very significant association that with the increase in the age of the patient the ambulatory prognosis is poor and 11 patients beyond the age of 10 years depended on the wheelchair.

There is a very strong association of the age of diagnosis with the ambulatory status (p value- 0.0139), in patients who were diagnosed below five years of age and were early on DFZ treatment 18 (60%) patients walked with difficulty or a stick where as when there was a late diagnosis beyond 5 years of age 44% of the patients were already wheelchair bound.

The association of the duration of treatment with the ambulatory status has a p value of 0.0235 and is statistically significant , 4 out of 16 patients i.e. 25 % of the patients were completely ambulatory in 1-10 months of DFX therapy compared to 5

out of 19 (26.3 %) in beyond 21 months showing that the drug has actually increased the ambulatory prognosis and slowed down the disease muscular dystrophy.

Corticosteroids are known to cause posterior sub-capsular cataract but most of the studies only mention the incidence of the cataract with the use and nothing has yet been mentioned about the visual prognosis or the grade of the cataract and its association with the variables.

In our study we examined both the eyes separately, but the earliest incidence of cataract was after the drug was used for a substantial period of 12 months after the diagnosis was confirmed.

In the right eye patients below 9 years of age 8 out of 30 (26 %)had PSC where as above ten years of age 8 out of 20 patients (40%) had PSC, so overall 16 out of 50 patients had cataract in their right eye amounting to 32%, where as in the left eye 11 out of 30 patients (36%) below the age of nine had PSC and 11 out of 20 patients (55%) above the age of ten had PSC with a over all incidence of 22 out of 50 patients (44 %) in the left eye had PSC . the p value is 0.226 & 0.2661 for respective eyes and is statistically insignificant

DeSilva[45] in 1987 had an incidence of 12.5 % PSC with prednisolone , Fenichel[47] in 1991 had a 10.8 % incidence of PSC with prednisolone , where as Biggar[48] in 2001 noted 30% PSC with DFZ , in 2006 had 55% incidence of PSC[51]

In a 2004 Toronto regimen[51] 30 % PSC with DFZ daily intake v/s no PSC was found in interrupted therapy with DFZ proving that interrupted therapy is better for the visual prognosis of the patient . Alman[52] in 2004 had a 33% PSC with DFZ and Houde [53] had a 49% incidence with DFZ.

The above studies show that prednisolone has a lower incidence of PSC compared to the incidence with DFZ but they lack information about the grades and the quantification of the PSC also the association was not proven earlier.

In the Right eye from 1 - 10 months on DFZ , 87% did not have PSC but 12.5% had grade 2 PSC compared to beyond 21 months where 7 out of 19 patients didn't have cataract but 3 patients had grade 9 cataract which need to be evaluated for surgery .

In the left eye in the first 10 months of treatment 87.5 % didn't not have PSC where as 12 .6 % have grade 3 PSC compared to beyond 21 months on treatment 21.1% were cataract free and 78.9 % had PSC such that 5.3 % patients i.e. 1 out of 19 need surgical intervention because the vision is poorer than 20/100 and the patients is visually impaired.

The p value in both the left and right eyes in association of duration of treatment with the incidence of cataract is statistically significant and shows that with the increase in the duration of treatment the incidence and the grade of cataract increases and this is the main stay of this study

The intraocular pressures of both the left eye and the right eye have a mean value of 13.2 and 14.01 mm of Hg with no optic disc changes were seen

There is no evidence of any other retinal insult caused by the daily regime of DFZ.

LIMITATION OF THE STUDY

1. It is a single centre study with a small number of patients
2. The patients were taken up for a child development clinic register and then enrolled for the study and were demographically unequally distributed
3. The compliance of the patient is only validated through history taking

IMPLICATION FOR FUTURE STUDY

1. The study should be at a multicenter level with a larger sample size
2. The drugs should be provided at the hospital level to ensure better compliance

CONCLUSION

1. This is the first national and international pioneer study conducted in India evaluating the ocular side effects of Deflazacort in patients diagnosed with Duchenne muscular dystrophy (DMD)
2. There is a very strong association of the incidence of cataract (PSC) with the consumption of this drug and the incidence is higher as compared to prednisolone
3. The median age of appearance of cataract is 15 months and none of the patients developed cataract below 12 months on deflazacort treatment .The evidence of cataract causes visual debilitation in the patients ,hence there is a need for follow up at 12 months of treatment and then forth every 3 months with surgical intervention to restore the vision
4. There is no evidence of rise in the intraocular pressure in either of the eyes with no glaucoma changes when compared to prednisolone
5. Deflazacort has decreased the progression of the disease by maintaining the ambulatory status and motor functions

SUMMARY

1. A a total of 50 patients were diagnosed with DMD at the child development clinic and started on DFZ at 0.75 mg per kg body weight on daily regimen
2. The patients were subjected to a complete ophthalmological examination of the anterior and the posterior segment , ambulatory status along with recording of the intraocular pressure, a dilated evaluation of the fundus and disc finding were recorded .
3. The mean age of the patients were 8.78 years with a standard deviation +/- 2.65 years. The mean age of diagnosis of DMD is 7 years with a standard deviation of 2.55 years.
4. The duration of the treatment is taken in months and is classified into three groups i.e 1- 10 months on R_x had 16 (32%) patients , 11- 20 months is 15 patients (30%) and beyond 21 months is 19 patients (32.21%)
5. 34 patients had perfect vision of 20/20 in the right eye where as 3 patients had a vision of 20/84 where as 34 patients had perfect vision of 20/20 in the left eye where as 3 patients had a vision of 20/84 , 2 patients had a VA of 20/100 which did not correct with refraction and needs surgical intervention
6. There is a strong association of the age of diagnosis with the visual acuity in the right eye with a p value of 0.028 which is statistically significant of the fact that the patients with an earlier age of diagnosis had a poor visual acuity on examination and the same reciprocates for the left eye.
7. There is a strong association of age of the patient , age of diagnosis and the months on treatment with the ambulatory status with a p value less than 0.05

8. 32 percent (16/50) had cataract (PSC) over all and there is no association of the age of the patient with the grade of cataract
9. Up till 10 months of treatment with DFZ, 2 patients out of 16 had grade 2 PSC; from 11-20 months, 2 patients had cataract out of 15 and beyond 21 months , 12 out of 19 patients had cataract in the right eye , Up till 10 months of treatment with DFZ, 2 patients out of 16 had grade 2 PSC; from 11-20 months, 5 patients had cataract out of 15 and beyond 21 months , 15 out of 19 patients had cataract in the left eye . There is strong association with p value 0.0106 for both eyes.
10. There was no rise in the intraocular levels above 21 mm of Hg and no disc findings of glaucoma were observed , there was evidence of any retinal insult with the usage of the drug in any subject . none of the patients turned out to be steroid responders

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ANNEXURE I – CONSENT FORM

CONSENT FOR PARTICIPATION IN RESEARCH STUDY

Mr _____ we are requesting you to enroll yourself in study titled **"ONE YEAR CROSS-SECTIONAL STUDY OFPREVALENCE OF OCULAR SIDE EFFECTS OF DEFLAZACORT TREATMENT IN DUCHENNE MUSCULAR DYSTROPHY"** conducted by Department of Ophalmology, J.N. Medical College, under KLE university, Belgaum.

we request you to participate in our study.

Your participation in research is voluntary. Your decision whether or not to participate in the study will not affect your relationship with J.N. Medical College. If you decide to quit you are free to withdraw at any time.

The purpose of research is to assess The Ocular Complications Of Deflazacort In Duchenne Muscular Dystrophy.

Procedure Involved:

If you agree to enroll yourself in my study, you will be interviewed regarding your present, past and family history, then you will be clinically examined in detail and investigated accordingly.

Risks and Benefits:

There is absolutely no risk involved in participating in this study the benefits are the early diagnosis of the ocular side effects and timely management of the same.

Voluntary Participation/Withdrawal:

Taking part in the study is voluntary. You may choose not to enroll yourself in this study. Your decision will not change present or future health care services offered to you at K.L.E.s hospital.

Alternatives:

Even if you decline the participation in the study, you will get the routine line of management.

Privacy and Confidentiality:

The only people to know that you are a research subject are members of the research team. No information about you or information provided by you during the research will be disclosed to other without your written permission except:

1. In emergency to protect your rights and welfare.
2. If required by law.

Authorization to Publish Results:

When the results of the research are published or discussed, in a conference, no information will be displayed that would disclose your identity. Any information that is

obtained in connection with this study and that can be identified with you will remain confidential.

Financial Incentives for participation:

No financial incentives are being offered to enrolled patients. It is purely being done with the idea of research and all the cost of the study will be borne by the investigator.

Questions:

If you need any further information regarding your rights as a study participant, you may also contact Dr.Ganga S. Pilli (Mobile No.9480275601), Chairman of Institutional Ethics Committee, JNMC, and Belagavi-10

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CONSENT STATEMENT

I voluntarily agree to take part in this study by signing below. I may withdraw at any time. I am not giving up any legal rights by signing this form. My signature below indicates that I have read, or it has been read to me, this entire consent form, and have had all my questions answered.

In case of the queries during the study or in future you may contact following person.

Principle investigator: DR. _____

Guide : DR. _____

Name of the participant: (signature/thumb print)

Name of the witness: (signature)

Name of the investigator: (signature)

Date: Place:

Address:

Phone no:

ANNEXURE-II

PROFORMA

PATIENTS ID NO: | | | |

NAME: | | | | | | | | | | | | | | | | | |

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AGE: | | | Years

SEX: | M |

ADDRESS: | | | | | | | | | | | | | | | | | |

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CONTACT NUMBER :- | | | | | | | | | | |

OP NUMBER: | | | | | | | | |

IP NUMBER: | | | | | | | | | |

DATE OF ADMISSION: | | | / | | | / | | | | |

DATE OF DISCHARGE: | | | / | | | / | | | | |

IS THE PATIENT ELIGIBLE FOR STUDY? (1-YES; 2-NO) | |

HAS INFORMED CONSENT BEEN GIVEN? (1-YES; 2-NO) | |

FINAL RESULT INFORMATION | |

1- INELIGIBLE
2- ELIGIBLE- REFUSAL
3- ELIGIBLE- PARTICIPATING

DATE: | | | / | | | / | | | | |

CHIEF COMPLAINTS:

DIMINUTION OF VISION RE ☐

Duration: _____ days/ months/years

LE ☐

Duration: _____ days/ months/years

HISTORY OF PRESENT ILLNESS:

1 .DIMINUTION OF VISION 1- Gradual; 2- Sudden ☐

1- Progressive; 2- Static ☐

1- Painless; 2- Painful ☐

1- For distance; 2- For near ☐

2. DIPLOPIA/POLYOPIA 1- Present; 2- Absent ☐

3. COLOURED HALOS 1- Present; 2- Absent ☐

4. BLACK SPOTS BEFORE THE EYES 1- Present; 2 - Absent ☐

5. WATERING 1- Present; 2 - Absent ☐

6. REDNESS 1- Present; 2 - Absent ☐

7. DISCHARGE 1- Present; 2 - Absent ☐

8. H/O WEARING GLASSES (1-Distance; 2-Near; 3-Both) ☐

Duration: ☐☐onths/years

PAST HISTORY:

TRAUMA TO THE EYE: 1- Present; 2- Absent ☐

OCULAR SURGERY: 1- Present; 2- Absent ☐

Type of surgery: _____

ANY OTHER MEDICAL DISORDERS: _____

PERSONAL HISTORY:

DMD: 1- Present; 2- Absent ☐

Duration: ☐☐ months/years

TREATMENT : 1- Present; 2- Absent ☐

Duration: ☐☐ months/years

NAME OF MEDICATION _____ DOSE ☐

Duration: ☐☐ months/years

GENERAL PHYSICAL EXAMINATION:

General Appearance:

1- Well built ,2- Moderately built, 3- Poorly built, 4- emaciated ☐

Pallor: 1- Present 2- Absent ☐

If present 1- Mild 2- Moderate 3- Severe ☐

Pulse: ☐☐☐/minute

BP:- ☐☐☐/ ☐☐☐mm of hg

Temperature: ☐☐☐gree Fahrenheit

Respiratory rate: ☐☐inute

SYSTEMIC EXAMINATION:

CVS: 1- Normal 2- Abnormal ☐
if 2, specify :_____

RS: 1- Normal 2- Abnormal ☐
if 2, specify: _____

CNS: 1- Normal 2- Abnormal ☐
if 2, specify :_____

Per Abdomen: 1- Normal 2- Abnormal ☐
if 2, specify :_____

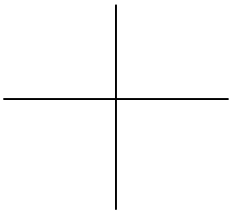
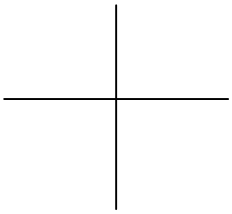
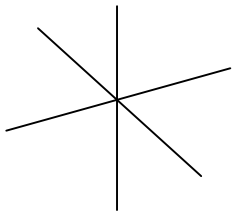
OCULAR EXAMINATION:

Head posture: 1- Erect ,2- Tilted ☐

Visual Axis: 1- Parallel, 2- Deviated ☐

Facial Symmetry: 1- Symmetrical, 2- Asymmetrical ☐

Extraocular movements:

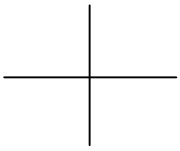
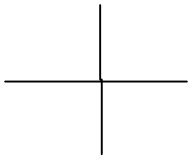
RE-  LE-  Binocular :- 

(N- Normal, R- Restricted) ☐

1) Visual Acuity:

	RE	LE
DISTANT		
PINHOLE		
NEAR		
AIDED		

REFRACTION/RETINOSCOPY:

Prescription	Spherical	Cylindrical	Axis	BCVA
RE				
LE				

2. Adnexa (1- Normal; 2-Abnormal)	☐	☐
3. Sclera (1- Normal; 2- Congested)	☐	☐
4. Conjunctiva (1-normal; 2-conjunctival congestion; 3-ciliary congestion; 4-chemosis)	☐	☐
5. Cornea (1- normal; 2-opacity; 3-vascularisation)	☐	☐
6. Anterior chamber (1- normal depth; 2-shallow; 3-deep)	☐	☐
7. Iris (1-normal colour & pattern; 2-Abnormal)	☐	☐
8. Pupil: Size- ____ in mm Shape- 1- Round & Regular; 2-Abnormal Reaction: Direct (1. Present, 2. Absent) Indirect (1. Present, 2. Absent) Near reflex (1. Preset, 2. Absent)	 ☐ ☐ ☐ ☐	 ☐ ☐ ☐ ☐
9. Lens Clarity- 1. Clear, 2. Opaque Cataract - (1) , PCIOL - (2) Cataract if present- 1.immature 2.mature 3. hyper mature A) CORTICAL- (1.Present, 2. Absent)	 ☐ ☐ ☐ ☐	 ☐ ☐ ☐ ☐
B) NUCLEAR SCLEROSIS- 1. PRESENT, 2- ABSENT If present- 1. Grade-1 2. Grade-2 3.Grade- 3 4. Grade-4	☐ ☐	☐ ☐
(C) POSTERIOR SUBCAPSULAR CATARACT PRESENT, 2. ABSENT	☐	☐

FUNDUS	RE	LE
GLOW		
MEDIA		
DISC Size Shape Color Nasalization Bayonetting Lamellar dot sign Haemorrhages Others:		
C:D RATIO		
BLOODVESSELS		
BACKGROUND		
MACULA		

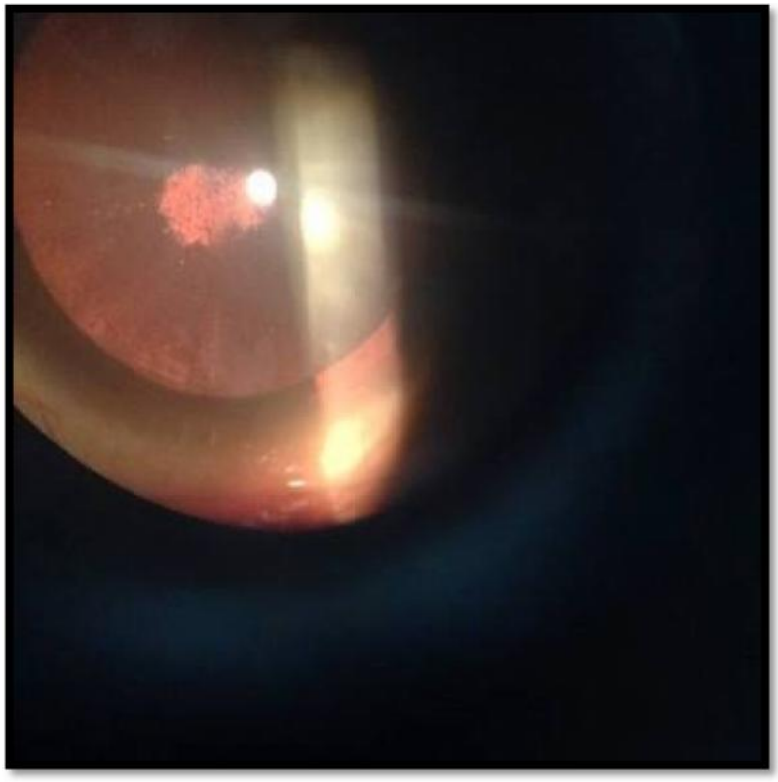
A) **:**IOP: (with NCT)

RE: _____ mm of hg

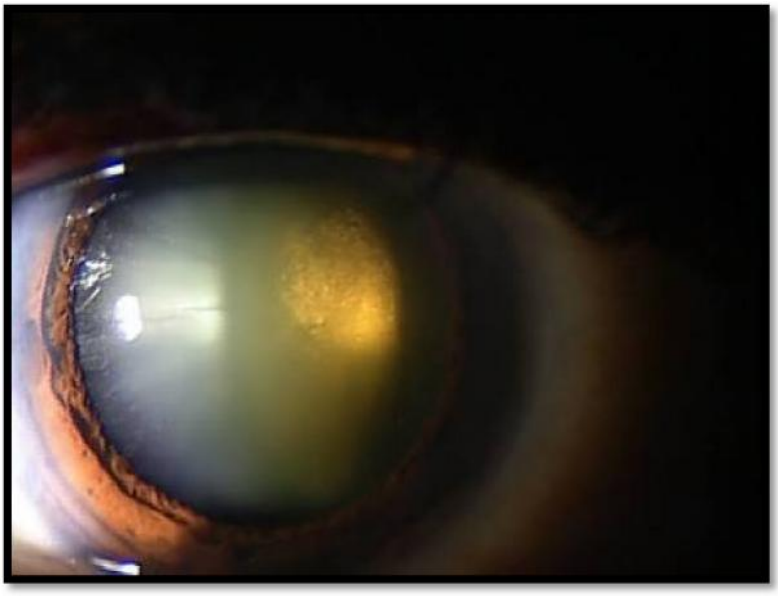
LE : _____ mm of hg

IMPRESSION:-

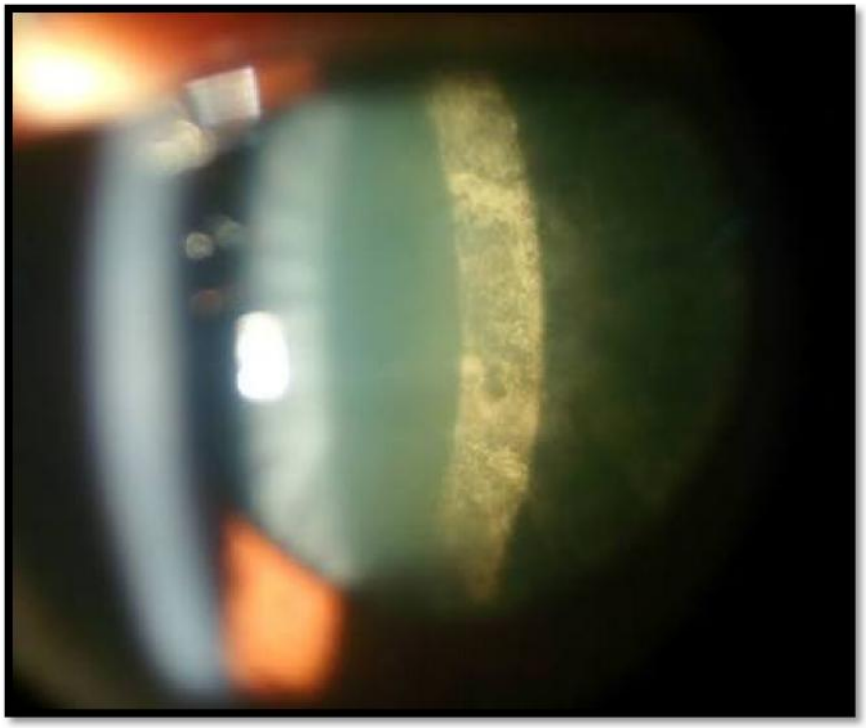
ANNEXURE III – PHOTOGRAPHS



Photpgraph 1 :- Grade I Psc



Photpgraph 2 :- Grade II Psc



Photpgraph 3 :- Grade IX PSC

ANNEXURE-IV - MASTER CHART

sr no	opd no	age	age of dx	months since on rx	va re	va le	iop re	iop le	ambulatory status	cataract re	cataract le	glaucoma	retinal pathology
1	3556936	10	6	24	20/20	20/20	12.4	12.2	4	-	-	-	-
2	3618945	12	11	12	20/20	20/20	13.6	14.3	1	-	-	-	-
3	3618937	10	9	12	20/20	20/20	11	12.2	3	-	-	-	-
4	2216695	6	4	24	20/84	20/84	12	14	3	present grade1	present grade1	-	-
5	3676696	11	10	12	20/20	20/20	12.4	12.8	1	-	-	-	-
6	3277803	10	9	12	20/20p	20/20p	15.6	17.3	3	-	-	-	-
7	3326170	9	4	12	20/20	20/20	14.3	12.2	3	-	-	-	-
8	1797971	15	10	60	20/25	20/25	11.6	14.3	1	present grade3	present grade3	-	-
9	3707343	8	8	2	20/20	20/20	11.5	11	4	-	-	-	-
10	852773	12	10	24	20/30	20/100	12.2	14.6	2	grade2 psc	grade2 psc	-	-
11	3823649	5	5	2	20/20	20/20	13.6	14.4	4	-	-	-	-
12	2168427	7	4	36	20/20	20/20	14.5	15.6	2	-	-	-	-
13	3864790	14	14	3	20/20	20/20	11.6	17.4	1	-	-	-	-
14	3745373	10	4	3	20/20	20/20	12.6	12.5	2	-	-	-	-
15	1769137	7	6	12	20/40	20/40	18	17.2	1	grade1psc	grade1 psc	-	-
16	3999672	10	7	36	20/40	20/40	12.6	12.5	1	grade2 psc	grade2 psc	-	-
17	3892576	8	8	3	20/20	20/20	14.6	18.5	3	-	-	-	-
18	3482901	6	4	14	20/20p	20/20p	18.5	14.6	2	grade1psc	grade1 psc	-	-
19	3912010	10	6	48	20/25	20/25	12.5	14.7	1	grade2 psc	grade2 psc	-	-
20	3978790	9	7	24	20/20	20/20	15	12.9	2	grade1psc	grade1 psc	-	-
21	2544619	6	5	12	20/20p	20/20p	14.7	16.7	3	grade1psc	grade1 psc	-	-
22	2897780	9	7	19	20/25	20/25	18.4	16.3	4	grade2 psc	grade2 psc	-	-
23	3409900	12	7	60	20/25	20/25	13.4	12.6	2	grade9 psc	grade 9 psc	-	-
24	3569989	10	9	12	20/20	20/20	17.5	16.4	1	grade1psc	grade1 psc	-	-
25	2309987	14	12	24	20/20p	20/20p	12.7	16.4	1	grade1psc	grade1 psc	-	-

26	2456889	5	4	12	20/20	20/20	17.5	16.4	2	-	-	-	-
27	2099877	7	5	24	20/25	20/25	14.7	12.5	2	grade2 psc	grade2 psc	-	-
28	3078898	9	6	36	20/30	20/30	18	16.4	2	grade3 psc	grade3psc	-	-
29	3549901	6	6	6	20/20	20/20	14.5	15.5	4	-	-	-	-
30	2309987	10	9	1	20/20	20/20	12.6	14.3	2	-	-	-	-
31	3045899	7	7	8	20/20	20/20	11	12.6	1	-	-	-	-
32	3019989	11	7	48	20/30	20/30	12.6	13.2	2	grade3 psc	grade3psc	-	-
33	2478897	5	5	3	20/20	20/20	11.5	12.6	4	-	-	-	-
34	3089909	12	10	24	20/20p	20/20p	10.6	13.4	1	grade1psc	grade1 psc	-	-
35	3780011	7	6	9	20/20	20/20	11.2	13.3	3	-	-	-	-
36	3670011	11	7	30	20/30	20/30	9.4	10.6	1	grade2 psc	grade2 psc	-	-
37	3401223	6	6	3	20/20	20/20	10.4	10.6	4	-	-	-	-
38	3780900	8	7	24	20/25	20/25	11	12.5	2	grade2 psc	grade2 psc	-	-
39	3769020	6	6	5	20/20	20/20	12	13.4	2	-	-	-	-
40	2309909	8	7	12	20/20	20/20	11	12	1	-	-	-	-
41	2340098	6	7	12	20/20	20/20	12	11.7	-	-	-	-	-
42	3089989	7	4	36	20/20	20/20	14.5	15.6	2	-	-	-	-
43	2098990	6	4	24	20/84	20/84	12	14	3	present grade1	present grade1	-	-
44	3078890	9	8	12	20/20	20/20	14.3	12.2	3	-	-	-	-
45	3045677	12	10	24	20/30	20/100	12.2	14.6	2	grade2 psc	grade2 psc	-	-
46	2014561	8	8	2	20/20	20/20	11.5	11	4	-	-	-	-
47	2011456	6	4	24	20/84	20/84	12	14	3	present grade1	present grade1	-	-
48	3016543	7	4	36	20/20	20/20	14.5	15.6	2	-	-	-	-
49	3012667	6	7	12	20/20	20/20	12	11.7	-	-	-	-	-
50	2012556	14	14	3	20/20	20/20	11.6	17.4	1	-	-	-	-

ANNEXURE-V

KEY TO MASTER CHART

Sr No	Serial number
dx	Diagnosis
rx	Treatment
va	Visual acuity
le	Left eye
re	Right eye
iop	Intra ocular pressure