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EFFECT OF STEROID ON INTRAOCULAR PRESSURE IN PAEDIATRIC PATIENTS WITH NEPHROTIC SYNDROME

Ophthalmology

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ABSTRACT

Aim: To evaluate the effect of Steroid on Intraocular Pressure in paediatric patient with Nephrotic syndrome. **Method:** A prospective cross sectional analytical case study was conducted at Heritage Institute of Medical Science (HIMS) from January 2017 to December 2017 in accordance with the Principle of the Declaration of Helsinki after approval from Institutional Ethical committee. 25 patients with Nephrotic syndrome were evaluated. Comprehensive ophthalmic assessment includes best corrected visual activity (BCVA), slit lamp & fundus examination was performed. Intraocular pressure (IOP) was measured by Applanation tonometry before steroid treatment, 1 month & 2 months after steroid treatment. Information on renal histological diagnosis and treatment regimen on each patient was noted. Data were analysed statistically. **Result:** 25 Patients with Nephrotic syndrome was evaluated. There was a statistically significant difference between IOP rise & total duration of steroid intake ($p = 0.0031$). No significant difference was noted between IOP and age of children with Nephrotic syndrome & total dose of steroid intake ($P > 0.05$). **Conclusion:** Nephrotic syndrome in children with longer duration of steroid therapy have greater risk of raised IOP & hence Glaucoma. So Paediatricians & Nephrologists are advice to refer Nephrotic syndrome patient for regular Ophthalmological evaluation.

KEYWORDS

Steroid , Intraocular Pressure, Glaucoma, Nephrotic Syndrome.

INTRODUCTION :

Nephrotic syndrome is one of the most common renal disease in children. It is defined by the presence of nephrotic range proteinuria (50mg/kg/day), edema, hyperlipidemia and hypoalbuminemia (less than 2.5 mg/ dl). These features that characterise nephrotic syndrome develops from primary alteration of the perm selective barrier of the glomerular capillary wall, which is no longer able to restrict the loss of protein to less than 100mg/m2 body surface per day.

Nephrotic range proteinuria has been variously defined by a urinary protein to creatinine ratio higher than 0.25 g protein per mmol creatinine or >2.0 mg protein per mg creatinine or ≥ 3 + proteinuria on urine dipstick.[1,2,3]

Worldwide the average incidence of Nephrotic syndrome is estimated to be 2-16.9 cases per 100000 children , in developing countries like India the incidence is still higher .[4]

Before the start of this century Nephrotic syndrome patient suffered high morbidity & mortality. Most commonly these patients died because of sepsis, peritonitis & malnutrition. Use of corticosteroids have reduced mortality rate to around 3% with infection remaining the most important cause of death. However corticosteroids have known side effects, such as increase of Intraocular pressure (IOP) & cataract and their use in Nephrotic syndrome requires prolonged high dose therapy usually for > 8 weeks. So patients should be referred to Ophthalmologist for regular monitoring [5,6.]

Prolonged use of high dose steroid therapy have multiple effects on the trabecular meshwork (TM) thereby increasing risk of glaucoma. The route of administration may influence the response of aqueous dynamics. Oppels et al in their study concluded that intravenous hydrocortisone or dexamethasone produced a decrease in outflow of aqueous humor 7. Other studies indicate that systematic administration of corticosteroids are likely to produce an increase in aqueous production 8-11. The Biphasic effect of corticosteroids may explain these conflicting results 12. An increase in circulation corticosteroid may cause an increase in aqueous production while topical administration of steroid may produce a decrease in aqueous outflow13-14. Nephrotic syndrome patients undergoing corticosteroid therapy should undergo slit lamp biomicroscopy and dilated fundus evaluation to detect any evidence of raised intraocular pressure. The ophthalmologist should check the contour and colour of optic disc, any asymmetric or elongation of the cupping and thinning of the neuroretinal rim and retinal nerve fiber layer on serial optic disc photos. If possible IOP of these children should be checked periodically. Based on these studies, the aim of the current study was to evaluate the effect of steroid on IOP and correlation of dose and duration of steroid therapy with intra ocular pressure in children with Nephrotic syndrome.

Material and Method: This is a prospective cross sectional study of patient with confirmed diagnosis of Nephrotic syndrome from Department Of Paediatric of HIMS from Jan. 2017 to Dec 2017. The study was conducted in accordance with ethical standards of declaration of Helsinki after approval was obtained from Instititional Ethical Committee. Written informed consent was obtained from parents of all the patients. A detailed history of diagnosis of nephrotic syndrome and steroid regimen (type, dose and duration of steroid use) was obtained from patients clinical records.

Inclusion Criteria:

1. Patients between 5-18 years of age with nephrotic syndrome havingproteinuria (72 gm/m2/day or50 mg/kg/day), hypoalbuminemia (less than 2.5gm/dl) or hypercholesterolemia.
2. Negative serology results for ANA , ANCA, anti ds DNA, C3, C4, CH5O, Hbs-Ag, anti HCV, anti HIV.
3. Patients with corticosteroid as main part of treatment.
4. Histopathology of FSGS or MCD proven by nephrologist.
5. Patient who accepted to attend the survey by signing the consent.

Exclusion Criteria:

1. Syndromic form of Nephrotic Syndrome.
2. Non cooperative patients for Ophthalmological examination.
3. Presence of any systemic disease other than Nephrotic syndrome.

A single examiner performed the ophthalmic examination of included patients which included BCVA (Best corrected visual activity) using the Snellen or illiterate E chart. IOP measurement with NCT (Non contact tonometry) and Applanation tonometer (Inami). Assessment of cornea and anterior segment with Slit lamp biomicroscope (Topcon Corp-Japan). Fundus was examined following dilation of pupils with 2.5% phenylephrine and 0.5% Tropicamide eyedrop.

Data was collected and analysed using statistical software. To assess the effect of steroid on IOP in relation to total dose and duration of steroid therapy unpaired t-test was used. Statistical analysis was performed using SPSS19.0 software version (SPSS Inc. Chicago,

Illinois, USA). A p-value of less than 0.05 was considered significant.

Result: Study was conducted at Heritage Institute of Medical sciences from Jan. 2017 to Dec. 2017 and 25 patients with Nephrotic syndrome were included in the study. From all the enrolled patients 16 were male and 9 female. Male and female ratio was 1.33. The median age at the time of examination was 9.5±3.3 years (Range 5 to 17 years). The mean age of onset of Nephrotic syndrome was 8.2±3 years.

Best corrected visual activity was normal 6/6 in 20 patients (80%) and less than 6/6 in 5 patients (20%), on measuring IOP it was normal (10-18 mmHg) in 19 patients (76%) & raised ≥ 19 mmHg in 6 patients (24%). On correlating IOP & age of patients there was no significant difference between IOP & age (P > 0.05).

Table 1: Correlation of IOP and Age in children with Nephrotic syndrome.

IOP	No of patients	Age	P value
Normal (10-18 mmHg)	21	10.5±3.2	0.066
Raised ≥ 19 mmHg	4	7.0±1.5	

On comparing the level of IOP with total dose of steroid therapy it was inferred that there is significant correlation between IOP & total dose of steroid therapy (P>0.05).

Table 2: Correlation of IOP & total dose of steroid therapy in Nephrotic syndrome.

IOP	Number of patients	Total dose of steroid in mg	P value
Normal 10-18 mmHg	21	6000± 500	0.062
Raised ≥ 19 mmHg	4	9000± 500	

On correlating the level of IOP with total duration of steroid intake it was concluded that there was significant correlation between IOP & long term duration of steroid intake (P<0.05).

Table 3: Correlation of IOP and Duration of steroid therapy

IOP	Number of patients	Duration of steroid therapy (weeks)	P- value
Normal (10-18 mmHg)	21	12±3	P 0.032
Raised ≥ 19 mmHg	4	14±2	

DISCUSSION:

Studies have shown that occurrence of ocular complication with steroid intake is well reported in the literature. Steroid induced glaucoma is iatrogenic secondary open angle glaucoma. In a study by Sihota et al. raised IOP in such eyes has been shown to lower with time after stopping steroid use[15].

The exact mechanism by which corticosteroids cause a rise in IOP is uncertain. Some authors believe there is a decrease in the facility of outflow, other an increase in aqueous production. It has been postulated that there may be abnormal functioning of cells in the area of trabecular meshwork leading to an abnormal or excessive deposition of mucopolysaccharides. Histopathology of steroid induced glaucoma in human has demonstrated excessive deposits of acid mucopolysaccharide or glycosaminoglycan (GAG) in the trabeculum[16].

In the present study various factors like age of patient, total dose of steroid intake & duration of steroid therapy were evaluated for their role in causing raised IOP. It was concluding that no significant correlation was there between IOP & age of children with Nephrotic syndrome and Total dose of steroid intake. These findings similar to the finding of Lennon rl et al who reported no significant correlation between IOP and age of children with Nephrotic syndrme and Hayasaka et al. who reported similar finding about IOP & total dose of steroid 17,18. Biednerbz et al. on the other hand in their study found association between high cumulative dose of steroid induced complication in Nephrotic syndrome19. The present study concludes that ocular complications like raised IOP is seen most commonly in patients with long term duration of steroid therapy. Despite the valuable information that can be obtained from this study it is essential to consider its limitation of small sample size. So further long term studies on larger population are needed to validate the same and study other ocular side effects of long term steroid therapy.

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