

The Effect of Steroid on Intraocular Pressure In Children with Nephrotic Syndrome

Masitha Dewi¹, Aryani A Amra²

Medical Faculty Sumatera Utara University, Medan, Indonesia
Corresponding Author: Masitha Dewi

Abstract: Nephrotic Syndrome (NS) is defined by the presence of nephrotic range proteinuria, edema hyperlipidemia and hypoalbuminemia. Nephrotic syndrome in children is the most common renal disease in Indonesia. Steroid in NS could lower mortality rate. Long term of steroid has gained notoriety due to its tendency to induce multiple side effects, including higher intraocular pressure (IOP). The aim of this current study to determine ocular abnormalities in children such as higher IOP with NS from prolonged corticosteroid therapy. A serial prospective analytic case study was conducted at the Adam Malik Hospital from march 2015 to august 2015 after approved by The Ethics Committee for Health Research Faculty of Medicine Sumatera Utara University. We analyzed IOP in 20 children with NS. The IOP was assessed before steroid treatment, 1st and 2nd month after steroid treatment. IOP was assessed until 2nd month after steroid treatment. After steroid treatment, from the statistical there is a significant differences correlation between IOP and duration of steroid in children with ns ($p=0,031$). No significant differences between IOP with age and total dose of steroid ($p>0,05$). NS in children with longer duration of steroid therapy have greater risk of higher IOP. So, Pediatricians are advised to refer NS patients to Ophthalmologist for evaluation.

Keywords: nephrotic syndrome, steroid, intraocular pressure (IOP)

Date of submission: 22-03-2018

date of acceptance: 07-04-2018

I. Introduction

Nephrotic syndrome is defined by the presence of nephrotic range proteinuria, edema hyperlipidemia and hypoalbuminemia. The constellation of features that characterize nephrotic syndrome develops from primary alterations of the perm selectively barrier of the glomerular capillary wall, which is no longer able to restrict the loss of protein to less than 100 mg/m² body surface per day. Nephrotic range proteinuria has been variously defined, including the increasingly popular use of spot urinary protein to creatinine ratio higher than 0,25 g protein per mmol, creatinine (or >2.0 mg protein per mg creatinine).^{1,2}

Nephrotic syndrome has reported incidence of two to seven per 100.000 children and a prevalence of nearly 16 cases per 100.000 and a prevalence of nearly 16 cases per 100.000. In development country, the incidence of nephrotic syndrome is highly. In Indonesia, nephrotic syndrome has reported incidence 6 cases per 100.000 in a year for children age lower than 14 years old.^{3,4}

Before twenty century, the morbidity and mortality of nephrotic syndrome is highly. Generally nephrotic syndrome patients died caused of septic, peritonitis and malnutrition. The majority of children with nephrotic syndrome respond to corticosteroids. Corticosteroid usage has reduced the mortality rate in children nephrotic syndrome to around 3%, with infection remaining the most important cause of death. However corticosteroids have known side effect such as increase of intraocular pressure and cataract. The use of corticosteroids in children with nephrotic syndrome usually with prolonged high dose steroid intake more than 8 weeks, so the patients need to be referred to an Ophthalmologist.^{5,6}

Steroids especially when taken in high doses and long term treatment, have multiple effects on the trabecular meshwork (tm), there by rising the risk of glaucoma. The route of administration may influence the response of aqueous dynamics. Oppels and colleagues found that intravenous hydrocortisone produced a minimal effect on aqueous humor formation and outflow, while topical hydrocortisone or dexamethasone produced a marked decrease in outflow. Other studies indicated that systemic administration corticosteroids are likely to produce an increase in aqueous production. Hayasaka and collagues in japan found that children with nephrotic syndrome with long term treatment of steroid have highly intra ocular pressure in about 20%. Clement cy in china reported one case child 9 years old with high dose steroid treatment for 8 days have highly intraocular pressure about 40 mmhg.^{7,8}

The biphasic effect of corticosteroids may explain these conflicting results. An increase in circulating corticosteroid may cause an increase in aqueous production, while topical administration of steroids may produce a decrease in aqueous outflow.⁹

Based on these studies, the aim of the current study was to investigate the effect of steroid on intraocular pressure in children with nephrotic syndrome and evaluate correlation dose and duration of steroid therapy with intraocular pressure in children with nephrotic syndrome.

II. Materials and methods

Subjects

This is a prospective cross sectional study of patients with diagnosis of nephrotic syndrome with steroid therapy for 8 weeks from the pediatric clinic of Adam Malik Hospital were recruited from march to august 2015. the study was conducted in accordance with ethical standards of declaration of Helsinki and approved by medical faculty University of Sumatera Utara ethics committee. Written inform consent was obtained from parents of these patients. A detailed history of diagnosis of nephrotic syndrome and steroid regimen was obtained from the patients clinical record.

All subjects underwent ophthalmologic examination included measured of best corrected visual acuity (bcva) using snellen chart, IOP measurement with non-contact tonometry (nt 530-nidek) and assessment of cornea and anterior chamber with slitlamp biomicroscope (topcon corp-japan). The inclusion criteria were nephrotic syndrome patients with age 6 to 15 years old with steroid therapy for 8 weeks. Eyes with secondary nephrotic syndrome and ocular trauma was excluded.

Statistical analysis

The collected data write in the research publication and keep in the computer. The collected data in computer analyzed by using the statistical software. To assess the effect of steroid on intraocular pressure based on total dose and longterm duration of steroid therapy, unpaired t test was used statistical analysis were performed with spss 19,0 and the level of significance was $p < 0,05$.

III. Result

The study was conducted from march 2015 to august 2015 in 20 children patient with neprotic syndrome

Table 1. The demographic data from 20 patients

Variable	N
Patients	20
Gender (m/f)	14/6
Age	9,6±3,15
Bcva snellen chart:	17/3
Normal (6/6)	
Abnormal (<6/6)	
Nutrition	(16/4)
-good	
-malnutrition	

Bcva : best corrected visual acuity

Table 2. Correlation intraocular pressure and age in children with ns

IOP	N	Age(y.o) X ±sd	P value
Normal (10-21 mmhg)	17	10,12±3,12	0,067
Abnormal (>22 mmhg)	3	6,67 ±1,15	

IOP: intra ocular pressure

From the table 2 , there was no significantly differences correlation between intraocular pressure and age ($p > 0,05$)

Table 3. Correlation intraocular pressure and total dose of steroid therapy in children with ns

IOP	N	Total dose (mg) X ± sd	P value
Normal (10-21 mmhg)	17	5323,41±4824,26	0,072
Abnormal (>22 mhg)	3	8978,67±2952,82	

From the table 3, there was no significantly differences correlation between intraocular pressure and total dose of steroid therapy ($p > 0,05$)

Table 4. Correlation intraocular pressure and duration of steroid therapy

IOP	N	Duration of steroid (months) X±sd	P value
Normal (10-21 mmhg)	17	12,59±13,90	0,031 ⁸
Anormal (>22 mmhg)	3	33,33±18,90	

From table 4, there was significantly differences correlation between intraocular pressure and long term duration of steroid therapy in children with ns ($p < 0,05$)

IV. Discussion

Studies have shown that occurrence of ocular complications with steroid intake is well reported in the literature. Our study found that ocular abnormalities were more common among children with nephrotic syndrome with long term duration of steroid therapy is higher intraocular pressure. Corticosteroid therapy has been recognized as a risk factor for glaucoma. In a study by Sihota, the raised IOP in such eyes has been shown to lower with time after stopping steroid use. 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, others 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 of excessive deposition of mucopolisaccharides and accumulation of extracellular matrix in the trabecular meshwork which in turn increases aqueous outflow resistance. Microstructural changes identified by Clark et al showed that actin stress fibers were reorganized into networks in trabecular cells in the presence of dexamethasone, causing a decrease in outflow facility. They postulated that this phenomenon was mediated via the meshwork glucocorticoid receptors. This effect was reversible once the drug was discontinued. Histopathology of steroid-induced glaucoma in humans has demonstrated an excessive deposit of acid mucopolisaccharides or glycosaminoglycan (gag), in the trabeculum.¹⁰

The table 2 found that there was no significantly differences correlation intraocular pressure and age children with ns. Lee Ryan and colleagues also reported there was no significantly differences correlation between intraocular pressure and age in children with ns.

From table 3 found that there was no significantly differences correlation intraocular pressure and total doses of steroid. This study also same with Hayasaka and colleagues study reported that there was no significantly differences between intraocular pressure and total doses of steroid. In other hand, study of Bagga and colleagues found association between high cumulative dose of steroid induced complication in ns.⁷

Table 4 found that there was significantly differences correlation intraocular pressure and long term duration of steroid therapy. A study by Ohji et al concluded that the ocular hypertensive response to topical dexamethasone was more severe in children than in adults. On the other hands, Biedner et al reported an opposite findings. A more recent Singaporean study reported that 28,3% of children with vernal conjunctivitis developed elevated IOP with topical steroids and with 5,5% developed glaucomatous nerve damage. Hayasaka and colleagues study reported that there was no significantly differences between intraocular pressure and duration of steroid therapy.^{11,12}

V. Conclusion

The present study concludes that ocular complication such as raising of intraocular pressure most commonly seen in children with nephrotic syndrome and have correlation between intraocular pressure and long term duration of steroid therapy, so further long term studies on larger population are needed for the evaluate another side ocular complication hence, Pediatricians are advised to refer the patients to Ophthalmologists for evaluation.

Acknowledgment

The authors are deeply indebted to Medical Faculty Sumatera Utara University for providing equipment and scientific apparatus

Conflict of interest

The authors declare that there are no conflicts of interest

References

- [1] Gordillo R, A Spitzer. The nephrotic syndrome in pediatrics in review/American academy of pediatrics. 2009;30(3):94-104
- [2] Arneil GC. The nephrotic syndrome. *Pediatr Clin North Am.* 1971;18:547-59
- [3] Srivastava T, Simon SD, Alon US. High incidence of focal segmental glomerulosclerosis in nephrotic syndrome of childhood. *Pediatr Nephrol* 1999;13:13-18
- [4] Lennon RL, Watson, Webb NJA. Nephrotic syndrome in children. *Paediatrics and child health.* 2010;20 (1):36-42
- [5] Gipson DS, Powell I, Massengill SF, Yao I. Management of childhood onset nephrotic syndrome. *Pediatrics.* 2009; 124(2):747-757

- [6] Kaye ld, kalenak jw, price rl,cunningham r. Ocular implications of longterm prednisone therapy in children. J pediatrophthalmol strab.1993;30:142-144
- [7] Hayasaka y, hayasaka s, matsukura h. Ocular findings in japanese children with nephrotic syndrome received prolonged corticosteroid therapy. Ophthalmologica.2006;220:181-185
- [8] Clementcy,joan sk, randa th, dennis sc." Intraocular pressure profile of a child on a systemic corticosteroid" in american journal of ophthalmology. 2004;137(1):198-201
- [9] Spaeth gl, rodrigues mm, weinreb s. Steroid-induced glaucoma: a persistent elevation of intraocular pressure and histological aspects. Trans am ophthalmol soc. 1977;75:353-381
- [10] Sihotar,konkalvl,dada t et al.prospective longterm evaluation of steroid induced glaucoma. *eye*.2008;22:26-30
- [11] Ohjim,kinoshitas,ohmie,kuwayama y. Marked intraocular pressure response to instillation of corticosteroids in children. Am j ophthalmol.1991;12:450-454
- [12] Biednerbz,davidr,grudsky a, scahs u. Intraocular pressure response to corticosteroids in children. Br j ophthalmol. 1980;64:430-431

Masitha Dewi."The Effect of Steroid on Intraocular Pressure in Children Withnephrotic Syndrome. "IOSR Journal of Pharmacy and Biological Sciences (IOSR-JPBS) 13.2 (2018): 18-21.