

Ocular and extra-ocular complications following long-term steroid consumption in children with idiopathic nephrotic syndrome

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ABSTRACT

Background: High dose of corticosteroids are required by patients with idiopathic nephrotic syndrome for long duration due to repeated relapse. The aims of this study were to analyze the ocular and extra-ocular complications of steroids on children with nephrotic syndrome.

Methods: This cross-sectional study was conducted at Dhaka Shishu (Children) Hospital from September 2017 to September 2019. Children with nephrotic syndrome between 1-16 years of age, who received steroid for at least three months, participated in this study. Total 70 children were enrolled. Detailed history was taken from parents regarding initial episode, drug history, visual problem, headache, hypertension, weight gain, psychosis, bone pain, epigastric pain and excessive growth of body hair. Comprehensive ophthalmologic assessment including visual acuity, intraocular pressure and cataract were performed. Detail of renal histopathology and treatment regimen in each patient was noted.

Results: A total of 70 patients were included, 61.4% were male and 38.6% were female. Median age at the time of examination was 60 months (range 17 to 216 months). The mean duration of disease was 33.71±21.12 months. The mean cumulative steroid dose at the time of examination was 8485.91±7326.83 mg. Fourteen (20%) patients had posterior subcapsular cataract. Among 70 patients, we could do visual acuity for 25 (35.7%) patients, intraocular pressure (IOP) in mm for 51 (72.85%) patients. Among them raised IOP was found in five (9.8%) patients. In right eye mean IOP was 14.16±3.57 and for left eye 14.77±3.55 mm. Renal biopsy was performed in 15 (21.43%) cases. Among the biopsy report, it was found that mesangial proliferative glomerulonephritis (MPGN) in 8 (53.33%), focal segmental glomerulonephritis (FSGS) in 2 (13.33%) and minimal change in 5 (33.34%) cases. Among all cases, 12 (17.14%) patients developed Cushingoid facies, 3 (4.2%) patients had hypertrichosis, 3 (4.2%) patients had central obesity and 4 (5.7%) patients had buffalo hump but none had hypertension, diabetes mellitus, epigastric pain, bone pain or psychosis.

Conclusion: Cataract formation was the most frequent ocular complication after large dose of oral corticosteroid therapy. The present study emphasizes the need for regular eye screening. Cushingoid facies was the most frequent among extra-ocular complications.

Key words: complication, nephrotic syndrome, steroid.

(*BIRDEM Med J* 2021; 11(1): 7-10)

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Received: December 31, 2019

Revision received: July 26, 2020

Accepted: October 31, 2020

INTRODUCTION

High dose steroid use is practiced by pediatrician in nephrotic syndrome (NS) for long duration. Most frequently seen glomerular disease, NS is characterized by having proteinuria >40 mg/m²/h, serum albumin <2.5 g/dl, oedema and hyperlipidemia. The commonest cause of NS is minimal change nephrotic syndrome (MCNS), where the relapse rate is high with significantly raised steroid dependency resulting in steroid toxicity. Patients receive repeated and prolonged courses of steroid during relapse.¹

Therefore, evaluation of the side effects of steroid is crucial in NS. Common side effects of steroid on eyes include increased intraocular pressure, cataract, ptosis, mydriasis, eyelid skin atrophy, keratitis, macular pigmentation changes, exacerbations of bacterial and viral infections. Among them cataract is the most frequent.² Besides ocular problems, long-term corticosteroid therapy is also responsible for osteoporosis, hypertension, Cushingoid appearance, psychosis, peptic ulcer, diabetes and growth retardation.

Besides individual susceptibility, many variables involve in forming cataract such as age, sex, systemic disease, duration of disease, duration of therapy and dosage schedule.³ The goals of this study were to determine the incidence of cataract and other ocular and extra-ocular side effects in a homogenous population of NS children and also to assess the correlation of cumulative dosage and duration of consumption of steroid with these complications.

METHODS

This cross-sectional study was conducted in Dhaka Shishu (Children) Hospital. Study duration was twenty five months from September 2017 to September 2019. NS children between 1-16 year of age, who received steroids for at least three months were included. This survey was carried out on 70 patients with minimal change disease, biopsy-proven focal segmental glomerulosclerosis (FSGS) and mesangial proliferative glomerulonephritis (MPGN). Demographic data, clinical findings and ophthalmologic symptoms were documented for every patient.

Inclusion criteria

Patients between 1-16 year of age with NS.

Negative serology results for antinuclear antibody (ANA), anti-double stranded DNA (anti dsDNA),

antineutrophil cytoplasmic antibody (ANCA), hepatitis B surface antigen (HBsAg), hepatitis C virus (HCV) and human immunodeficiency virus (HIV) and normal complement (C3, C4, CH50) level.

Corticosteroid consumption for more than 3 months as the main or adjunctive part of the treatment.

Patient's attendant who accepted to attend the survey by signing the consent.

Exclusion criteria

Syndromic forms of NS.

Patients being non-cooperative for ophthalmologic examination.

Presence of any systemic disease other than NS.

Eyes screened with a history of ocular trauma or previous surgery were excluded.

Ethical issues

The study was approved by the local ethics committee of Dhaka Shishu (Children) Hospital. Informed consents of the parents and/or patients were obtained.

Ocular examination

Ophthalmological examination was performed for all patients by a pediatric ophthalmologist. Full ophthalmologic examination included determining visual acuity with Snellen visual acuity chart, cataract by slit lamp biomicroscopy and measurement of intraocular pressure (IOP) by tonometry.

RESULTS

A total of 70 patients were included in the study, 61.4% of whom were males and 38.6 % females. The median age at the time of examination was 60 months (range, 17 to 216 months).

The mean duration of disease was 33.71 ± 21.12 months. The mean duration of steroid use was 404.46 ± 293.6 days. Out of 70 cases, renal biopsy was performed in 15 (21.43%) cases. Among the biopsy reports, it was found that MPGN in 8 (53.33%) cases, FSGS in 2 (13.33%) and minimal change in 5 (33.34%) cases. Among 70 patients, we could do visual acuity for 25 (35.7%) patients and IOP in mm for 51 (72.85%) patients. Among them raised IOP was found in five (9.8%) patients. In right eye mean IOP was 14.16 ± 3.57 and left eye mean IOP was 14.77 ± 3.55 mm.

Table I Predictors for developing cataract in nephrotic syndrome patients (N=70)

Duration of steroid use	Cataract Present (n, %)	Cataract Absent (n, %)	P value
<1 years (41)	5 (12.2)	36 (87.8)	0.104 ^{ns}
1-2 years (19)	5 (26.3)	14 (73.7)	
3-4 years (10)	4 (40)	6 (60)	
Steroid doses			
<5000 mg (31)	3 (9.7)	28 (90.3)	0.05 ^s
5001-10000 mg (19)	4 (21.1)	15 (78.9)	
10001-15000 mg (10)	2 (20)	8 (80)	
>15000 mg (10)	5 (50)	5 (50)	
Types of treatment given			
Monotherapy (13)	1 (7.7)	12 (92.3)	0.205 ^{ns}
Combined therapy (57)	13 (22.8)	44 (77.2)	

Patients were given combined therapy (prednisone with either cyclophosphamide or tacrolimus/ mycophenolate mofetil) in 57 cases and 13 were given oral prednisolone alone. The mean steroid dose at the time of examination was 8485.91±7326.83 mg. Among all cases, 12 patients (17.14%) had Cushingoid facies, 3(4.2%) patients had hypertrichosis, 3 (4.2%) patients had central obesity and 4 (5.7%) patients had buffalo hump but none had hypertension, diabetes, epigastric pain, bone pain or psychosis. Fourteen (20%) patients had cataract. The predictors developing cataract in NS were described in Table I. Analysis of data showed no significant association between the duration of corticosteroid treatment and cataract formation ($p = 0.104$), but a significant association between the steroid doses and development of cataract ($p=0.05$). There was no significant association between the type of treatment and cataract.

DISCUSSION

In this study the incidence of cataract increased with higher doses of corticosteroid therapy. Among 70 children, 14 (20%) cases had cataract. Percentage of incidence is comparable with previous reports.⁴⁻⁶

We found that cataract was the most common ocular complication. Similar results were reported in the study by Gheissari A et al.¹ Study by Olonan LRN et al., also found the incidence of cataract to be 13.6% and glaucoma to be 4.5%.⁷ Study by Hayasaka Y et al., stated that

cataract was present in 33.3% and glaucoma in 20% patients receiving prolonged corticosteroids.⁸ Bagga A et al., also found association between high cumulative dose of steroid and steroid induced complications in NS.⁴ Study by Ng JS et al., also found that high doses of steroid in NS were associated with steroid related complications especially cataract.⁹ Similar results were obtained by Ryan NL et al. in Philippines children.⁷ The increased IOP but not its damage is reversible. This symptom was reported as the most common finding by Mohan et al.¹⁰ However, the steroid dependent ocular abnormalities were not found in Turkish children with steroid sensitive NS.¹¹

It remains unclear if combined therapy increased the incidence of cataract formation and glaucoma development in pediatric NS patients. A study conducted by Kaye and associates¹² found no association between steroid therapy and ocular hypertension as opposed to the study done by Grossman et al.¹³ Only one patient in this study was diagnosed to have steroid-induced glaucoma. However our finding contrasted by Jezheela K et al¹⁴, where duration of steroid therapy was found to be associated with development of cataract.

Dikshit and Avashi deemed that susceptibility of an individual is an important factor with regard to posterior subcapsular cataract formation.¹⁵ In this study, after a wide range of steroid consumption cataract occurred but it was not possible to predict the individual who were likely to develop cataract which is similar to the study by J.T Brocklebank.³

Conclusion

Our study concluded that, higher cumulative doses of steroid therapy were significantly associated with cataract. The present study emphasizes the need for regular ocular evaluation and also to explore additional factors in causation of steroid induced ocular problems. Among extra-ocular complications Cushingoid facies was the most prevailing.

Authors' contribution: GNC designed the study, prepared the manuscript. TK reviewed the manuscript. TF edited the manuscript. RAC did literature search. SA had the study concept. MH designed the study and reviewed the manuscript. All authors read and approved the final version for submission.

Conflict of interest: Nothing to declare.

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