DOI: 10.7860/JCDR/2017/24694.9334

Original Article

Paediatrics Section

Study on Steroid Induced Ocular Findings in Children with Nephrotic Syndrome

VIJAY AGRAWAL[1], KUSUM DEVPURA[2], LAXMIKANT MISHRA[3], SAJAN AGARWAL[4]

ABSTRACT

Introduction: Long term use of corticosteroids in Nephrotic Syndrome (NS) is associated with ocular complications such as Posterior Subcapsular Cataract (PSC), glaucoma, increased intra-ocular pressure, ptosis, mydriasis, eyelid skin atrophy, keratisis, thinning of cornea and sclera, repeated hordeolum exacerbations.

Aim: To determine ocular abnormalities in children with NS and their association with steroid dosing and duration.

Materials and Methods: Hundred patients with NS in the age group of 2-18 years, with no evidence of other systemic disease, were considered for the study. Group I included cases (66) who took standard steroid regimen for first episode of NS. Group II included cases (34) who took steroid irrationally (daily basis for long time) other than standard regimen. Steroid induced ocular complications were compared in both groups after detailed ophthalmological examination. Statistical analysis was done using Statistical Package for Social Science (SPSS-20.0).

Results: Ocular abnormalities were found in 12 patients out of 66 in Group I (18%) and 16 patients out of 34 patients in Group II (47%). Out of 12 patients of Group I who had ocular problems, three had myopic astigmatism, eight patients had PSC and one had temporal disc pallor. While in Group II, out of 16 patients who had ocular complications, two patients had raised intra ocular pressure and two patients had myopic astigmatism and 12 patients had posterior sub capsular cataract. The difference in mean cumulative steroid doses in both groups was statistically significant but no such difference was there between duration of steroid intake in both group.

Conclusion: Our study concluded that ocular complications were more common in patients with irrationally steroid intake and cumulative steroid dose intake was also significantly higher in same patients.

Keywords: Corticosteroid, Idiopathic nephrotic syndrome, Ocular complications

INTRODUCTION

Idiopathic Nephrotic Syndrome (INS) is the most common glomerulopathy in children, with an annual incidence of approximately 2-3 new cases per 100,000 populations under the age of eighteen years [1]. NS is defined by proteinuria > 40mg/m^2/h, serum albumin <2.5g/dl, oedema formation and hyperlipidemia [1]. Minimal Change Nephrotic Syndrome (MCNS) is the most common cause of NS. MCNS however has a high relapse rate, with approximately half of the patients developing steroid dependency resulting in steroid toxicity [2]. Relapse is defined as three consecutive days with 3+ on urinary albumin dipstick [3].

Long term use of corticosteroids is associated with ocular complications such as PSC, glaucoma, increased intra-ocular pressure, ptosis, mydriasis, and eyelid skin atrophy, keratisis, thinning of cornea and sclera, repeated hordeolum exacerbations [4]. Furthermore, NS is reported as a one of clinical syndromes with specific eye involvements such as Pierson syndrome, Wilms tumor-Aniridia syndrome and congenital NS [5]. Ocular side-effects of steroid consumption are well described. However, there are only few reports studying the steroid dependent and non-steroid dependent ophthalmic findings in patients with nephrotic syndrome [6,7]. Hence, this study was undertaken on children less than eighteen years of age and on steroids. The aim of the present study was to determine ocular abnormalities in children with NS on steroid therapy.

MATERIALS AND METHODS

This observational study was conducted in the Department of Paediatric Medicine in association with the Department of Ophthalmology of S.M.S. Medical College, Jaipur, Rajasthan, India from August 2014 to July 2016.

The sample size was calculated to a minimum of hundred cases of NS, assuming 50% chances of developing ocular changes at an allowable error of 10% [7]. Informed written consent was taken from the guardians and ethical clearance for the study was taken from institutional ethical committee. Hundred patients of NS in the age group of 2-18 years with no evidence of other systemic disease were included in the study. Detailed history was taken; general physical and systemic examinations were done. Detailed eye examination was done with the help of consultant faculty. Non co-operative patients for complete ophthalmological examinations and presence of other systemic diseases (anaemia, hypertension, diabetes) other than NS were excluded from the study. The patients in the study were divided into two groups. Group I included patients taking steroid as per standard regime 60 mg/mt^2 daily for six weeks followed by 40 mg/mt^2 on alternative day for six weeks for their first episode and patients who developed further episodes (relapse) were treated as per standard protocol for relapse. Patients taking steroids therapy irrationally (either daily basis for long time) other than standard regimen were included in group II.

STATISTICAL AYALYSIS

Statistical analysis was done using computer software Microsoft Excel, SPSS-20.0 and Primer. Quantitative values are expressed as mean and standard deviations and qualitative values in percentages and proportion. Student t-tests were performed for comparing means of groups. Significance levels for tests was determined as 95% ($p<0.05$). Correlation coefficient was calculated between cumulative steroid dose and duration of steroid intake. A p-value <0.05 was considered significant.

RESULTS

Out of 100 patients, 66 were in Group I and 34 were in Group II. The age of onset of disease was found to be 5±1.39 years in Group I and 5.09±1.31 years in Group II (p-value=0.76). Distribution of patients according to aetiology of nephrotic syndrome has been shown in [Table/Fig-1].

Variable	Group I	Group II	Total	χ^2(df)	p-value
FRNS	8	24	32	42.76 (3)	0.001
SDNS	31	1	32		
IFRNS	13	8	21		
INS	14	1	15		
Total(N)	66	34	100		

[Table/Fig-1]: Distribution of cases according to aetiology of Nephrotic syndrome. χ^2 Chi-square, FRNS: Frequently relapsing nephrotic syndrome; SDNS: Steroid dependent nephrotic syndrome; IFRNS: Infrequently relapsing nephrotic syndrome; INS: Idiopathic Nephrotic Syndrome, df: Degree of freedom.

Variable	Group I	Group II	Total	χ^2(df)	p-value
Increase IOP	0	2	2	13.10 (4)	0.011
Myopic astigmatism	3	2	5		
PSC	8	12	20		
Temporal disc pallor	1	0	1		
No findings	54	18	72		
Total	66	34	100		

[Table/Fig-2]: Distribution of cases according to ocular disease. IOP: Intra ocular pressure, PSC: Posterior subcapsular cataract.

Variable	Mean±SD		t-value(df)	p-value
	Group I(n -66)	Group II (n -34)		
Cummulative dose of steroid (mg)	6700.86±3908.87	11659.85±7743.87	3.511(41.86)	0.001
Duration (months)	21.47±16.87	17.74±11.80	1.287(89.0)	0.201

[Table/Fig-3]: Mean cumulative steroid doses and duration in cases.

Ocular abnormalities were found in 12 patients out of 66 in Group I (18%) and 16 patients out of 34 patients in Group II (47%). The p-value for ocular abnormality in different group was found to be 0.002. Out of 12 patients of Group I who had ocular problems, three had myopic astigmatism, eight patients had PSC and one had temporal disc pallor, while in Group II, out of 16 patients who had ocular complications, two patients has raised intra ocular pressure and two patients had myopic astigmatism and 12 patients had PSC as shown in [Table/Fig-2]. The mean cumulative steroid dose in Group I was 6700.86±3908.87 mg and in Group II was 11659.85±7743.87 mg. The p-value was 0.001 which was highly significant as shown in [Table/Fig-3]. Mean duration of steroid intake in Group I was 21.47±16.87 months and in Group II was 17.74±11.80 months. The p-value was 0.201 which was insignificant. Negative correlation was found between dose and duration of steroid intake in Group II which was stastically significant.

DISCUSSION

Occurrence of ocular complications with steroid intake is well reported in the literature. Ocular abnormalities are common among patients with NS receiving steroids. Our study found that ocular abnormalities were more common among patients who received steroids irrationally than patients who received steroids according to the standard regimen as described earlier. PSC is the most common complication seen with systemic steroid intake. The posterior polar region of steroid-associated cataractous lenses consists of: 1) a superficial zone of liquefaction; and 2) a deep zone of segmentally swollen lens fibres. Cytoplasm at knob and socket junctions has become lucent and plasma disappears leaving empty spaces. Steroid-induced glaucoma is highly elevated IOP and is always associated with steroid administration. Pressure elevation generally correlates with steroid doses and is most common with topical administration although it also occurs with systemic steroid use.

We found that PSC cataract was the most common ocular abnormality followed by myopic astigmatism. Similar results were reported in the study by Gheissari A et al., [7]. Study by Olonan LRN et al., also found the incidence of cataract to be 13.6% and Glaucoma to be 4.5% [8]. Study by Hayasaka Y et al., stated that PSC was present in 33.3% and glaucoma in 20% patients receiving prolonged corticosteroids [6]. Difference in incidence of PSC among cases with history of steroid therapy and healthy controls was statistically significant.

Another study by Kyrieleis H et al., found 10 cases of myopia and three cases of cataract as steroid dependent complications among 15 cases [9]. While in our study we found PSC was most common ocular abnormality. However, our findings were contrasted by Ozaltin F et al., study where they found no ocular abnormality in Steroid Sensitive Nephrotic Syndrome (SSNS) [8,10]. This might be due to small sample size in their study.

The mean cumulative dose of steroid was higher in Group II and the difference was found to be significant. Greater number of steroid dependent ocular complications was also observed in the same group. Study by Ng JS et al., also found that high doses of steroid in NS were associated with steroid related complications especially PSC [11]. Study by Hayasaka Y et al., also found association between total dose and duration of corticosteroid and cataract formation [6]. Study by Bagga A et al., also found association between high cumulative dose of steroid and steroid induced complications in NS [3].

CONCLUSION

The present study concludes that ocular complications are more commonly seen in nephrotic syndrome with irrational steroid intake and higher steroid doses intake.

REFERENCES

[1] Robson WL, Leung AK. Nephrotic syndrome in childhood. Adv Pediatr. 1993;40:287-323.
[2] Saha TC, Singh H. Minimal change disease: A review. South Med J. 2006;99 (11):1264-70.
[3] Bagga A. Revised guidelines for management of steroid-sensitive nephrotic syndrome. Indian Journal of Nephrology. 2008;18(1):31-39.
[4] Liu D, Ahmet A, Ward L, Krishnamoorthy P, Mandelcorn ED, Leigh R, et al. A practical guide to the monitoring and management of the complications of systemic corticosteroid therapy. Allergy, Asthma and Clinical Immunology. 2016;9:30.
[5] Chesney RW. The idiopathic nephrotic syndrome. Curr Opin Pediatr. 1999;11:158-61.
[6] Hayasaka Y, Hayasaka S, Matsukura H. Ocular findings in Japanese children with nephrotic syndrome receiving prolonged cortico-steroid therapy. Ophthalmologica. 2006;220(3):181-85.
[7] Gheissari A, Attarzadeh H, Sharif H, Pourhossein M, Merrikhi A. Steroid dependent and independent ocular findings in Iranian children with nephrotic syndrome. Int J Prev Med. 2011;2(4):264-68.
[8] Olonan LRN, Pangilinan CAG, Yatco MM. Steroid induced cataract and glaucoma in pediatric patients with nephrotic syndrome. Phillip J Ophthal. 2009;34(2):59-62.
[9] Kyrieleis H, Löwik M, Pronk I, Cruysberg H, Kremer J, Oyen W, et al. Long-term outcome of biopsy-proven, frequently relapsing minimal-change nephrotic syndrome in children. Clin J Am Soc Nephrol. 2009;4(10):1593-600.
[10] Ozaltin F, Heeringa S, Poyraz CE, Bilginer Y, Kadayifcilar S, Besbas N et al. Eye involvement in children with primary focal segmental glomerulosclerosis. Pediatr Nephrol. 2008;23(3):421-27.
[11] Ng JS, Wong W, Law RW, Hui J, Wong EN, Lam DS. Ocular complications of paediatric patients with nephrotic syndrome. Clinical and Experimental Ophthalmology. 2001;29:239-43.

PARTICULARS OF CONTRIBUTORS:
1. Assistant Professor, Department of Paediatric, JK Lon Hospital, SMS Medical College, Jaipur, Rajasthan, India.
2. Professor, Department of paediatric, JK Lon Hospital, SMS Medical College, Jaipur, Rajasthan, India.
3. Senior Resident, Department of paediatric, JK Lon Hospital, SMS Medical College, Jaipur, Rajasthan, India.
4. Senior Resident, Department of Paediatric, JK Lon Hospital, SMS Medical College, Jaipur, Rajasthan, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Vijay Agrawal,
Assistant Professor, Department of Paediatric, JK Lon Hospital, SMS Medical College, Jaipur-302004, Rajasthan, India.
E-mail: vijayagrawal30111974@gmail.com

FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Submission: **Oct 08, 2016**
Date of Peer Review: **Nov 01, 2016**
Date of Acceptance: **Dec 06, 2016**
Date of Publishing: **Mar 01, 2017**