

Steroid-induced Ocular Hypertension and Cataract in Children with Nephrotic Syndrome

A Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

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List of Abbreviations

<i>Abbr.</i>	<i>Full-term</i>
ACE	: Angiotensin-converting enzyme
ARF	: Acute renal failure
BID	: Twice daily
BMI	: Body Mass Index
BUN	: Blood Urea Nitrogen
CNF	: Congenital nephrotic syndrome of the Finnish type
CNS	: Congenital Nephrotic Syndrome
CPM	: Cyclophosphamide
Cr	: Creatinine,
CS	: Corticosteroids
ENaC	: Sodium epithelial channel
EPO	: Erythropoietin
FN	: Finnish nephropathy
FSGS	: Focal segmental glomerulosclerosis
HBV	: Hepatitis B Virus
HCV	: Hepatitis C Virus
HDL	: High density lipoprotein
HIV	: Human Immunodeficiency Virus

HMG-CoA	: Hydroxymethylglutaryl coenzyme A
HSP	: Henoch-Schoë'nlein purpura
IDL	: Intermediate-density lipoprotein
IgA	: Immunoglobulin A nephropathy
IOP	: Intra-ocular pressure
LDL	: Low density lipoprotein
LN	: Lupus nephritis,
MCD	: Minimal-change disease
MCNS	: Minimal change nephrotic syndrome
MMF	: Mycophenolate mofetil
MN	: Membranous nephropathy
MPGN	: Membranoproliferative glomerulonephritis
NS	: Nephrotic syndrome
NSAIDs	: Non-steroidal anti-inflammatory drugs
PAS	: Microscopic level (PAS
POAG	: Primary open angle glaucoma
PSC	: Posterior subcapsular cataract
PSGN	: Poststreptococcal glomerulonephritis
RAA	: Renin-angiotensin-aldosterone
SD	: Standard deviation
SDNS	: Steroid dependent nephrotic syndrome

SLE	: Systemic lupus erythematosus
SPSS	: Statistical package for social sciences
SSNS	: Steroid sensitive nephrotic syndrome
T3	: Triiodothyronine
TBG	: Thyroid-binding globulin
TE	: Thromboembolism
TIGR	: Trabecular-meshwork-inducible-glucocorticoid-response gene
Up/c	: Urinary protein/creatinine ratio
UPr	: Urine protein
VA	: Visual acuity
VLDL	: Very-low-density lipoprotein

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ABSTRACT

Background: Long term use of corticosteroids in Nephrotic Syndrome (NS) is associated with ocular complications such as Posterior Subcapsular Cataract (PSCC), glaucoma, increased intra-ocular pressure (IOP), ptosis, mydriasis, eyelid skin atrophy, keratitis, thinning of cornea and sclera, repeated hordeolum exacerbation. Among these side effects is ocular hypertension, and cataract which can result in severe and permanent visual disturbances. However, the exact prevalence, severity and timing of development of these complications have yet to be fully explored in the pediatric patient group.

Objective: To estimate the burden of ocular complications like posterior subcapsular cataract (PSCC) and raised intra ocular pressure (IOP) in children with nephrotic syndrome on steroid therapy or after cessation of treatment and to assess the correlation between the duration of consumption of steroids with these ocular complications.

Subjects and Methods: This cross-sectional study was conducted in the Department of Pediatrics in association with the Department of Ophthalmology of Ain Shams University Hospitals. We studied 60 children with primary nephrotic syndrome with no evidence of other systemic diseases. Demographic, clinical and treatment details were obtained from case records. Detailed ocular evaluation was performed to detect PSCC and to measure IOP and to assess the visual acuity.

There ages ranged from 5 to 18 years. Ocular examination including determining the best corrected visual acuity by Snellen visual acuity charts, slit lamp biomicroscopy of the anterior segment and measurement of intraocular pressure by air puff tonometer.

Results: We found high prevalence of children with decreased visual acuity (53.3 %), cataract (15 %) and increased IOP, (38.3%), most of them were mild to moderate elevations. There was positive correlation between the duration of steroids and the IOP. Cataract was not reported in children receiving steroids for less than 6 months.

Conclusion: Our study concluded that ocular complications were common among children with nephrotic syndrome and the IOP was positively correlated with the duration of steroid therapy, the ocular findings were also detected after cessation of steroids. The present study emphasizes the need for regular ocular evaluation and to explore additional factors in causation of steroid induced ocular complication.

Key words: Steroid-induced Ocular Hypertension, Cataract Children, Nephrotic Syndrome

Introduction

Idiopathic nephrotic syndrome (NS) is the most common glomerular disease in children. It is defined as the association of gross proteinuria with hypoalbuminemia, edema or hyperlipidemia, a condition that usually requires prolonged and combined treatments, and one that may recur over years. Nephrotic syndrome appears to be a clinically heterogeneous disease characterized by different histological variants (**Caridi et al., 2010**).

Both the disease per se and the immunosuppressive medications could cause complications leading to significant morbidity. Complications in various organs, for instance renal failure, peritonitis, thromboembolism, hypertension, hyperlipidemia and failure to thrive, have been reported (**Gorensek et al., 1988**).

Investigated ocular complications arising from nephrotic syndrome and/or its treatments in children. They concluded that children who have nephrotic syndrome often require prolonged, intermittent high dose of systemic corticosteroid therapy. Paediatricians should be aware of the potential risk of developing steroid-related complications, especially posterior subcapsular cataract. It appears to have a higher risk when steroid therapy is used in very young patients. Early detection would help to prevent amblyopia development, particularly in

the group of immature eyes (**Joan SK Ng, William Wong and Ricky WK Law et al., 2001**).

Prednisolone, the first-line treatment for children with nephrotic syndrome, causes severe side effects. One of these side effects is the presence of elevated fluid pressure inside the eye (intraocular pressure) which can result in optic nerve damage or visual field loss (normal range of intraocular pressure is between 10-21 mmHg) (**Kawaguchi et al., 2014**).

Chronic corticosteroid use, either topically or systematically, can result in posterior subcapsular cataract formation. However, surprisingly, Cushing's syndrome, which results from an overproduction of endogenous corticosteroids, has not been associated with a high incidence of cataract formation. In 60 patients having Cushing's syndrome from 1 to 20 years only two patients had posterior subcapsular cataracts; these were bilateral and symmetric (**Taylor and Hoyt, 2005**).

Determined the incidence and severity of cataracts in a homogeneous population of children with steroid-responsive nephrotic syndrome and determined the relationship of steroid dosage to the compaction and stiffening of the central lens material in 58 children with steroid-sensitive nephrotic syndrome. Eight (14%) children had cataracts. Visual acuity was normal in all but one child. There was no relationship between total dose or mean daily dose of prednisolone

(corrected for body surface area) and cataract formation. Alternate-day treatment with prednisolone for an average of half the total treatment time did not prevent cataracts. They showed that there is little risk of causing permanent visual handicap in children with steroidsensitive nephrotic syndrome, provided prednisolone treatment is carefully controlled (**Brocklebank JT, Harcourt RB and Meadow SR., 1982**).