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

A Thesis

Submitted in Partial Fulfillment of Master Degree in Pediatrics

By

Moamen Mohamed Abdelwahab
M.B., B.ch., 2008
Diploma in Pediatrics, 2015
Faculty of Medicine - Ain Shams University

Under the Supervision of

Prof. Dr. Sawsan Sayed El Moselhy
Professor of Pediatrics
Faculty of Medicine - Ain Shams University

Dr. Mohamed Samy El-Farsy
Lecturer of Pediatrics
Faculty of Medicine - Ain Shams University

Dr. Hisham Samy Saad-Eldeen
Lecturer of Ophthalmology
Faculty of Medicine - Ain Shams University

Faculty of Medicine
Ain Shams University
2018

أعوذ بالله من الشيطان الرجيم

بسم الله الرحمن الرحيم

قَالُوا۟ سُبْحَٰنَكَ لَا عِلْمَ لَنَآ

إِلَّا مَا عَلَّمْتَنَآ ۖ إِنَّكَ أَنتَ ٱلْعَلِيمُ ٱلْحَكِيمُ

سورة البقرة ٣٢

صدق الله العظيم

Acknowledgments

First and foremost, I feel always indebted to **Allah**, *the* **Most Beneficent** *and* **Merciful** *who gave me the strength to accomplish this work.*

My deepest gratitude to my supervisor, **Prof. Dr. Sawsan Sayed El Moselhy,** *Professor of Pediatrics , Faculty of Medicine - Ain Shams University, for her valuable guidance and expert supervision, in addition to her great deal of support and encouragement. I really have the honor to complete this work under her supervision.*

I would like to express my great and deep appreciation and thanks to **Dr. Mohamed Samy El-Farsy,** *Lecturer of Pediatrics, Faculty of Medicine - Ain Shams University, for his meticulous supervision, and his patience in reviewing and correcting this work. I greatly appreciate his efforts.*

I must express my deepest thanks to **Dr. Hisham Samy Saad-Eldeen,** *Lecturer of Ophthalmology, Faculty of Medicine - Ain Shams University Ain Shams University, for guiding me throughout this work and for granting me much of his time.*

Special thanks to my **Parents** *and my* **Wife** *for their continuous encouragement, enduring me and standing by me.*

Last but not least, I would also like to thank my colleagues, my patients and everyone helped me in this study.

Moamen Mohamed Abdelwahab

List of Contents

List of Abbreviations

Abbr.	Full-term
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-Scho¨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 : Membranopoliferative glomerulonephritis

NS : Nephrotic syndrome

NSAIDs : Non-steroidal anti-inflammatory drugs

PAS : Microscopic level (PAS

POAG : Primary open angel glucoma

PSC : Posterior subcabsular 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

List of Tables

List of Figures

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, keratisis, 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)**.