بسم الله الرحمن الرحيم

MONA MAGHRABY

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

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جامعة عين شمس

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قسم

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MONA MAGHRABY

Effect of Galactose on Proteinuria in Pediatric Steroid Resistant Nephrotic Syndrome

Thesis

Submitted for Partial Fulfillment of Master Degree in Pediatrics

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Mohammed Abdel-hamid Elshenawy

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List of Abbreviations

Abb.	Meaning
ACE	Angiotensin-converting enzyme
ARBS	Angiotensin receptor blockers
ARF	Acute renal failure
CS	Corticosteroids
CVT	Cerebrovascular thrombosis
DPGN	Diffuse proliferative glomeruloneohritis
EPO	Erythropoietin
FR	Frequent relapse
FSGS	Focal segmental glomerulonephritis
FSPF	Focal sclerosis permeability factor
G-1P	Glucose -1-phosphate
GBM	Glomerular basement membrane
GFR	Glomerular filtration rate
HDL	high density lipoprotein
INS	Idiopathic nephrotic syndrome
LDL	Low density lipoprotein
MCD	Minimal change disease
MCNS	Minimal change nephrotic syndrome
MGN	Membranous glomerulonephritis

List of Abbreviations cont...

Abb.	Meaning
MMF	Mycophenolate mofetil
MN	Membranous nephropathy
MPGN	Membranoproliferative glomerulonephritis
NS	Nephrotic syndrome
PTE	Pulmonary thrombo embolism
RAS	Rennin angiotensin system
RNS	Reactive nitrogen species
ROS	Reactive oxygen species
SDNS	Steroid dependant nephrotic syndrome
SNI	Calcineurin inhibitors
SRNS	Steroid resistant nephrotic syndrome
SSNS	Steroid sensitive nephrotic syndrome
TBG	Thyroid binding globulin
TNF	Tumor necrotic factor
UDP	Uridine diphosphate
VPF	Vascular permeability factor

INTRODUCTION

Nephrotic syndrome (NS) is primarily a pediatric disorder and is fifteen times more common in children than adults. The vast majority of affected children will have steroid sensitive minimal change disease (SSNS). The characteristic features of NS are heavy proteinuria >40 mg/m^2/hr, hypoalbuminemia (<2.5 g/dL), edema and hyperlipidemia ***(Vogt and Avner, 2011).***

The majority of children who present with idiopathic nephrotic syndrome (NS) have minimal change disease (MCD), which is generally responsive to steroid therapy. As a result, empirical steroid therapy is given to most children who present with idiopathic NS ***(Trachtman et al., 2013).***

However, approximately 10 to 20 percent of patients will fail to respond to initial steroid treatment. Most children with steroid-resistant nephrotic syndrome (SRNS), the underlying cause is not known. However, advances in molecular genetics of glomerular diseases have shown single gene defects that affect glomerular podocyte differentiation and function are responsible for a quarter to a third of all pediatric cases of isolated and syndromic SRNS in many parts of the world ***(Saleem et al., 2013).***

The International Study of Kidney Disease in Children (ISKDC) defined steroid resistant as a minimum exposure of 8 weeks of prednisone with 60 mg/m^2/day; or 2 mg/kg/day for

4 weeks followed by 40 mg/m^2 or 1.5 mg/kg on alternate days for 4 weeks. The minimum duration of prednisone required to define resistance is unresolved. A kidney biopsy is recommended to evaluate SRNS to determine the underlying pathology, which may dictate therapy ***(Colquitt et al., 2017).***

Idiopathic steroid-resistant nephrotic syndrome (SRNS) in children is characterized by a high risk of progression to end-stage renal disease, post-transplant disease recurrence (***Sgambat et al., 2013)*** and an overall increased risk of mortality. Approximately 80 % of children with idiopathic SRNS show focal segmental glomerulosclerosis (FSGS) on renal biopsy, whereas the remaining may show minimal change or mesangial proliferation in the early stages. Current therapies for SRNS, including cyclosporine, tacrolimus, mycophenolate Mofetil and rituximab, may induce partial or complete remission in 25–50 % of children. However, these therapies confer a risk of immunosuppression and nephrotoxicity over time. Thus, there is an urgent need for investigating novel and non-toxic therapies to treat this disease ***(Greenbaum et al., 2012).***

One or more proteinuria-inducing circulating factors have been identified in children with idiopathic SRNS. This notion is further supported by the rapid recurrence of proteinuria after renal transplant and response to plasmapheresis in some patients. Focal sclerosis permeability factor (FSPF) is one of such circulating factors identified in the

serum of patients with idiopathic SRNS. Galactose bound to FSPF with high affinity and inactivated and decreased FSPF activity in vitro, but it did not improve proteinuria in a patient with post-transplant FSGS recurrence .The proposed mechanism is the presence of galactose-binding sites on FSPF which interact with galactose of the glomerular glycocalyx to induce proteinuria. Free galactose supplementation may block the FSPF binding sites, thus rendering it inactive and promoting clearance of the FSPF–galactose complex via asialoglycoprotein receptors in the liver. ***(Greenbaum et al., 2012).***

Another case report described partial remission during treatment with oral galactose in two pediatric SRNS patients. Since no prospective data are available, we had investigated the effect of oral galactose therapy on FSPF and the clinical response in children with idiopathic SRNS ***(De Smet et al., 2009).***

AIM OF THE WORK

To study the effectiveness and safety of galactose as a possible therapeutic modality of treatment on steroid resistant nephrotic syndrome in pediatric patients.