THE LONG TERM OUTLOOK TO FINAL OUTCOME AND STEROID TREATMENT RESULTS IN CHILDREN WITH IDIOPATHIC NEPHROTIC SYNDROME

Nida Dinçel[1], Ebru Yılmaz[2], Şükriye Hacıkara[3], İpek K. Bulut[3], Sevgi Mir[3]

[1]Children's Hematology Oncology Training and Research Hospital, Pediatric Neprology, Ankara, [2]Dr Behcet Uz Children Research And Education Hospital, Pediatric Nephrology, [3]Ege University Medical Faculty, Pediatric Nephrology, IZMİR, TURKEY.

Objectives:

- Idiopathic Nephrotic Syndrome (INS) was defined as combination of a nephrotic syndrome and non-specific histological abnormalities of the kidney including minimal change nephrotic syndrome (MCNS), focal segmental glomerulosclerosis (FSGS) and diffuse mesengial proliferation (DMP) (1). The annual incidence of INS in the general pediatric population is 2–7 per 100,000 and the prevalence is 16 per 100,000. (2).
- MCNS is the most common cause of INS in children, accounting for more than 75% of all pediatric cases and for 90% of cases in children younger than 5 years of age (3).
- The causes of INS by definition remain unknown but evidence exists that a primary T-cell disorder may be responsible in MCNS and FSGS. The best prognostic indicator in all the histological variants of the INS is the response of proteinuria to therapy (4). Therefore, the objectives of treatment are threefold: to lower proteinuria, to reduce the frequency of relapses and to sustain the basal level of GFR (glomerular filtration rate) thus prevent progression to renal failure. Most children with MCNS respond to steroid. However up to 50% of patients with MLH develop frequently relapsing and/or 10-15 % SRNS (steroid resistant nephrotic syndrome) and often required immunosuppressive treatment (5). The long term prognosis is generally good, but almost 25% of the cases required prolonged treatment (18 weeks) with corticosteroids (6).
- Although previous data reported better prognosis with the long term treatment, there were any clear consensus about steroid treatment duration. We report our experience with MCNS; its clinical course, treatments and outcomes.

Methods:

- We assessed 120 children (66 male, 54 female) with MCNS admitted to Ege University Children Hospital Nephrology Department, Izmir, between 1987-2009.Their clinical presentations, treatment and disease courses were retrospectively reviewed. The mean duration of follow-up was 11.5±1.9 years.
- At presentation; presence of any accompanying diseases, majority of initial complaints, common physical findings, anthropometric parameters (height, weight, body surface area), albumin and lipid values, levels of proteinuria in 24hours collected urine were evaluated. None of the patients had haematuria (microscopic or macroscopic), hypertension, uremia and hypocomplementemia at presentation. Patients having secondary nephrotic syndrome were excluded from study. Remission is defined as a Up <4mg/m2/hour or Up/Ucr <0.2 mg/mg for three consecutive days. Absence of remission after four week of daily steroid therapy at a dose of 2 mg/kg/day, followed by three high doses of pulse steroid is called, resistance. Frequent relapses were having relapses more than two, within six months or four within twelve months. Also patients having relapse with steroid taper or within 2 weeks of steroid withdrawal, were referred to as steroid dependent (SDNS).
- Initially, all patients were treated with a single dose of 2mg/kg/ day (maximum 60mg/day) prednisolone for 4 weeks, followed by 8 weeks of the same daily dose given every other day. During the first 4 week, penicillin V, gastro protective agent, calcium plus D vitamin were given. After twelfth week, prednisone doses were gradually decreased with a rate of 0.5mg/kg per 15 daily intervals until complete discontinuation had been achieved by week 18th.The response to therapy was classified according to the definitions from the International Study of Kidney Disease in Children (ISKDC), as mentioned above. Renal biopsy was performed in the following situations by obtaining the informed consent: 1) age of onset younger than 2 and older than eight years 2) Steroid resistant or dependent Frequent relapsers and SRNS were treated with cyclophosphamide and /or cyclosporine, after performing renal biopsy. The patients were evaluated for the side effects of steroid therapy,

Results:

- Steroid responsive patients (n=106) were called as group I, steroid resistant patients (n=14) were called as group II. Then group 1 was divided into 3 subgroups. The demographic characteristics, physical and laboratory data at the time of first admission are given in table 1.
- Among frequent relapsers (SDNS) group, 11 patients (45.8 %) had the second episode within the first year of diagnosis (n=11), 4 of these 11(17%) patients had the second episode within six months of the initial response. At the end of study, 19 of 24 SDNS patients reached recovery, 5/24 progressed to SRNS. One patient had NPHS2 gene mutation, progressed to ESRD, the other one that followed as stage 1-CKD (chronic kidney disease), had NPHS1 mutation. End of the follow up period, 82 patients were steroid responsive without any adverse effect of treatment.
- Sixty-two patients had no any episode. Total 85% of patients achieved recovery within 5 years, 94% in 10 years. 19 steroid dependent patients (19/24, 79%) recovered in 10 years while the rest 5 were observed as SRNS. Therefore at the end of study, 19 patients were called as steroid resistant. During the follow up, 12/19 SRNS patients achieved recovery (63%), 5 progressed to CKD, 1 to ESRD and 1 patient died. The recovery rates of non relapsers, rare relapsers, SDNS and SRNS were found as, 100%, 100%, 79% and 63% respectively. Outcome of patients were shown in figure1 and table 2.
- Patients younger than 2 years, older than 8 years and SRNS, as a total number of 38 (32%) underwent biopsy. Histopathological analysis of biopsy revealed the underlying conditions of these 38 patients to be minimal change nephritic syndrome (17 patient;44.8%), focal segmental glomerulosclerosis (14 patients;37%) ,IgM nephropathy (5 patients;13%) and C1q nephropathy (2 patients; 5.2%).MCNS was found in 17of the patients underwent biopsy and the total incidence of MCNS(presumptive and biopsy proven) was 82.5%.

Table 1. Data at the time of admission

	Group 1 (n=106)			Group 2 (n=14)	p
	Non relapsers (n=62)	Frequent relapsers (SDNS)(n=24)	Rare relapsers (n=20)	SRNS	
F/M	35/27	11/13	8/12	5/9	
Age	196±81	29±18	181±12	27±12	
İncidental/edema/oliguria	-/57/10	1/24/17	-/19/2	-/14/10	
Consanguinity	2	7	1	3	
Positive family history	8	4	1	5	
Additional presence of atopy/urticaria/URTI/UTI	1/2/17/5	-/1/11/2	3/-/3/-	-/-/2/1	
Birth week: term/preterm	48/14	22/2	17/3	14/-	
Birth weight: <2.5/2.5-4/>4 kg	19/36/7	2/16/6	5/14/1	1/11/2	
Mean proteinuria (mg/m²/h)	134±12	127±52	111±23	189±19	0.01*
Mean albuminemia (mg/dl)	1.73±0.65	0.81±0.95	1.1±0.65	0.85±0.22	0.05*
GFR (ml/m²/min)	90±12	110±7	108±12	131±21	0.07*
Mean lipid values	363mg/dl	278mg/dl	391mg/dl	342mg/dl	0.06

SDNS: Steroid Dependent Nephrotic Syndrome, SRNS: Steroid Resistant Nephrotic Syndrome, F: female, M:male, URTI: Upper Respiratory Tract Infection , UTI: Urinary Tract Infection , GFR: Glomerular Filtration Rate
*p, group 1 vs group 2 statistically significant

Figure 1. Distribution of patients at the 4th week and 10 year

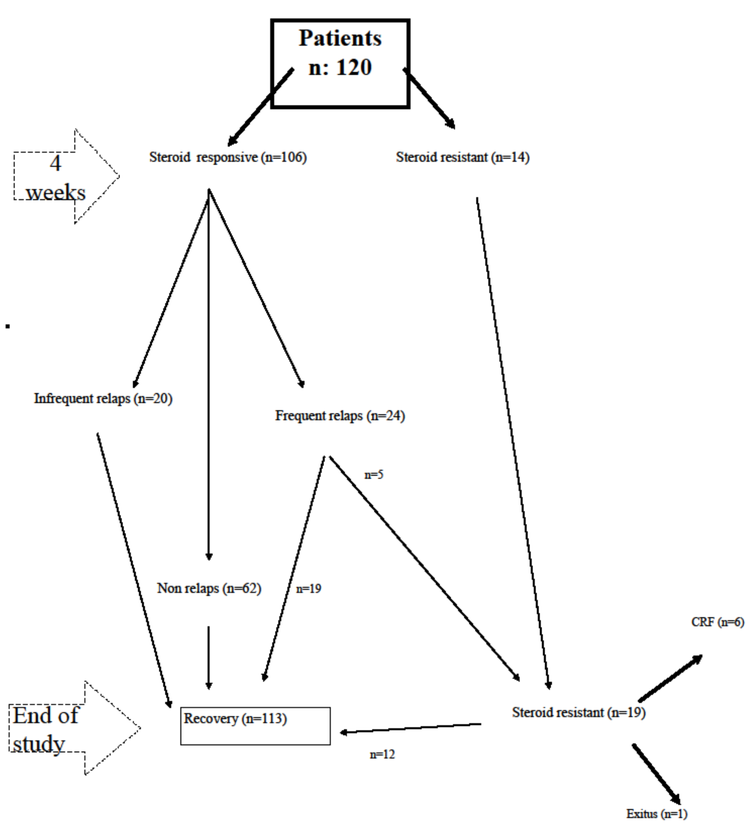

Table 2 Full recovery status of patients

Time	Number	Percentages
6th week	106	88
6th month	102	85
1st year	93	77,5
5th year	102	85
10th year	113	94

Table 3. Outcome in group 1 patients

	No relapsers (n=62, 58.4%)	Rare relapsers (n=20, 18.8%)	Frequent relapsers (n=24, 22.6%)	p
Relaps within first 6 mo	-	1	4	0.01***
Relaps within 6-12 mo	-	5	7	0.21***
Relaps within after 12 mo	-	14	13	0.34***
Therapy	LTST*	LTST	LTST + cytostatic agent**	
Complication	none	None	none	
Mean height z score (±SD)	2.3±0.5	1.3±1.1	0.3±1.8	0.03*** 0.01****
Full recovery	62	20	22	

*LTST: Long term steroid therapy, **cytostatic agent: cyclosporine and /or Cyclophospamide
*** p value : rare relapsers vs frequent, **** p value : non relapsers vs frequent

Conclusions:

- By using the long term corticosteroid treatment modality consisting of 20 weeks, we had the remission rate was 88% (106/120) at the end of 4 week, it rised to 94% (113/120) by the end of follow up period. Among the frequent relapsers, 79% of patients achieved recovery.
- Most of patients entered remission by our therapy end of follow up time. With the support of our satisfactory results among the whole study group, long term prednisolone treatment still remains valid.

References:

1. Niaudet P, Boyer O (2009). Idiopathic Nephrotic Syndrome in Children: Clinical Aspects. In Pediatric Nephrology Sixth ed. Avner ED, Harmon ED, Niaudet P, Yoshikawa N.eds. Springer-Verlag Berlin, Heidelberg: 667-702.
2. AA Eddy, JM Symons. Nephrotic syndrome in childhood. Lancet 2003; 362(9384):629–639.
3. DC Cattran, E Alexopoulos, P Heering, PF Hoyer, A Johnston, A Meyrier et al. Cyclosporin in idiopathic glomerular disease associated with the nephrotic syndrome: Workshop recommendations. Kidney Int 2007; 72: 1429–1447.
4. Troyanov S, Wall CA, Miller JA (2005). Focal and segmental glomerulosclerosis: definition and relevance of a partial remission. J Am Soc Nephrol 16: 1061–1068.
5. Beco A, Castro-Ferreira I, Coentrao L, Neto R, Sampaio S, Pestana M. Rituximab for steroid-dependent nephrotic syndrome Clin Nephrol. 2010 Oct;74(4):308-10.
6. Kyrieleis HA, Levtchenko EN, Wetzels JF. Long-term outcome after cyclophosphamide treatment in children with steroid-dependent and frequently relapsing minimal change nephrotic syndrome. Am J Kidney Dis 2007;49: 592-597.

52 ERA 915--SP
N) Paediatric Nephrology.
Ebru Y&305;lmaz
DOI: 10.3252/pso.eu.52era.2015
ePosters supported by F. Hoffmann- La Roche Ltd.
52nd ERA-EDTA CONGRESS London 2015 UNITED KINGDOM MAY 28 '31
PosterSessionOnline.com