THE EFFICACY OF CYCLOSPORINE ADMINISTRATION IN NEPHROTIC SYNDROME IN ADULTS

Anna Matyjek[1], Aleksandra Rymarz[1], Maria Sobol[2], Stanislaw Niemczyk[1]

[1] Department of Internal Medicine, Nephrology and Dialysis, Military Institute of Medicine, Warsaw, Poland.
[2] Department of Human Biophysics and Physiology, Medical University of Warsaw, Warsaw, Poland.

INTRODUCTION AND OBJECTIVES

The international recommendations suggest administering cyclosporine *(CsA)* at 3-5 mg/kg/day in primary glomerulonephritis in adults. The aim of the study was to estimate the efficacy of CsA treatment in nephrotic syndrome *(NS)*.

METHODS

24 adult patients with NS treated with CsA for inducing remission were included into the retrospective analysis. The cyclosporine trough level *(CsA_{C0})* was measured every 6-12 weeks. The initial remission was recognized at the albumin level >3.5 g/dl. The complete remission *(CR)* was defined as proteinuria <0.5 g/day, the partial remission *(PR)* as proteinuria >0.5 g/day without others signs of nephrotic syndrome. Nonparametric tests (Mann-Whitney test, Spearman rank order correlation) were used in a statistical analysis *(Statistica 13)*.

RESULTS

24 adult patients (17 males, 71%) with a mean age 50±18 years were enrolled. The histological diagnosis was: membranous glomerulonephritis *(MGN)* in 15 (63%), followed by minimal change disease *(MCD)* in 7 (29%) and focal segmental glomerulosclerosis *(FSGS)* in 2 patients (8%).

Table 1. Patients characteristics at baseline (n=24).

Variable	Min.	Max.	Mean ± SD
Age [years]	21	80	49±18
Serum albumin [g/dl]	1.1	3.4	2.4±0.7
Daily proteinuria [g/day]	4.3	40.9	11.5±9.9
Creatinine [mg/dl]	0.7	2.0	1.1±0.3
eGFR [ml/min/1.73m^2]	35	90	76±21
Total cholesterol [mg/dl]	146	760	298±137
LDL [mg/dl]]	61	568	200±112
HDL [mg/dl]	41	142	70±24
Total body weight (TBW) [kg]	52	140	90±19
Ideal body weight (IBW) [kg]	49	82	69±9
Initial CsA total dose [mg/day]	100	400	198±71
Initial CsA-WD_{TBW} [mg/kg/day]	1.9	3.2	2.3±0.7
Initial CsA-WD_{IBW} [mg/kg/day]	1.9	4.9	3.1±0.7
Initial CsA_{C0} [ng/ml]	46	306	130±79

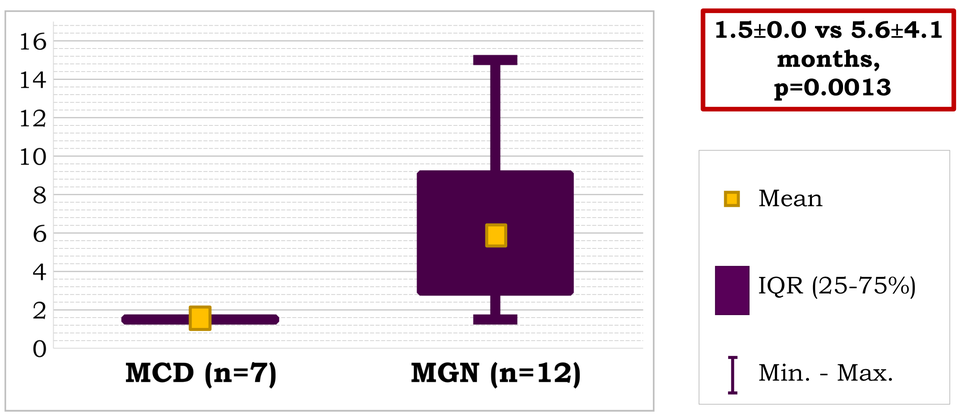
Ideal body weight (for men) = 50 + 0.9* (height [cm] – 152.4)
Ideal body weight (for women) = 45.5 + 0.9* (height [cm] – 152.4)
CsA-WD – daily dosage of CsA per 1kg of weight
CsA-WD_{TBW} = CsA dose [mg/day] / TBW
CsA-WD_{IBW} = CsA dose [mg/day] / IBW

During the induction of remission, the mean weight-adjusted CsA dosage was: 2.3±0.7 mg/kg/day – based on total body weight *(TBW)* and 3.1±0.7 mg/kg/day – based on ideal body weight *(IBW)*. The mean CsA_{C0} obtained in the induction of remission was 130±79 ng/ml.

The initial remission was achieved in 20 patients (83%) in the mean time 4.2±3.7 months. This time was significantly different in MCD and MGN [Figure 1].

In 3 patients (13%) the nephrotic syndrome persisted (2 with MGN, 1 with FSGS), in 1 patient (4%) CsA was discontinued due to deterioration of renal function.

Figure 1. Comparison of remission achievement in MCD and MGN



In result, the CR was achieved in 10 patients (7 with MCD, 2 with MGN, 1 with FSGS) and PR in 10 patients (10 with MGN) [Figure 2.].

There was no significant difference between CR and PR group in immunosupressive treatment [Table 2].

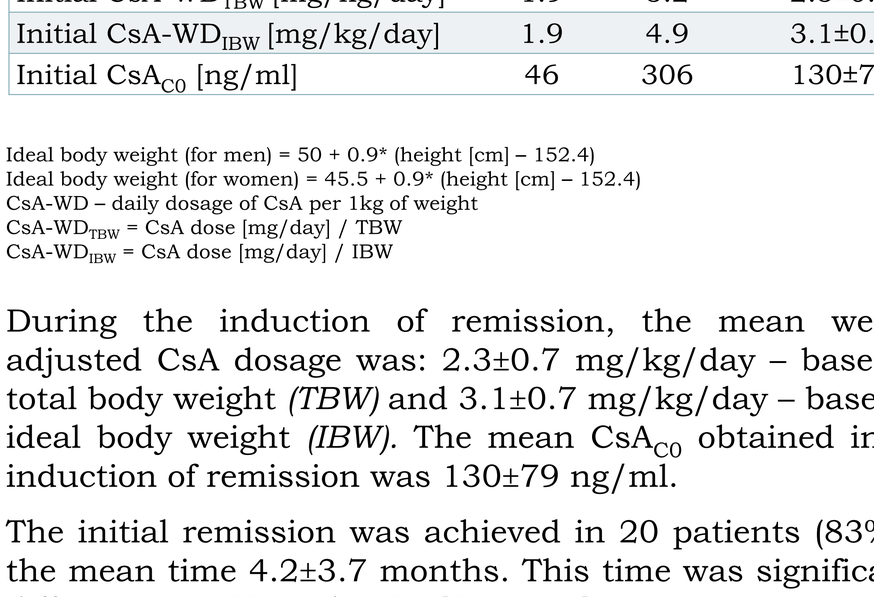
Table 1. Comparison of immunosupressive treatment in CR and PR group.

Variable	Complete remission	Partial remission	P-value
CsA dose [mg/day]	174±28	184±49	0.631
CsA-WD_{TBW} [mg/kg/day]	2.3±0.6	2.0±0.7	0.247
CsA-WD_{IBW} [mg/kg/day]	2.8±0.4	2.6±0.6	0.796
CsA_{C0} [ng/ml]	115±15	112±28	0.684
$C_0WD\text{-}R_{TBW}$	53.9±17.9	58.8±20.1	0.739
$C_0WD\text{-}R_{IBW}$	43.0±10	45.7±18.4	0.912
Prednisone dose [mg]	6.2±4.3	11.4±7.1	0.063

C_0WD-R – CsA concentration obtained from 1mg of CsA per 1kg of weight
$C_0WD\text{-}R_{TBW}$ = CsA_{C0} / (CsA dose [mg/day] / TBW)
$C_0WD\text{-}R_{IBW}$ = CsA_{C0} / (CsA dose [mg/day] / IBW)

In the patients before remission reaching, the significant inverse correlations were observed between CsA_{C0}–to–weight-based-dose ratio and cholesterol level (r=-0.62, p=0.043 for IBW), as well as LDL (r=-0.72, p=0.013 for IBW). There was no correlation with cholesterol and LDL in patients with remission (CR or PR).

Figure 2. The summary of the observational study.



Nephrotic syndrome – daily proteinuria >3.5 g and hypoalbuminemia <3.5 g/dl
Initial remission – daily proteinuria <3.5 g and normoalbuminemia (serum albumin >3.5 g/dl)
Complete remission – daily proteinuria <0.5 g
Partial remission – daily proteinuria between 0.5 and 3.5 g

CONCLUSIONS

- ❑ The moderate doses of CsA (2.3–3.1 mg/kg/day) were sufficient to elicit the initial remission of NS.
- ❑ The sufficient trough CsA levels were: 130 ng/ml to induce remission and 112-115 ng/ml to maintain remission.
- ❑ The achievement of recommended trough CsA level suggests that calculation on IBW is more reliable than on TBW.
- ❑ The influence of hypercholesterolemia due to nephrotic syndrome on CsA_{C0}-to-weight-based-dose ratio should be take into account when adjusting the drug dose in the induction of remission.
- ❑ Achievement only PR in most of the patients with MGN may suggest, that CsA doses and CsA_{C0} should be higher to reach CR in this type of glomerulonephritis.

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Anna Matyjek
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