ORIGINAL RESEARCH PAPER

Paediatrics

KEY WORDS: Nephrotic syndrome, prednisolone, urine albumin, SSNS.

STUDY ON OUTCOME OF SINGLE MORNING TOTAL DOSE OF ORAL PREDNISOLONE VERSUS DIVIDED DOSE OF ORAL PREDNISOLONE IN TREATMENT OF STEROID SENSITIVE NEPHROTIC SYNDROME

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ABSTRACT

Nephrotic syndrome is a common renal disorder characterised by Massive proteinuria (>40 mg/m2/day); hypoalbuminemia and edema. Relapses of nephrotic syndrome are usually treated with prednisolone. Study was aimed to compare the efficacy, complication and compliance of single morning daily total dose versus divide daily dose of oral prednisolone in treating steroid sensitive nephrotic syndrome(SSNS). The study was conducted on patients diagnosed as 1st attack Nephrotic Syndrome or relapse case with SSNS visiting nephrology clinic and admitted in pediatric ward in S.S.G Hospital Vadodara. Total 60 patients were taken in prospective randomised observational study.Patients with 1st attack or relapse were randomized to receive prednisolone 2 mg/ kg per day, either as a single dose (Group A) or in divided doses (Group B) until remission, followed by 1.5 mg/kg on every alternate day. Complication parameters Blood Pressure, Random Blood Sugar, urine output and GI upset were noted. Data was analysed by applying standard statistical test and Med CalC. We observed that average time take for remission after starting the treatment in group A and group B was 14.13 and 17.13 days. Compliance was observed better with single dose then divided dose and fluctuation in blood pressure, random blood sugar, GI upset were observed more with divided dose. Study concluded that single dose did not suppress HPA axis.

Introduction:

Nephrotic syndrome is a common renal disorder .In Indian subcontinent it is to be estimated at 90 to 100 per million population .It is characterised by massive proteinuria; hypoalbuminemia and edema. Hypercholestrolemia microscopic hematuria ,raised urea level are also observed.

Protienuria results from altered permeability of glomerular filteration barrier which comprises the podocyte slit diaphragm glomerular basement membrane and fenestrated capillary endothelium. The barrier to protein excreation is at the level of glomeruli where size of protein molecule and their negative charge inhibits glomerular filteration. Steroids in nephrotic syndrome is the core treatment in inducing remission by reducing inflammatory process and thereby reducing proteinuria. However steroids lead to various side effects like cushingoid features(obesity, hirsuitism,striae) hypertension ,impaired glucose intolerance, posterior subcapsular lenticular opacities ,growth retardation etc[1].

Aims and Objectives:

To compare the efficacy, complication and compliance of single morning daily total dose versus divide daily dose of oral prednisolone in treating steroid sensitive nephrotic syndrome(SSNS).

Materials and Methods:

The present study was conducted among patients diagnosed as first attack nephrotic syndrome or relapse case with steroid sensitive nephrotic syndrome visiting nephrology clinic at OPD 13 B or admitted in pediatric ward in S.S.G Hospital, Vadodara. Total 60 patients were enrolled during study period.

INCLUSION CRITERIA:

1) Children who were freshly diagnosed as primary attack nephrotic syndrome from 1year to 17 years on OPD basis or admitted for same in Paediatric ward.
2) Children who were already enrolled in Paediatric Nephrology Clinic with regular follow up and labeled as frequent or infrequent relapse in Nephrotic syndrome from 1year to 17years.

EXCLUSION CRITERIA:

1) Children on alternate regimen in primary or in relapse (frequent or infrequent) relapse of Nephrotic Syndrome
2) Children diagnosed as steroid resistance nephrotic Syndrome and are already on alternate drug therapy.
3) Children with congenital or FINNISH type of nephritic syndrome.
4) Children with breakthrough proteinuria (with urine albumin +2 or urine protein to creatinine ratio <2 and responds to anti-biotic treatment) were be excluded from the study

Method of data collection:

Children fitting in the inclusion criteria will be enrolled into the study after taking written and informed consent from the parents and tested for urine protein creatinine (p/c) ratio and routine blood and urine investigations. Patients participating in the study will be randomized into group 'A' or group 'B' by lottery method.

Group A : patients will receive single morning total dose of oral prednisolone.

Group B : patients will receive divided total dose of oral prednisolone.

Efficacy of the two groups will be compared:

1) Time taken for urine albumin to become nil or trace by sulphosalacilic acid spot test .
2) Time taken for edema to get resolved .

Complications to steroid regimen in two groups will be noted:

1) Blood Pressure monitoring.
2) GI upset like nausea, vomiting, abdominal pain.

Compliance of the two groups will be compared by:

1) No of blisters completed
2) School dropouts
3) Duration of stay in the hospital.

DATA ANALYSIS AND STATISTICAL METHODS:

Data collected from the study was analysed CHI SQUARE TEST and Independent T Test. Odds ratio was calculated when question was in Yes or No. Data analysis was done by using Med CalC.

Study Design: Prospective Randomised Observational Study.

RESULT AND DISCUSSION:

Comparing complications of two Groups :

GI upset

GI uspet	Group A Yes: No	Group B Yes: No
Pre treatment	18 : 12	19 : 11
Post Treatment	5 : 25	20 : 10
p value(odd ratio)	0.0011(2.24 to 25.06)	0.7(0.29 to 2.49)

Patients when presents with ascites in Nephrotic Syndrome often complained of vague abdominal pain which was explained either secondary to acsites or subacute bacterial peritonitis. In group A there were 18 patients out of 30 who had complains regarding GI upset and in Group B there were 19 patients out of 30 with similar complains.

The above table shows that only 5 out of 30 patients had GI complains in form of either abdominal pain , or bloating feeling or vomiting and requiring antacids to surpass complaints of gastritis secondary to Prednisolone when given in total single morning dose in group A; while 20 out of 10 patients were having GI complains requiring antacids frequently when Prednisolone was given in divided dose in Group B with statistically significant (p= 0.0002),other side effects or prednisolone like peptic ulcer formation and haemorrhage,abdominal discormfort and oesophageal ulceration was not observered in our study.

Comparing blood pressure difference Post treatment of Group A and Group B

Post treatment parameters	Group A	Group B	P value
SBP	95.4(±8.17)	109.27(±10.33)	0.0002
DBP	57.87(±4.61)	62.8(±4.94)	0.0002
Wether on any antihypertensive	5:25	20:10	

The above table shows that there is statistical significance in blood pressure in two groups and more patients require medication for controlling BP when treated with divided dose as compared to single dose with pvalue =0.0002.

In study done by Bimal K. Ekka, Arvind Bagga, and R. N. Srivastava at AIIMS, New Delhi: Single- versus divided-dose Prednisolone therapy for relapses of Nephrotic syndrome they compared blood pressure of two groups .mean SBP for single dose group was 101.9±7.5mmhg and for divided group was 105.6±12.3mmhg. In sample size of 106 patients. they found no significant differences in side effects in patients treated with Prednisolone in single or divided doses which is in contrast to our study. The degree of adrenocortical suppression was, however, not measured[2].

In other study done by Premala.S et al titled as Predictors of remission and relapse in idiopathic Nephrotic syndrome: a prospective cohort study, concluded that: There was no statistically significant association between relapse of Nephrotic syndrome and blood pressure from baseline to total duration of study and in between relapse[3].

Comparing Efficacy of two Groups:

Post Treatment Parameters	Group A (n = 30)	Group B (n = 30)	P-Value
Remission Time taken (in days)	14.13(±5.56)	17.13(±6.68)	P = 0.0637
Time Taken for resolution of edema (in days)	5.4(±2.87)	6.93(±3.36)	P = 0.0629

Average time taken for remission (in days) for Group A is 14.13 days(±5.56) and for Group B is 17.13 days(±6.68) ; which suggests that time taken for occurrence of remission in two groups is similar in both groups with no difference observed statistically (p=0.0637). Average time taken for resolution of edema (in days) after starting Prednisolone therapy in Group A is 5.4 days(±2.87) and for Group B is 6.93 days(±3.36) which suggests that time taken for resolution of edema is similar in both groups with no difference observed statistically (P = 0.0629).

Hence both groups did not show any significant difference statistically in average time taken for remission & resolution of edema.

In one study done by Bimal K. Ekka, Arvind Bagga, and R. N. Srivastava titled as Single- versus divided-dose Prednisolone therapy for relapses of nephrotic syndrome. After 9 months' follow-up, there were no differences in the frequency of relapses and cumulative dose of prednisolone received in the two groups which is comparable to our study also[2].

Comparasion of compliance in two Groups:

Compliance	Single dose (n = 30) (Group A)	Divided dose (n = 30) (Group B)	P-Value
No of Drugs/Blisters missed by the Patient	0.55(±1.87)	3.2(±1.3)	P < 0.0001
Compliance observed (YES : NO)	29 : 1	20 : 10	P = 0.0076

Our study has compared Post Treatment parameters showing compliance of Group A and Group B. Average number of drugs missed by the patients in Group A is 0.55(±1.87) and in Group B is 3.2(±1.3) which shows that patients in group B has missed more no of drugs or blisters when compared to Group A which is also statistically significant (p= <0.0001).

Compliance was observed clinically in 29 patients out of 30 in Group A; hence maximum patients had completely taken Prednisolone when given in single total morning dose; however 20 patients out of 30 in Group B had completely taken Prednisolone in divided dose and rest 10 patients did not show good compliance to the divided dose and which was also significant statistically (p=0.0076)

In study proposed by Honq S. Lau, Karin S et al. Non-compliance in elderly people: evaluation of risk factors by longitudinal data analysis more complex drug regimen. Concluded that The increased risk was similar for a regimen of two times daily and more than two times daily compared to a regimen of once daily. This relation is consistent with the findings of Pullar et al, and Hulka et al.[4]; and suggests that drug regimens should be as simple as possible. It can be argued that an increase in the number of drugs also leads to a more complex drug regimen, but our results indicate that these two factors can and should be treated separately[5].

Conclusion:

It is evident from our study that complication in terms of Blood pressure and GI upset were more when patient was given divided total dose of oral prednisolone as compared to single morning total dose of oral prednisolone. Both treatment therapy were equally effective in inducing remission .Compliance is better observed when patient were given single morning total dose as compared to divided daily total dose.

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