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TO STUDY THE EFFECT OF TOTAL CHOLESTEROL, FINAL HT(CM), FINAL HEIGHT DIFFERENCE WITH VITAMIN D, SERUM CA AND ALP IN CHILDREN WITH NEPHROTIC SYNDROME

Paediatrics

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ABSTRACT

Nephrotic Syndrome is the clinical manifestation of glomerular diseases associated with heavy (nephrotic range) proteinuria.
1. To correlate between linear growth velocity and biochemical bone markers in nephrotic children on steroid therapy. The study population constituted patients who are children and adolescent admitted in Department of Paediatrics in Midnapore Medical College and Hospital, WB diagnosed with Nephrotic syndrome. The study participants who fulfilled inclusion criteria were included in this study. Taking into consideration of availability of patients during data collection period, a total of 75 children and adolescent diagnosed with nephrotic syndrome were enrolled in the study and 75 controls were taken. Difference of mean ALP vs. group was statistically significant (p=0.0216). Difference of mean total cholesterol vs. group was statistically significant (p<0.0001). Difference of mean serum Ca vs. group was statistically significant (p<0.0001). Present study found that in case, the mean serum Vitamin D and Ca lower in cases which was statistically significant. We found that correlate between linear growth velocity and biochemical bone markers in nephrotic children on steroid therapy.

KEYWORDS

Linear growth velocity, Vitamin D, Serum Calcium, ALP and Children with Nephrotic Syndrome

INTRODUCTION

Nephrotic range proteinuria is defined as proteinuria >3.5 g/24hr or >40 mg/m²/hr or a urine protein:creatinine ratio >2. The triad of clinical findings associated with nephrotic syndrome arising from the large urinary losses of protein are hypoalbuminemia (<2.5g/dl), edema and hyperlipidemia (cholesterol >200mg/dl).[1]

Approximately 90% of children with nephrotic syndrome have idiopathic nephrotic syndrome. Idiopathic nephrotic syndrome includes multiple histologic types, in which minimal change nephrotic syndrome (MCNS) is the most common type (approximately 85% of total cases of nephrotic syndrome in children). More than 95% of children with minimal change disease respond to corticosteroid therapy.[2]

Idiopathic nephrotic syndrome is more common in boys than in girls (2:1) and most commonly appears between the ages of 2 and 6 years. However, it has been reported as early as 6 months of age and throughout adulthood.[3]

Corticosteroids are the mainstay of therapy for MCNS. Response is defined as the attainment of remission within the initial 4 weeks of corticosteroid (CS) therapy.

In children with presumed MCNS , prednisolone should be administered as a single daily dose or divided doses of 60 mg/m²/day or 2 mg/kg/day to a maximum of 60 mg daily for 6 wk2,5followed by alternate day prednisolone (starting at 1.5 mg/kg or 40mg/m²) for a period ranging from 6 week to 5 months[1], with tapering of the dose.

Relapse of nephrotic syndrome is defined as a urine protein: creatinine ratio of >2 or ≥3+ protein on dipstick testing for 3 consecutive days.

Growth in patients with idiopathic nephrotic syndrome is influenced by several factors. Prior to the onset of the disease, growth in children who later develop nephrotic syndrome and that in other healthy children is influenced by the same factors. On onset of the disorder, the children suffer from proteinuria caused by the increase in glomerular permeability, leading to hypoproteinemia associated with urinary loss of several substances important for homeostasis. In most cases, after the start of steroid therapy, proteinuria subsides quickly; however, the side effects of glucocorticoid treatment persist.[4]

Nephrotic syndrome often occurs as a part of a systemic illness with an inflammatory state. The increased osteoclastic bone resorption accompanying inflammation is thought to be mediated by TNFα and other cytokines rather than by the RANKL, RANK, OPG pathway. On the other hand, it was reported that both 25(OH) vitamin D and calcitriol are transported by vitamin D binding globulin and albumin, which are depleted by heavy proteinuria-albumin losses. These changes contribute to secondary hyperparathyroidism and increased bone turnover.

A reduced bone mineral density is common, particularly in the first several months of treatment, when prednisolone doses exceed 5 mg/day. Glucocorticoid use is associated with reducedosteoblastic bone formation, increased apoptosis ofboth osteocytes and osteoblasts. Glucocorticoids also indirectly affect bone. It causes reduced intestinal calcium absorption and increased urinary calcium losses.

Glucocorticoids (GC) alter growth by directly acting on the growth cartilage or via altering the levels of growth factors.Growth is an essential feature of childhood. It depends on genetic, nutritional, social and emotional factors.It is affected by chronic systemic disease. Growth follows a sigma shaped curve with a high velocity in the early postnatal period and during puberty, but a steady rate during mid-childhood. Nephrotic syndrome occurs most commonly in the age group of 2-8 years when the growth rate is at a steady state. Patients having frequent relapses and requiring repeated courses of steroids often develop steroid toxicity, including growth retardation.[5]

Chronic steroid treatment has long been recognized as a major risk factor for growth retardation in children. A high correlation was found between growth retardation and cumulative steroid dose6. Loss of bone and deterioration in short term growth are dependent on the type and dose of GC and occur most prominently over the first six months of treatment. GC induced growth failure may also be due to direct effects on the growth plate. Infusion of GC into the growth plate leads to a temporary reduction in the growth rate of that leg and may disrupt the growth plate vasculature.[7]

High dose corticosteroid treatment causes a decrease in bone formation as shown by the changes in alkaline phosphatase level. The higher the cumulative dose of CS used the more marked the changes in

biochemical bone markers.[4]

THE AIM OF OUR STUDY

1. To compare the linear growth velocity in children with nephrotic syndrome receiving steroid with that of known available reference standard for children of same age and sex groups.
2. To correlate between linear growth velocity and biochemical bone markers in nephrotic children on steroid therapy.

MATERIALS AND METHODS

Study population:

The study population constituted patients who are children and adolescent admitted in Department of Paediatrics in Midnapore Medical College and Hospital, WB diagnosed with Nephrotic syndrome. The study participants who fulfilled inclusion criteria were included in this study. Taking into consideration of availability of patients during data collection period, a total of 75 children and adolescent diagnosed with nephrotic syndrome were enrolled in the study and 75 controls were taken.

Study Duration:

This studywas carried out from April 2018 to September 2019.

INCLUSION CRITERIA:

- Children between 2-12 age group of years.
- Diagnosed case of nephrotic syndrome.
- Idiopathic nephrotic syndrome.
- On steroid therapy.
- Steroid sensitive Nephrotic Syndrome

EXCLUSION CRITERIA:

- Children <2 years and >12 years.
- Children with secondary causes of nephrotic syndrome.
- Children who are steroid resistant (defined as failure to achieve Remission after 8 wkof corticosteroid therapy) or steroid dependent (Occurrence of 2 consecutive relapses during alternate days steroid therapy or within 2 weeks of its discontinuation).
- Children on alternative therapies to corticosteroids.
- Short stature due to other causes excepting steroidtherapy.
- Very sick children.
- Unwilling for study.
- On any calcium, phosphorus or vitamin-D containing preparations.

Statistical Analysis:

For statistical analysis data were entered into a Microsoft excel spreadsheet and then analysed by SPSS 24.0. and GraphPad Prism version 5. Two-sample t-tests for a difference in mean involved independent samples or unpaired samples. Unpaired proportions were compared by Chi-square test or Fischer's exact test, as appropriate. p-value ≤ 0.05 was considered for statistically significant.

RESULT AND ANALYSIS

Our study showed that in case, the mean age (mean± s.d.) of patients was 6.6867 ± 2.7751 years. In control, the mean age (mean± s.d.) of patients was 6.4533 ± 2.8119 years. Difference of mean age vs. group was not statistically significant (p=0.6098) and the mean age at diagnosis (mean± s.d.) of patients was 5.4067 ± 2.4143 years.

We found that in case, the mean albumin (mean± s.d.) of patients was2.2733 ± 1.8598 mg/dl. In control, the mean albumin (mean± s.d.) of patients was 4.4847 ± .6601 mg/dl. Difference of mean albumin vs. group was statistically significant (p<0.0001).

It was found that in case, the mean total cholesterol (mean± s.d.) of patients was 332.9467 ± 55.2940 mg/dl. In control, the mean total cholesterol (mean± s.d.) of patients was 166.6800 ± 18.4707 mg/dl. Difference of mean total cholesterol vs. group was statistically significant (p<0.0001) and in case, the mean Final ht (mean± s.d.) of patients was 114.2960 ± 18.5996 cm. In control, the mean Final ht (mean± s.d.) of patients was 124.8773 ± 104.4226 cm. Difference of mean Final ht vs. group was not statistically significant (p=0.3890).

We found that in case, the mean final height difference (mean± s.d.) of patients was 5.4613 ± 2.4978. In control, the mean final height difference (mean± s.d.) of patients was 5.3573 ± 1.9650. Difference of mean final height difference vs. group was not statistically significant (p=0.7773) and according to final height difference in case, 4(5.3%) patients had ≥-2 to <+2 and 71(94.7%) patients had ≥+2. According to final height difference in control, 3(4.0%) patients had ≥-2 to <+2 and 72(96.0%) patients had ≥+2. Association of final height difference vs. group was not statistically significant (p=0.6986).

Our study showed that in case, the mean Vitamin D (mean± s.d.) of patients was 12.6293 ± 3.4974. In control, the mean Vitamin D (mean± s.d.) of patients was 17.8907 ± 4.6069. Difference of mean Vitamin D vs. group was statistically significant (p<0.0001) and in case, the mean serum Ca (mean± s.d.) of patients was 6.8000 ± .9672. In control, the mean serum Ca (mean± s.d.) of patients was 9.6907 ± .9218. Difference of mean serum Ca vs. group was statistically significant (p<0.0001).

It was found that in case, the mean serum P (mean± s.d.) of patients was 5.2147 ± .9998. In control, the mean serum P (mean± s.d.) of patients was 5.1135 ± .8854. Difference of mean serum P vs. group was not statistically significant (p=0.5145) and in case, the mean serum Mg (mean± s.d.) of patients was 2.0947 ± .5162. In control, the mean serum Mg (mean± s.d.) of patients was 2.0027 ± .4353. Difference of mean serum Mg vs. group was statistically significant (p=0.2399).

We found that in case, the mean ALP (mean± s.d.) of patients was 136.3200 ± 66.3598. In control, the mean ALP (mean± s.d.) of patients was 113.4267 ± 53.7341. Difference of mean ALP vs. group was statistically significant (p=0.0216) and in case, 30(40.0%) patients had female and 45(60.0%) patients had male. In control, 25(33.3%) patients had female and 50(66.7%) patients had male. Association of sex vs. group was not statistically significant (p=0.3968).

Our study showed that in case, 59(78.7%) patients had Hindu, 11(14.7%) patients had Muslim and 5(6.7%) patients had Christian. In control, 57(76.0%) patients had Hindu, 10(13.3%) patients had Muslim and 8(10.7%) patients had Christian. Association of religion vs. group was not statistically significant (p=0.6790).According to residence in case, 42(56.0%) patients had rural and 33(44.0%) patients had urban. In control, 44(58.7%) patients had rural and 31(41.3%) patients had urban. Association of residence vs. group was not statistically significant (p=0.7412) and in case, 64(85.3%) patients had relapse 1 and 11(14.7%) patients had relapse 2.

DISCUSSION

We found that in case, the mean age (mean± s.d.) of patients was 6.6867 ± 2.7751 years. In control, the mean age (mean± s.d.) of patients was 6.4533 ± 2.8119 years. Difference of mean age vs. group was not statistically significant (p=0.6098). Present study found that the mean age at diagnosis (mean± s.d.) of patients was 5.4067 ± 2.4143 years. Present study found that in case, 30(40.0%) patients had female and 45(60.0%) patients had male. In control, 25(33.3%) patients had female and 50(66.7%) patients had male. Association of sex vs. group was not statistically significant (p=0.3968).

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According to residence in case, 42(56.0%) patients had rural and 33(44.0%) patients had urban. In control, 44(58.7%) patients had rural and 31(41.3%) patients had urban. Association of residence vs. group was not statistically significant (p=0.7412).

Biyikli NK et al8 found that serum ALP, OC, and iPTH levels were within normal limits at the time of study entry. However, both serum OC and ALP levels showed a significant decrease after the completion of CS treatment (OC from 13.6+/-9.2 ng/ml to 6.7+/-5.2 ng/ml and ALP from 151.8+/-60.2 U/l to 116+/-43.8 U/l). 25-Hydroxyvitamin D levels increased to 17.2+/-8.9 microg/l from 9.9+/-6.9 microg/l after CS treatment. The effects of recurrent use of CSs were assessed by dividing nephrotic patients into two subgroups: infrequent relapsers (IFR) and frequent relapsers (FR). The cumulative dose of CS was 28,125 mg/m(2) for IFR and 105,000 mg/m(2) for FR. The changes in OC, ALP, and 25-hydroxyvitamin D levels after CS treatment were significantly different between IFR and FR.

We found that in case, the mean albumin (mean± s.d.) of patients was 2.2733 ± 1.8598 mg/dl. In control, the mean albumin (mean± s.d.) of

patients was 4.4847 ± .6601 mg/dl. Difference of mean albumin vs. group was statistically significant (p<0.0001).

Present study found that in case, the mean ALP (mean± s.d.) of patients was 136.3200 ± 66.3598. In control, the mean ALP (mean± s.d.) of patients was 113.4267 ± 53.7341. Difference of mean ALP vs. group was statistically significant (p=0.0216).

We found that in case, the mean total cholesterol (mean± s.d.) of patients was 332.9467 ± 55.2940 mg/dl. In control, the mean total cholesterol (mean± s.d.) of patients was 166.6800 ± 18.4707 mg/dl. Difference of mean total cholesterol vs. group was statistically significant (p<0.0001).

In case, the mean Final ht (mean± s.d.) of patients was 114.2960 ± 18.5996 cm. In control, the mean Final ht (mean± s.d.) of patients was 124.8773 ± 104.4226 cm. Difference of mean Final ht vs. group was not statistically significant (p=0.3890).

We found that in case, the mean final height difference (mean± s.d.) of patients was 5.4613 ± 2.4978. In control, the mean final height difference (mean± s.d.) of patients was 5.3573 ± 1.9650. Difference of mean final height difference vs. group was not statistically significant (p=0.7773).

According to final height difference in case, 4(5.3%) patients had ≥-2 to <+2 and 71(94.7%) patients had ≥+2. According to final height difference in control, 3(4.0%) patients had ≥-2 to <+2 and 72(96.0%) patients had ≥+2. Association of final height difference vs. group was not statistically significant (p=0.6986).

Koşan C et al 9 found that mean serum calcium (Ca) and osteocalcin levels were found to be significantly lower than those at the beginning of the therapy. Mean serum total alkaline phosphatase (t-ALP), bone-specific alkaline phosphatase (b-ALP) and urine calcium creatinine ratio (Ca/Cr), urinary deoxypyridinoline levels were significantly increased in comparison to the beginning of therapy. There was no significant relationship between serum levels of phosphate and parathyroid hormone (PTH) at the beginning of treatment and at the 4th and 12th week of treatment.

We found that in case, the mean Vitamin D (mean± s.d.) of patients was 12.6293 ± 3.4974. In control, the mean Vitamin D (mean± s.d.) of patients was 17.8907 ± 4.6069. Difference of mean Vitamin D vs. group was statistically significant (p<0.0001). Present study found that in case, the mean serum Ca (mean± s.d.) of patients was 6.8000 ± .9672. In control, the mean serum Ca (mean± s.d.) of patients was 9.6907 ± .9218. Difference of mean serum Ca vs. group was statistically significant (p<0.0001).

Present study found that difference of mean serum P vs. group was not statistically significant (p=0.5145).

Present study found that in case, the mean serum Mg (mean± s.d.) of patients was 2.0947 ± .5162. In control, the mean serum Mg (mean± s.d.) of patients was 2.0027 ± .4353. Difference of mean serum Mg vs. group was statistically significant (p=0.2399). In case, 64(85.3%) patients had relapse 1 and 11(14.7%) patients had relapse [2].

Mohamed GB et al 10 found that alkaline phosphatase (ALP), and 24-hour urinary Ca and proteins were measured. The NS patients revealed a significantly lower serum OPG and parameters of bone formation (ALP and OC) and a significantly higher 24- hour urinary Ca than controls. A short course of glucocorticoids therapy for one month resulted in a significant decrease of serum OPG, ALP and OC levels and a significant increase of 24- hour urinary Ca, while serum PTH levels were not significantly affected by this therapy; the FR revealed a significantly lower serum level and a significantly higher 24- hour urinary Ca and serum PTH than the IFR. OPG had significant negative correlations with markers of disease activity and severity (ESR, serum cholesterol, 24- hour urinary protein and cumulative steroid dose), PTH and 24- hour urinary Ca. On the other hand, OPG had significant positive correlations with ALP, OC, and serum albumin.

CONCLUSION

We found the difference of mean serum Vitamin D and serum Ca were lower in case compared to control which was statistically significant. Along with this in our study we found that the difference of mean ALP (higher in cases) and Cholesterol (higher in cases) compared to control was statistically significant. We found the correlation between linear growth velocity and biochemical bone markers in nephrotic children on steroid therapy.

Table: Distribution of Mean Age, Albumin, Total cholesterol, Final ht(cm), Final height difference, Vitamin D, Serum Ca, Serum P, Serum Mg and ALP: Group

		Number	Mean	SD	Minimum	Maximum	Median	p-value
Age (years)	Case	75	6.6867	2.7751	2.5000	12.0000	6.0000	0.6098
	Control	75	6.4533	2.8119	1.5000	12.0000	6.0000	
Albumin	Case	75	2.2733	1.8598	1.3000	18.0000	2.1000	<0.0001
	Control	75	4.4847	.6601	3.2000	5.5000	4.8000	
Total cholesterol	Case	75	332.9467	55.2940	244.0000	440.0000	322.0000	<0.0001
	Control	75	166.6800	18.4707	124.0000	210.0000	163.0000	
Final ht(cm)	Case	75	114.2960	18.5996	83.0000	165.2000	113.0000	0.3890
	Control	75	124.8773	104.4226	81.5000	1005.0000	110.2000	
Final height difference	Case	75	5.4613	2.4978	0.8000	13.2000	5.2000	0.777
	Control	75	5.3573	1.9650	0.5000	11.0000	5.6000	
Vitamin D	Case	75	12.6293	3.4974	4.2000	22.0000	12.4000	<0.0001
	Control	75	17.8907	4.6069	8.8000	32.0000	17.9000	
Serum Ca	Case	75	6.8000	.9672	5.0000	9.6000	6.7000	<0.0001
	Control	75	9.6907	.9218	7.8000	11.6000	9.6000	
Serum P	Case	75	5.2147	.9998	2.7000	7.0000	5.4000	0.514
	Control	74	5.1135	.8854	3.0000	6.5000	5.2000	
Serum Mg	Case	75	2.0947	.5162	1.4000	3.6000	2.1000	0.2399
	Control	75	2.0027	.4353	1.0000	3.4000	2.0000	
ALP	Case	75	136.3200	66.3598	18.0000	310.0000	118.0000	0.0216
	Control	75	113.4267	53.7341	36.0000	256.0000	100.0000	

REFERENCE

1. "Nephrotic Syndrome in Adults".National Institute of Diabetes and Digestive and Kidney Diseases. February 2014. Retrieved 9 November 2017.
2. Ferri, Fred F. (2017). Ferri's Clinical Advisor 2018 E-Book: 5 Books in 1. Elsevier Health Sciences.p. 889.ISBN 9780323529570.
3. Kher, Kanwal; Schnaper, H. William; Greenbaum, Larry A. (2016). Clinical Pediatric Nephrology, Third Edition. CRC Press.p. 307.ISBN 9781482214635.
4. Kelly, Christopher R.; Landman, Jaime (2012).The Netter Collection of Medical Illustrations - Urinary System e-Book.Elsevier Health Sciences.p. 101.ISBN 1455726567.
5. Behrman, Richard E.; Robert M Kliegman; Hal B. Jenson (2008).Nelson Tratado de Pediatria (in Spanish). Elsevier, España. p. 1755.ISBN 8481747475.
6. "Electronic Learning Module for Kidney and Urinary Tract Diseases".Archived from the original on 2008-12-20.Retrieved 2015-12-25.
7. Freedberg, Irwin M. et.al, ed. (2003). Fitzpatrick's dermatology in general medicine (6th ed.). New York, NY [u.a.]: McGraw-Hill. p. 659.ISBN 0-07-138076-0.
8. Biyikli NK, Emre S, Sirin A, Bilge I. Biochemical bone markers in nephrotic children. Pediatric Nephrology. 2004 Aug 1;19(8):869-73.
9. Koşan C, Ayar G, Orbak Z. Effects of steroid treatment on bone mineral metabolism in children with glucocorticoid-sensitive nephrotic syndrome. West Indian Medical Journal. 2012 Sep;61(6):627-30.
10. Mohamed GB, Abdel-Latif EA. Serum osteoprotegerin (OPG) in children with primary nephrotic syndrome. Saudi Journal of Kidney Diseases and Transplantation. 2011 Sep 1;22(5):955.