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Plasma Histamine And Serotonin Levels In Children With Nephrotic Syndrome And Acute Poststreptococcal Glomerulonephritis

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Abstract

Plasma histamine and serotonin concentrations were measured using fluorimeteric assay in 40 children with renal diseases. Minimal change nephrotic syndrome (15) focal segmental glomerulosclerosis(10) and acute poststreptococcal glomerulonephritis(15) to determine the relation between plasma levels of histamine and serotonin and these various types of renal diseases in children. Plasma histamine level was significantly increased in group of children with acute poststreptococcal glomerulonephritis. Plasma serotonin levels were significantly increased in all 3 groups of patient, when compared with those of controls. Raised plasma histamine in acute poststreptococcal glomerulonephritis group may be evidence of the acute immunological inflammation and defective renal excretion due to mild renal impairment in these children. Raised plasma serotonin in all 3 groups of patients may be due to diminished uptake and release of serotonin from platelets in children with minimal change nephrotic syndrome and focal segmental glomerulosclerosis and due to defective renal execretion in children with acute poststreptococcal glomerulo-nephritis.

Introduction

Histamine plays an important role in the regulation of the functions and changes which result from inflammation and trauma. It is one of the main constituents of tissue mast cells (Range and Dale ,1993.) blood basophils (Hartman *et al*,1961) and it is also present in gastric mucosa (Kiahlson , *et al.*,1964), vascular endoth-elial and smooth muscle cells (Abboud *et al* ,1982. and Hollis *et al.*, 1983) The kidney forms and stores histamine. but very little is known about the role of histamine in renal pathophysiology (Gill *et al* , 1991). Markle *et al*.,(1986) demonstrated increased renal histamine content in experimental diabetes with nephropathy. In adults impaired clearance of injected labelled histamine has been reported in chronic renal failure (CRF) (Beal and Vavarsdal , 1959).

Serotonin is a vasoactive amine, ninety% of the body's stores of serotonin are found in gastrointestinal tract, while the remainder is divided between the central nervous system and platelets (Aberg and Engstron , 1990). It was found that there is a Significant increase in plasma serotonin in all types of nephrotic syndrome (Malyszko *et al*, 1996). (Parbtani *et al.*, 1980). demonstrated non significant differences between free plasma serotonin in normal individuals and patients with minimal change nephrotic syndrome (MCNS), and acute poststreptococcal glomerulonephritis (APSGN), but signifi-cant increase in cases of focal segmental glomerulosclerosis (FSGS) and systemic lupus erythmatosjs (SLE) was found. Little is known about the relation between the plasma histamine and serotonin levels and renal diseases in children. In the present study we determine the plasma histamine and serotonin levels in children with various renal diseases (MCNS, FSGS and APSGN), and evaluated a curative' relation between these renal diseases and plasma levels of histamine and sterotonin.

Subjects And Methods

Forty children with renal diseases (chronic illness considered as handicapped had been studied in Menoufiya and Al Azhar, universities, hospitals in the following three clinical groups:

Group I: Fifteen children with minimal change nephrotic syndrome with previous frequent relapses. (MCNS), ten boys (66.6.6%) and five girls (33.33%) with median age 7.1 years (range 2-14 years), and median weight was 23.3 Kg (range 13-32Kg). The diagnosis of MCNS was done on histopathological basis after renal biopsy. None of the children was on steroids, and all were normotensives. The median duration of nephrotic syndrome illness was 2.6 years, (range 1-6 years).

Group 2: Ten children with focal segmental glomerulosclerosis (FSGS), six boys (60%) and four girls (40%), range 3-14 years. The weight was range 13-23Kg. The duration of illness range 1-4 years.

The diagnosis of FSGS was done on histopathological basis after renal biopsy. None of the children was on steroid therapy, two (20%) of these children were hypertensives and both of these children were being treated with beta blockers (atenolol mg /kg/day orally).

Group 3: Fifteen children with acute poststreptococcal glomerulo-nephritis (APSGN), nine boys (60%) and six girls (40%) range 4-11 years. The weight range 15-30Kg. The diagnosis of APSGN was done on a clinical and laboratory basis. None of these children was taking steroids, five (33.33%) were hypertensive and all were being treated with beta blockers (atenolol 2mg/kg/ day orally). But, the blood sample collection was taken before starting the antihypertensive therapy.

Controls: Controls (C) consisted of twelve children were seven boys (58.3%) and five girls (41.7%) range 2-14 years. The weight range 11-36 Kg.

None of these controls had any history of renal, allergic disease or diabetes mellitus, and none of these children had taken any medication for at least two weeks before the study. The 3 groups of patients and their control were subjected to full clinical evaluation, laboratory investigations including hemoglobin estimation, renal function (blood urea nitrogen & plasma creatinine), 24 hours urinary protein, serum albumin, and plasma levels of histamine and serotonin.

Methods:

Determination of histamine: This was performed according to the modification of the method reported by Lorenz *et al.*, (Lorenz, W, *et al*, (1971) . For fluorimetric assay of the amine, the fluorescence was measured using Schimadzu fluorescence spectrophotometer (RF 500).

Determination of plasma serotonin: This was carried out according to the modification of the method of Schlumpf et al (Schlumpf, M *et al*, 1974). For fluorimetric assay of the amine, reading of fluorescence intensity has been recorded using schimadzu fluorescence spectrophotometer (RF 500).

Statistical analysis

The statistical analysis was done using the appropriate methods (Mean and standard deviation SD was done using student table (t.table). The level of significance was set as P.value.

Results

The clinical data of patients and control are summarized in table(l) There is a significant increase in the mean values of blood pressure (systolic & diastolic) in groups of FSGS and APSGN in comparison with the control group ($P<0.05$).

As regards the duration of illness, there is no significant difference between MCNS group and FSGS group ($P>0.05$).

Table (2) shows the laboratory data of patients and controls. Comparison between the control group and the three groups of patients indicates a significant decrease in hemoglobin (Hb) in APSGN group ($P<0.05$), and a significant increase of BUN & S. creatinine ($P<0.05$), a significant decrease in serum albumin in both MCNS and FSGS group ($P<0.05$), and a significant increase in 24 hours urinary protein in MCNS, FSGS and APSGN group ($P<0.05$). Table (3) shows plasma histamine and serotonin in patients and controls.

Comparison between the controls and group of patients demonstrates a significant increase in plasma histamine in APSGN group (P<0.05). And also a significant increase in plasma serotonin in all group of patients MCNS, FSGS and APSGN (P<0.05).

Table(1): Clinical data of patients and controls.

Group	Age (ys)	P	Weigt (kg)	P	Blood.preasure (MM Hg) (Systolic)	P	(Diastolic)	P	Duration of the disease(yr.)	P
Control	7.66±3.6	-	23.8±7.6	-	98.3±10.9	-	65.0±4.3	-		-
MCNS	7.1±3.6	-	22.3±6.2	-	101.7±11.1	-	65.7±10.0	-	2.6±1.7	-
FSGS	7.7±2.8	-	18.8±3.6	+	112.5±16.2	+	73.5±10.1	+	2.4±1.2	-
APSGN	7.3±2.4	-	21.8±4.2	-	118.0±17.1	+	77.0±11.8	+		-

P value P<0.05 (+) is Significant.
P value P>0.05 (-) is Non significant.

Table (2): Laboratory data of patients and controls.

Group	Hb (gm/dL)	P	BUN (mg / dL)	P	S.Creatinine (mg /dL)	P	S.Albumin (gm /dL)	P	Urinary Protein (gm/24hrs)	P
Controls	12.3±0.5	-	14.3±1.0	-	0.69±0.02	-	4.09±0.38	-	0.07±0.009	-
MCNS	12.2±0.3	-	14.9±1.2	-	0.79±0.11	-	2.12±0.28	+	2.63±0.28	+
FSGS	12.4±0.3	-	15.5±1.8	-	0.88±0.13	-	1.83±0.19	+	2.4±0.31	+
APSGN	10.8±0.5	+	20.5±6.1	+	1.04±0.36	+	3.88±0.34	-	0.28±0.04	+

P value P<0.05 (+) is Significant.
P value P>0.05 (-) is Non significant.

Table(3):Plasma histamine and serotonin in patients and controls

Group	P.Histamine (ug/mL)	P	P.Serotonin (ug/mL)	P
Controls	32.3±4.9	-	10.9±4.2	-
MCNS	32.8±7.4	-	31.1±18.2	+
FSGS	38.5±7.4	-	56.5±21.5	+
APSGN	48.9±7.4	+	41.3±12.5	+

P value P<0.05 (+) is Significant.
P value P>0.05 (-) is Non significant.

Discussion

The idiopathic nephrotic syndrome and acute poststreptococcal glomerulonephritis are the most common renal disorders in children (Sabayti *et al*. ,1990). The term "idiopathic nephrotic syndrome" includes at least two subgroups of glomerulonephritis, namely minimal change nephrotic syndrome (MCNS) and focal segmental glomerulosclerosis (FSGS) a which probably represent different evalutionary

stages of the same disease in children (Ponticellic and Passerini 1991).

The data clearly show a substantial increase in histamine level in patients with APSGN. The increase plasma histamine in APSGN is similar to that previously reported in adults (Wetterquist , 1978.and Stokenhuber *et al*. ,1981, Kasahara *et al.*, 2001). They attributed this increase due to some degree of renal impairment, because histamine, a relatively small hydrophilic molecule is normally excreted in urine. There is no data in the literature about plasma histamine level and APSGN in children. Our results can be explained by the occurance of APSGN as acute immunological inflammatory renal disease with increase histanine released from inflammed renal tissues, and also by the impairement of renal function in APSGN and hence the slow renal excretion of intrinsic histamine from the circulation, this impairment was clear in our APSGN group. As regards the non significant differences in plasma histamine between MCNS and FSGS group and control group, this is supported in adults by (Barradas *et al*., 1991), but (Gill *et al*.,1991.and Lang , Towers, 2001.and Masaskiene, 2003), reported increase plasma histamine in patients with nephritic syndrome in adults. There is no data in the literature concerning the relation between plasma histamine and nephrotic syndrome in children. The clinical implications of these observation, though not obvious are potentially interest as increase histamine concentration may participate in the induction of glomerular damage through increase glomerular capillary permeability and the leakage or deposition of macromolecules such as immuno- globulins and complement. Also our results obviously show increase in plasma serotonin in all our patients (MCNS, FSGS, and APSGN), this increase is similar to that previously supported in adults (Aberg *et al*.,1990 , Malyszko *et al*., 1996. and Ceniz *et al*.,2005). they attributed this to the uptake and its release of serotonin from platelets which were markedly diminished in patients with nephrotic syndrome, and the slow renal excretion due to renal impairment in cases of APSGN. Also, there is no data in the literature clears the relation between plasma serotonin and MCNS, FSGS and APSGN in children. The possible mechanism underlying the increase in plasma serotonin in children with MCNS, FSGS and APSGN recquire further investigations.

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مستوي الهيستامين و السيروتينين في الأطفال المصابين بمرض نوفروتك و إلتهابات الكلي

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تتعرض الدراسة لقياس نسبة الهستامين و السيروتونين في الدم في عدد 40 طفل يعانون من أمراض بالكلي و قد وجد تغيرات في المرضي الذين يعانون من مرض النفروتيك و إلتهاب حويصلات الكلي المتجزء. و ما بعد إلتهاب حرثومة الستريتوكوكس لحويصلات الكلى حيث تزيد نسبة الهستامين في الدم في الأمراض الثلاثة و خاصة المجموعة الثالثة و كذلك الحال بالنسبة للسيروتونين و الزيادة الكبيرة في المجموعة الثالثة و ذلك للإلتهاب و نقص إدرار الكلي.