MEDICAL CHANNEL

Original Article

THE COMPARISON OF THE BODY AND RENAL WEIGHT IN LITHIUM CARBONATE AND L-ARGININE TREATED ALBINO RATS

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ABSTRACT

Objective: To make comparison of the weight in grams (mean body weight, absolute renal weight and relative renal weight) of the albino rats after treatment with Lithium carbonate and L-Arginine.
Design: A prospective experimental study.
Place: Department of Anatomy, Basic Medical Sciences Institute, Jinnah Post Graduate Medical Centre Karachi
Duration: July 2007 to November 2007
Methodology: Forty five adult albino rats of either sex were taken and divided into three groups as A, B and C which were further subdivided into three subgroups according to the period of treatment they received i.e. two, four and six weeks respectively. Animals were weighed before the commencement of study. Group 'A' animals served as control and Group 'B' animals received lithium carbonate (Neurolith, Adamjee Pharma) in a dose of 20 mg/kg/day with feed. Group 'C' animals received lithium carbonate 20 mg/kg/day with feed and L-Arginine (Arginine, General nutrition corporation, Pittsburg USA) 300 mg/kg/day with feed. At the end of period of treatment animals were again weighed and then sacrificed. The kidneys were removed and their weights were recorded.
Results: Comparison showed an insignificant ($P>0.05$), significant ($P<0.05$) and highly significant increase ($P<0.001$) in body weights in subgroups, A1, A2 and A3. The significant ($P<0.05$), moderately significance ($P<0.01$) and highly significant decrease ($P<0.001$) in body weight were noted in subgroups B1, B2and B3 when they were compared with themselves and highly significant ($P<0.001$) results were obtained when they were compared to control. Subgroups C1, C2 and C3 showed insignificant ($P>0.05$), significant ($P<0.05$), moderately significance ($P<0.01$) increase in body weights when compared with themselves and insignificant results were obtained when compared to control. Absolute kidney weights showed significant increase ($P<0.05$) in subgroup B1. Moderately significant ($P<0.05$), and highly significant decrease ($P<0.001$), results were found in subgroup B2 and B3. Relative kidney weights were found increased in lithium treated subgroups.
Conclusion: The lithium carbonate treated rats show significant ($P<0.05$) weight changes. Insignificant ($P>0.05$) results are obtained with concomitant administration of L-Arginine with Lithium carbonate.

Key Words: Lithium carbonate, comparison, L-Arginine.

INTRODUCTION

Lithium is in group one of periodic table among the alkali metals and is the lightest solid element. It is from Greek word Lithos; stone, with symbol 'Li' and atomic number 3 [(1)]. Lithium salts are also useful in treatment of Bipolar and unipolar depression [(2)]. Lithium carbonate is often referred to as an antimanic drug but in many parts of world it is considered as a mood stabilizinzing agent because of its role in preventing mood swings with Bipolar affective (manic depressive) disorder[(3)].

Bipolar affective disorder symptoms include depression and feeling of hopelessness during the depression phase of the condition, other depressive symptoms include thoughts of suicide, alterations in sleep pattern and loss of interest in activities that were once the source of pleasure. What differentiate Bipolar disorder from major depression is the occurrence manic episodes often described as the emotional 'highs' between the episodes of depression [4].

In 1970 the food and drug administration of United States of America F.D.A. approved the lithium as a treatment for mania. Four years later the F.D.A also approved the use of lithium as preventive or prophylactic treatment for manic depressive illness [5]. Lithium carbonate used for long term treatment of manic depressive illness and has been reported to lead progressive renal impairment in rat and humans [6]. Early signs of renal insuffiency include glucose urea, polyuria and reduced urinary concentrating ability. Subsequent clinical deterioration is evidence by electrolyte disturbances, reduced creatinine clearance, oligurea and dehydration [7]. In long term use, therapeutic concentration of lithium has been thought to cause histological and functional changes in kidney. The significance of such changes is not clear but is of sufficient concern to discourage long term use of lithium unless it is definitely indicated [1].

L-Arginine is classified as a semi essential or conditionally essential aminoacid depending on the developmental stage and health status of individual. Infants are unable to effectively synthesize making it nutritionally essential for infants. Adults however are able to synthesize it in urea cycle. Arginine was isolated from lupin seedling extract in 1886 by the Swiss Ernst Schulze [8].Arginine is considered semi essential aminoacid because although it is normally synthesized in sufficient amounts by the body, supplementation is some times required (for example due to in born errors of urea synthesis protein malnutrition, excess ammonia production excess lysine intake, burns, infection, peritoneal dialysis, rapid growth or sepsis [9]. L-Arginine can ameliorate kidney dysfunction induced by Cyclosporin via a mechanism which involves the production of nitric oxide. In addition L-Arginine may therefore be a beneficial for cyclosporin nephrotoxicity and can be used to improve the therapeutic index of cyclosporin [10].

MATERIAL AND METHODS

The present study was conducted in the Department of Anatomy Basic Medical sciences institute Jinnah postgraduate medical centre Karachi. 45 adult albino rats of either sex between 90-120 days were taken for the study, and were observed for any abnormality for one week before the commencement of this study. The animals were weight and were divided into three groups A, B, and C and each group was further subdivided into three subgroups AI, A2 and A3 according to period of treatment they received, i.e. 2, 4 and 6 weeks respectively. Each subgroup comprised of 5 animals. Group 'A' animals served as control and Group 'B' animals received lithium carbonate (Neurolith, Adamjee Pharma) at the dose of 20 mg/kg/day with feed and Group 'C' received Lithium carbonate 20mg/kg/day and L-Arginine (Arginine General Nutrition Corporation, Pittsburg USA) 300mg /kg per day with feed.

The animals were weighed before anaesthetizing them with ether in a glass chamber and were sacrificed, and fixed on dissecting board after the end of their respective periods of treatment. Abdomen was opened by midline incision. Kidneys were excised and weighed (absolute weight of kidney) on triple beam balance. The relative weight of kidney was obtained by multiplying the weight of kidney in grams with 100 and then dividing it into final body weight of animal in grams.

RESULTS

GROUP A

The mean value of initial body weights (G) were 223.200±0.860, 226.000±0.707 and 232.000±1.581 respectively and the mean values of final body weights (G) were 231.400±0.927, 241.800±1.031 and 255.600±0.927 respectfully (Comparision is shown in table 1). The mean values of absolute kidney weights (G) were 0.602±0.836, 0.641±0.076 and 0.677±2.135 respectively (Comparision is shown in table 3). The mean values of relative kidney weights (G) were 0.259±0.734, 0.264±1.318 and 0.261±3.443 respectively (Comparision is shown in table 4).

GROUP B

The mean values of initial body weights (G) were 221.830±0.718, 223.000±0.582 and 235.000±0.447 respectfully and the mean values of final body weights (G) were 215.000±1.139, 204.800±1.318 and 194.000±1.580 respectively (Comparision is shown in table 1 and table 2). The mean values of absolute kidney weights (G) were 0.625±3.605, 0.603±2.230 and 0.580±2.826 respectively (Comparision is shown in table 3).The mean values of relative kidney weights (G) were 0.290±1.341, 0.294±1.757 and 0.299±2.271 respectively (Comparision is shown in table 4).

GROUP C

The mean values of initial body weights (G) were 224.200±0.373, 228.000±0.632 and 230.000±1.139 respectfully and the mean values of final body weights (G) were 231.40±0.927, 240.000±1.002 and 257.000±1.736 respectively (Comparision is shown in table 1, table 2). The mean values of absolute kidney weights (G) were 0.599±0.538, 0.637±0.677 and 0.674±2.153 respectively (Comparision is shown in table 3).The mean values of relative kidney weights (G) were 0.258±0.812, 0.266±1.744 and 0.261±1.516 respectively (Comparision is shown in table 4).

DISCUSSION

Lithium is now the drug of choice for treating Bipolar affective disorder, it is also used to treat alcoholism, schizoaffective disorders and clusture headaches. Thus lithium is an indispensable pharmaceutical component of modern psychiatric therapy [11].

Bipolar affective disorder (manic depression) is a frequently diagnosed serious psychiatric disorder. Patients with cyclic attacks of mania, have many symptoms of paranoid schizophrenia (grandiosity, bellicosity, paranoid thoughts and over activity). The gratifying response to lithium therapy of patients with Bipolar disorder has made such diagnostic distinction important [3]. Long term use in therapeutic concentrations of lithium have been thought to cause histological and functional changes in kidney. The significance of such changes is not clear but it is of sufficient concern to discourage long term use of lithium unless it is definitely indicated [1].

The L- Arginine/nitric oxide pathway seems to have a slightly protective effect on the kidney after renal ischaemic injury in rats (12).Therefore this study was planned to make the comparison of weights (body weight ,absolute kidney weight and relative kidney weight), and observe changes in weight when L-Arginine and lithium carbonate are administered simultaneously. The animals in group A were used as control and they appeared to have put on

TABLE -1

COMPARISON OF THE DIFFERENCE IN THE MEAN BODY WEIGHT WITHIN SAME SUBGROUPS OF THE ALBINO RATS.

Statistical Comparison	P-value
Initial & Final Weights at 2nd week in Group-A1	P>0.05*
Initial & Final Weights at 4th week in Group-A2	P<0.05**
Initial & Final Weights at 6th week in Group-A3	P<0.001****
Initial & Final Weights at 2nd week in Group-B1	P<0.05**
Initial & Final Weights at 4th week in Group-B2	P<0.01***
Initial & Final Weights at 6th week in Group-B3	P<0.001****
Initial & Final Weights at 2nd week in Group-C1	P>0.05*
Initial & Final Weights at 4th week in Group-C2	P<0.05**
Initial & Final Weights at 6th week in Group-C3	P<0.01***

Key: ***Insignificant** ****Significant** ***** Moderately significant** ****** highly significant**

TABLE -2

COMPARISON OF THE DIFFERENCE IN THE MEAN BODY WEIGHT BETWEEN DIFFERENT SUBGROUPS OF THE ALBINO RATS

Groups	P-value
A1 vs B1	P<0.01****
A1 vs C1	P>0.05*
C1 vs B1	P<0.01***
A2 vs B2	P<0.001****
A2 vs C2	P>0.05*
C2 vs B2	P<0.001****
A3 vs B3	P<0.001****
A3 vs C3	P>0.05*
C3 vs B3	P<0.001****

Key:
Insignificant** ** Moderately significant**
****Significant** ****** Highly significant**

TABLE -3

COMPARISON OF THE MEAN AND THE ABSOLUTE KIDNEY WEIGHT BETWEEN DIFFERENT SUBGROUPS OF THE ALBINO RATS

Statistical Comparison	P-value
A1 vs B1	P<0.05**
A1 vs C1	P>0.05*
C1 vs B1	P<0.05**
A2 vs B2	P<0.001****
A2 vs C2	P>0.05*
C2 vs B2	P<0.01***
A3 vs B3	P<0.001****
A3 vs C3	P>0.05*
C3 vs B3	P<0.001****

Key:
Insignificant** ** Moderately significant**
****Significant** ****** highly significant**

weight, this may be due to free access to balanced laboratory diet and water. The animals of group B after one week showed decreased interest in eating, this could be due to loss of appetite leading to decrease in weight. This is in agreement with Allagui et al 2005 [13]). They worked on renal, thyroid and sexual functions in male and female rats and observed a dose dependent loss of appetite. Animals of group C put on weight which could be due to increase in appetite caused by L-Arginine and could be also due to reduction of renal damage to minimum. This was in agreement with Mahmoud et al 2002 [10]. They noted increase in appetite on their work on protective role of L-Arginine against nephrotoxicity induced by cyclosporin.

The absolute kidney weights in group B showed an initial increase in subgroup B1 as compared to control which could be due to accumulation of drug and its metabolites and may also be due to accumulation of inflammatory products in kidney. This could be due to adaptive mechanism operating to detoxify the substance [16].

The absolute kidney weights were decreased in subgroup B2, and B3. This could be due to damage caused by the drug which is in agreement with Affone et al 2002 [14]. According to them toxic metals can reduce kidney weight significantly.

The relative kidney weights were found increased in all groups of lithium treated animals. This is due to increase in absolute kidney weight initially , later the subgroup B2 and B3 showed an increase in relative kidney weights in spite of decrease in absolute weight

TABLE – 4

COMPARION OF THE MEAN RELATIVE KIDNEY WEIGHT BETWEEN DIFFERENT SUBGROUPS OF THE ALBINO RATS

Statistical Comparison	P-value
A1 vs B1	P<0.001****
A1 vs C1	P>0.05*
C1 vs B1	P<0.001****
A2 vs B2	P<0.001****
A2 vs C2	P>0.05*
C2 vs B2	P<0.01***
A3 vs B3	P<0.001****
A3 vs C3	P>0.05*
C3 vs B3	P<0.001****

Key:
***Insignificant** *** Moderately significant**
****Significant** **** Highly significant**

on account of a decrease in body weight. This is in agreement with the study of Hirsch 1973(15) who stated that increase in kidney weight; body weight ratio was partly due to decline in body weight but the associated increase in kidney weight also contributed to the kidney weight, body weight ratio.
The absolute and relative weights of group C were found to have no difference between them and control group A [(15).]

CONCLUSION

The present study suggests that insignificant (P>0.05) changes in weights are obtained when L-Arginine and lithium carbonate are administered simultaneously.

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