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Effect of herbal combination on biochemical and behavioral responses in rats

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Abstract: Use of herbal drugs has been exponentially increased all over the world due to their minimum side effects in comparison with synthetic drugs used in allopathetic medicine. Sharbat-e-Ahmed Shah (SAS) is herbal drug prescribed for the treatment of Schizophrenic patients as major tranquilizer in Hikmat since long time due to its minimum side effects as compared to other neuroleptic drugs. SAS is made up of different combination of herbs. The present study was designed to establish biochemical and behavioral effects of this herbal preparation. Administration of SAS for six weeks decreased the body weight, food intake as well as plasma cholesterol levels where as plasma glucose levels are remained comparable between the two groups.

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INTRODUCTION

Schizophrenia is a severely debilitating neuropsychiatric disorder characterized by disturbance of thoughts, auditory hallucinations and multiple delusions[1]. It is generally considered to be a syndrome, which produces a diverse disturbance in cognition, reality testing, mood, interpersonal relations, social and work function. It is chronic severe mental illness affecting large number of population[2,3].

The first line treatment for schizophrenia is usually the chronic use of antipsychotic or neuroleptic medication. These neuroleptics not only produce extrapyramidal symptoms[4] but also produce other side effects including, weight gain[5,6], hyper cholesterolemia[7, 8], hyperglycemia and the onset of diabetes mellitus[9-12]. One promising way for the treatment of schizophrenia without these side effects is the use of herbal drugs.

The use of herbal drugs has been exponentially increased with the passage of time by majority of people, both in developing and developed countries because of their natural origin and fewer side effects[13].

Sharbat-e-Ahmed Shah (SAS) is a herbal drug prescribed for the schizophrenic patients in Hikmat since long time due to its minimum side effects as compared to neuroleptic drugs. SAS is made up of different combination of herbs. The current study deals with biochemical and behavioral effects of SAS in rats.

MATERIALS AND METHODS

Animals and treatment

Locally bred Albino Wistar rats weighing 170-220g purchased from HEJ Research Institute of Chemistry, University of Karachi were used for the experiments. Rats were randomly assigned as control and test. They were housed individually in plastic cages with sawdust covered floor in a quiet room with free access to cubes of standard rodent diet and water for 5 days before starting the experiment. Food intake and body weights were monitored daily. Growth rates were calculated as the percent changes in body weight compared to previous body weight.

Drug dose

A dose of 0.3ml/day of SAS was given for 6 weeks. Equal volume of water was given to control rats for the same period of time.

Biochemical estimation

After 6 weeks of treatment the rats were decapitated to collect plasma. Glucose levels in plasma were estimated by O' Toludine method[14]. Plasma Cholesterol levels were estimated by Zlatkis method[15].

Statistical analysis

Data were analyzed by Student's two tailed "t" test. P values<0.05 were considered significant.

RESULTS

Figure 1 shows the effect of SAS on cumulative food intake and growth rate. Data analyzed by student's t-test revealed significant decrease (*p<0.05) in both food intake and growth rate following repeated administration of SAS. Figure 2 and 3 show the effects of SAS on plasma glucose and cholesterol levels respectively. Data analyzed by student's t-test revealed non-significant effect on plasma glucose level where as plasma cholesterol level significantly decreased (*p<0.05) following repeated administration of SAS.

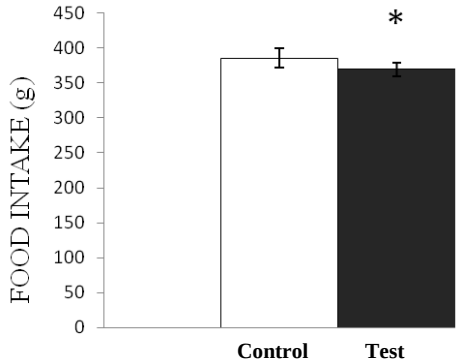

Figure 1: Effects of SAS on cumulative food intake and growth rate. Values are mean±SD (n=6) significant difference by Student *t*-test *p<0.05 with respect to controls.

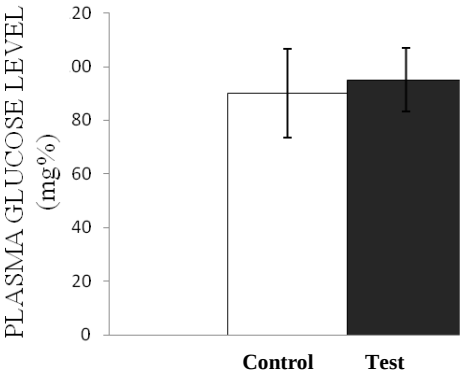

Figure 2: Effects of SAS on plasma glucose levels. Values are mean±SD (n=6) significant difference by Student *t*-test *p<0.05 with respect to controls.

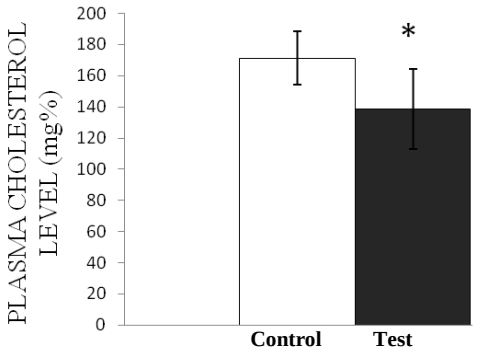

Figure 3: Effects of SAS on plasma cholesterol levels. Values are mean±SD (n=6) significant difference by Student *t*-test *p<0.05 with respect to controls.

DISCUSSION

The primary findings in the present study are that administration of SAS for six weeks did not increase the plasma glucose level and significantly decreased food intake, growth rate and plasma cholesterol level.

Obesity and being overweight are associated with reduced quality of life, greater morbidity (cardiovascular diseases, diabetes mellitus, osteoarthritis and some types of cancer) and mortality[16]. Most of antipsychotic medications have been associated with weight gain, with a wide range of average gain for different medications. Typical and atypical antipsychotic medications occupy both ends of spectrum, with Molindone, Aripiprazole, Ziprasidone, Fluphenazine and haloperidol causing less weight gain, and chlorpromazine, thioridazine, olanzapine and Clozapine causing the most weight gain[5,6].

Neuroleptic induced weight gain has been suggested to contribute patient noncompliance with treatment and may adversely affect clinical outcome[17]. After six weeks SAS taking animals did not increase the body weight. SAS significantly reduces the growth rate and food intake (Figure 1). Most of the neuroleptic drugs increase glucose level for example Clozapine and Olanzapine as being associated with highest risk. Quetine and Risperidone seem to confer lower risk, while Ziprasidone and Aripiperazole apparently do not cause hyperglycemia[18]. Moreover Hyperglycemia, new onset diabetes, and diabetic ketoacidosis occur at increased rates with atypical antipsychotic medications, even in absence of weight gain[19, 20]. The mechanism of action for hyperglycemia is unclear but may involve insulin resistance[18, 20]. In the present study plasma glucose levels were not increased by SAS after six weeks of treatment (Figure 2). This may be suggested that SAS did not cause insulin resistance.

Atypical antipsychotic medications cause increase in triglycerides and cholesterol level[7,8], which may be related to weight change[18]. Clozapine and Olanzapine confer the greatest risk, while Quetiapine and Risperidone are intermediate, and Ziprasidone and Aripiperadone have not been reported to cause an increased in serum lipids[18].

A number of studies reported that Chlorpromazine stimulate cholesterol synthesis by HMG Co-A reductase enzyme via inhibition of sphinomylinase also it is reported that chlorpromazine inhibited LDL and non-LDL dependent cholesterol esterification, thereby increasing cholesterol[21]. SAS unlike atypical antipsychotic drugs reduced the plasma cholesterol level (Figure 3).

SAS is the combination of different herbs used to treat schizophrenia in Hikmat. The side effects, including increase body weight, increase plasma glucose and cholesterol level, previously observed following the administration of neuroleptic were not

seen after 6 weeks administration of SAS. It can be suggested that the herbs present in this preparation may act synergistically not only to treat schizophrenia but also prevent the patient from metabolic dysregulation. *Cuscuta reflexa*, constituent of SAS, has been reported as having anti-hyperglycemic effect[22]. This promising herbal combination should be further explored for the treatment of schizophrenia. Each herb present in this herbal preparation should be investigated for the potential of anti-schizophrenic and metabolic regulatory effects, their biological active components and the mechanism of their action should also be examined.

CONCLUSION

In conclusion it is suggested that preparation of different herbal combination, SAS is a better alternative of neuroleptic drugs because the side effects like weight gain, increased cholesterol and glucose levels observed following neuroleptic treatment are not observed following the repeated administration of SAS.

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