Comparative Safe-Reduction of Body Weight in Rats by Using Different Doses of Formalin

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Abstract---Body weight gain and obesity have a significant influence on quality of life since they are related with comorbidities and psychological issues. The latter is far more significant than most people think. Formoline L112, a formulation containing polyglucosamine, a chitosan derivative, is one of the most often used products in Europe to help people lose weight. Aim of the study: to evaluate dose-related body weight reduction in rats with possible measuring of drug’s safety. Materials and method: 30 rat were classified into 3 groups; group 1 (No.=10) used as control, group 2 (No.=10) given 1 tablet of formoline, and group 3 (No.=10) was given 2 tablet each 12 hours/day. The body weight of each rat was taken before and 30 days after treatment. Blood urea and serum creatinine was assessed before and after using the drug to exclude renal injury. Results: there was significant reduction (at P<0.05) in body weight by using either single or double doses of formoline as compared to control group with no statistical significance of using single dose as compared to double dose.

Keywords---blood urea, formalin, obesity, safe-reduction, serum creatinine.

Introduction

Obesity is a word used to describe a wide range of weight for a person of a certain height that is connected with negative health consequences (Blüher 2020). Adult definitions of overweight and obesity are based on set cutoff criteria that are directly tied to a person’s body mass index. This definition requires that a high degree of body weight be with a large amount of fatty tissue (Weihrauch-Blüher...
Despite the fact that BMI goes parallel to body fat, there is also a correlation with gender and age in children more than that in adults. Therefore, determining whether a child or teenager (2-9 yrs. old ages 2 to 19 years) is overweight or obese is dependent on a comparison of his / her height and weight (Wang, Beydoun et al. 2020). The percentiles used to classify children as overweight or obese are predetermined and based on data collected from 1963 to 1980 (or 1963 to 1994 for children ages 2 to 6 years).

Excessive body weight was shown to be increased in USA for ten’sss of years, but it has leveled off in recent years. The best screening metric used to assess presence or absence of obesity is a BMI (Caussy, Pattou et al. 2020). The BMI is a proxy measure for body fat because it correlates positively with body fat, especially when BMI value is abnormally high. In addition, it is feasible and simple tool, and is affordable and simple to be implemented in practice. One of its drawbacks is that BMI cannot discriminate between contribution of fat or muscle mass to the total body weight both in case of children and adults (Heslehurst, Vieira et al. 2019).

Overweight becomes an increasingly growing public concern in USA, and it is linked to a variety of negative health outcomes in children and adults, such as increase chance of development of cardiovascular disorders, malignancy, psychological disturbances, asthma, and diabetes mellitus. Some study has established a link between obesity and early puberty and menarche in girls, whereas other research has revealed disparities in puberty timing even after adjusting for BMI in the population (Geserick, Vogel et al. 2018). As a result, it’s unclear how much the obesity pandemic is contributing to early puberty. In general, overweight occurs when food intake exceeds physical activity (calory gain exceeds calory expenditure). Childhood obesity, similarly, develops when calorie gain overweighs consumption such as in case of decreased physical activity (Polyzos and Margioris 2018).

Researchers are also investigating the effect of environmental chemical exposures on the development of obesity in children. Such chemical materials are suggested to affect the metabolism (catabolism/anabolism) balance in human body causing increased fatty mass are termed “obesogens”. Adults have also been linked to diabetes after being exposed to specific toxins, according to studies. According to some researches, diabetes (Type 2) in adults is associated with exposure to certain toxins that cause disrupted function of insulin to reduce blood glucose level in response to a meal, and it is linked to rising obesity rates in the United States (Russo and Lumeng 2018).

As an intestinally active lipid adsorber (Schönbach 2019), Formoline L112 has a glucosamine-containing fiber, a β-1,4 polymer consisting of D glucosamine and N-acetyl-D-glucosamine (Otto, Stoll et al. 2008). The polymer is an indigestible fiber or roughage that is expelled naturally after passing through the digestive system. The pill dissolves in the acidic environment of the stomach after orally eating the active component with 250 ml of a low-calorie drink (Stoll, Bitterlich et al.). Protonation of the basic amino groups forms positively charged sections of the molecule, resulting in a solution in the stomach. β-1,4-poly-D-glucosamine is then deprotonated in the somewhat alkaline intestinal environment. The
hydrophilic profile of the compound is reduced as a result of the loss of charge; the polymer becomes almost insoluble and its viscosity rises (Sanhueza, Moreno et al. 2018).

**Materials and Method**

This study was conducted for 6 months in 2021 in animal house with optimal conditions and regular watch up. A 30 Sprague-Dawley rats were used as an experimental model, aged between 11-14 months old. The animals' welfare was ensured in conformity with the European Communities' general rules governing the use of animals in studies. These rats ranged between 320-387 gm body weight and were divided into 3 equal groups; first group was given a placebo, second group was given a single dose/day of formoline tablets (The main ingredient of the Formoline is the polyglucosamine fiber), while the 3rd group received 2 doses at 12 hour intervals. The study was takes 30 days.

The animals were given 13 mg of ketamine per kilogram of body weight. Blood samples were taken for all rat (a cannula was inserted into the vena jugularis while the animals were anesthetized) before and after using the drug to assess renal function (blood urea and serum creatinine), and body weight was recorded before and after this period. Statistical analysis was done by using SPSS v.22 program by evaluating the significance at P< 0.05 using ANOVA (Kruskal-Wallis One Way Analysis of Variance on Ranks) and paired t-test to compare the mean±SD for the results between these groups.

**Results**

This study showed that there was significant reduction of body weight after taking single or double dose of formoline for 1 month as compared to control group, however, no statistical significance in difference of Ranks between using single and double dose of formoline as shown in table (1).

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Diff of Ranks</th>
<th>Q</th>
<th>P&lt;0.05</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single dose before vs single dose after</td>
<td>315</td>
<td>5.704</td>
<td>Yes</td>
</tr>
<tr>
<td>Double dose before vs double dose after</td>
<td>342</td>
<td>5.541</td>
<td>yes</td>
</tr>
<tr>
<td>Control vs double dose after</td>
<td>298</td>
<td>5.396</td>
<td>Yes</td>
</tr>
<tr>
<td>Control vs single dose after</td>
<td>289.5</td>
<td>5.242</td>
<td>Yes</td>
</tr>
<tr>
<td>Single dose after vs double dose after</td>
<td>8.5</td>
<td>0.154</td>
<td>No</td>
</tr>
</tbody>
</table>

Another finding that found is the high margin of safety of formoline use on renal function even when it was used at higher doses (the double dose) manifested as preserved fixed levels of urea and creatinine as shown in table (2).
Table 2
Show levels of urea and creatinine when formoline used in different doses. The data represented as mean±SD

<table>
<thead>
<tr>
<th>Test</th>
<th>Before</th>
<th>After</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood urea by using single dose of formoline</td>
<td>37.1±3.742</td>
<td>36.6±5.354</td>
<td>0.758</td>
</tr>
<tr>
<td>Blood urea by using double dose of formoline</td>
<td>34.5±2.665</td>
<td>35.33±2.160</td>
<td>0.462</td>
</tr>
<tr>
<td>Serum creatinine by using single dose of formoline</td>
<td>0.35±0.138</td>
<td>0.333±0.103</td>
<td>0.822</td>
</tr>
<tr>
<td>Serum creatinine by using single dose of formoline</td>
<td>0.342±0.111</td>
<td>0.35±0.0974</td>
<td>0.479</td>
</tr>
</tbody>
</table>

Discussion

A nearly four-fold rise in worldwide prevalence of obesity has been noticed since 1980 and is now an important cause of death, having a significant impact on death and morbidity rates, cost effectiveness of health system, and type of living conditions (Cnubben, Tel et al. 2016). The effectiveness of polyglucosamines as therapeutic age-lowering agents has being investigated recently. They may replace the current therapies of obesity because of their availability, cost effectiveness and lower level of side effects (Perna, Basharat et al. 2020). Increased free fatty acid concentrations appear to play a major role in the etiology of insulin resistance, according to a growing body of research. A recent study investigated the effect of free fatty acids (FFA) on insulin sensitivity. Results of the study revealed that increased level of FFA is associated with insulin resistance and development of inflammatory conditions insulin-targeted tissues such as skeletal muscle, liver, and endothelial cells.

Thus FFA acts as a vital risk factor in the occurrence of type 2 diabetes, hypertension, dyslipidemia, coagulation problems, and atherosclerotic vascular disease. Meanwhile, decreased level of FFA potentiates tissue sensitivity to insulin both in obese individuals and in patients with type 2 diabetes melitus (T2DM) (Barrea, Altieri et al. 2019). Using of formoline was associated with beneficial effect with potential FFA-reducing effect as demonstrated in a study on rats (Lütjohann, Marinova et al. 2018). The impact of formoline (Chitosan) on blood glucose in diabetic patients is larger than that of overweight/obese participants, but it has no effect on subjects with dyslipidemia, according to a stratified analysis of the research populations. This finding might be explained by the fact that people with dyslipidemia were not always diabetic.

The normal physiological control of blood glucose and insulin may be unaffected by chitosan use (He, Wang et al. 2020). Previous research on formoline (Chitosan anti-obesity)'s properties focused on its impact on leptin resistance and fat production (Liu, Chen et al. 2020). Increased thermogenesis has been shown to be useful in the fight against obesity in recent studies (Naveed, Phil et al. 2019). In high-fat diet caused obesity and diabetic animal models, low-molecular weight formoline has been proven to be a more potent anti-obese and anti-diabetic drug (Chiu, Yen et al. 2020). It dramatically lowered blood levels of CHO and LDL-C (Jo, Ha et al. 2013). With the administration of formoline, hepatic lipid deposition was decreased, and liver cell necrosis was improved, suggesting that these medications lower lipid levels to some extent (Saleh and El-Shorbagy 2020).
References


