Dose Effects of D-Ribose on Glucose and Purine Metabolites

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Citation

Abstract

Background: D-ribose enhances the recovery of cellular energy levels. Increases in uric and lactate levels with lower blood glucose values have been reported post D-ribose consumption.
Aims of the Study: A dose response evaluation of these effects has been lacking; this investigation studied these effects in varying doses of D-ribose.
Materials and Methods: Ten healthy adult subjects ingested 0, 2, 5, 10 grams of D-ribose. Glucose, lactate, uric acid and insulin levels were assessed at 0, 15, 30, 45, 60, and 120 minutes post each dose.
Results: Serum glucose levels were significantly lower at 45 and 60 minutes post ingestion of 10 grams of D-ribose, unlike 2 and 5 grams. This hypoglycemia was not associated with a sustained increase in insulin values. Significant differences in lactate levels were found between 0 and 120 minutes post ingestion of D-ribose at all doses. Uric acid levels were higher at the 5 and 10 gram consumption, not observed in 2 grams.
Conclusions: Quantitative dosing of D-ribose is well tolerated without significant persistent abnormalities in glucose and purine metabolites.

Work was performed at the Human Performance Laboratory, St. Cloud State University, St. Cloud, MN, USA

INTRODUCTION

Interest in nutritional supplements continues to soar. Adenosine triphosphate (ATP) levels are necessary to maintain cellular integrity and function. Myocardial ischemia produces a decline in ATP levels with impaired function.[1] Further, strenuous exercise also produces a decline in muscular ATP levels. With ATP degradation, nucleosides can be washed from the cell, limiting the regeneration of high-energy phosphates.[2]

Supplemental D-ribose (DR), a natural occurring 5-carbon carbohydrate, has shown to regenerate low ATP levels in both skeletal and cardiac muscle. Abnormal levels of glucose and purine metabolites have been reported with supplemental DR; however, a dose response evaluation of these abnormalities has been lacking in the literature; and therefore, this study investigated the effect of different doses of DR on glucose and purine metabolic products in healthy individuals.

METHODS

Study approval was obtained from the St. Cloud State University Institutional Review Board prior to securing informed written consent from each subject. Ten healthy adult male and female subjects (24-50 years of age) comprised the study population. Six subjects were between 24 and 30 years of age with the remaining four between 40-50 years of age. Each subject fasted for at least 8 hours prior to evaluation. Oral doses of DR (0, 2, 5, 10 grams dissolved in 250 ml of water) were consumed by each subject with a 24 hour washout interval between doses.

Blood sampling (10 cc) at each tested dose of DR was collected in Becton Dickinson Vacutainers (Becton Dickinson, Inc., Franklin Lakes, NJ). Duplicate analyses of glucose, insulin, uric acid and lactate levels were performed at 0, 15, 30, 45, 60 and 120 minutes following DR consumption. Glucose and lactate levels were measured using a LA, YSI 2300 Stat Glucose Lactate Analyzer (YSI Life Sciences, Yellow Springs, OH). Plasma was analyzed for insulin (INS, RIA, Medgenix Diagnostics, Brussels, Belgium) and uric acid (UA, Sigma Kit #685, Sigma-Aldrich, Inc., St. Louis, MO) levels.

STATISTICS

Glucose, insulin, lactate, and uric acid levels underwent repeat-measure analyses of variance to further compare differences overtime, between age groups, and between dose treatment levels. Tukey HSD post hoc tests were administered to differentiate means for significance, using an alpha level of significance ($p<0.05$). Analyses were performed with MINITAB 12.1 (Minitab Incorporated, PA).

RESULTS

No adverse subjective effects of DR were observed. Each tested DR dose demonstrated a fall in glucose levels, reaching a nadir at 45 minutes after ingestion with a rebound effect approaching baseline approximately two hours later. As expected, this decline in glucose levels was dependent upon the DR dose with the most noted significant decline observed in 10 grams compared to 2 grams ($p<0.05$). Lower doses of DR (2 and 5 grams) maintained blood glucose levels similar to baseline. Both age groups demonstrated similar trends. (Figure 1)

Figure 1

Figure 1: Blood Glucose Treatment Differences Over Time (n=10)
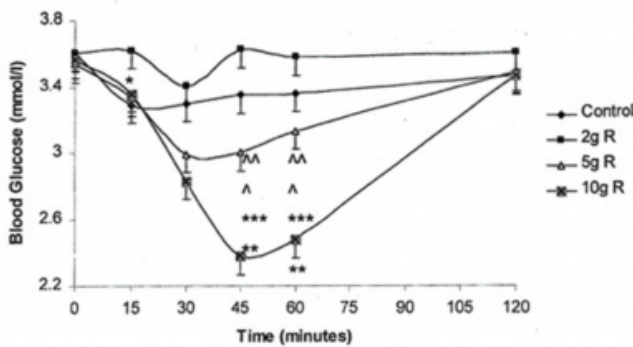
*10 g at 15-min different from 10 g at 45-min (P < 0.05).

**10g different from 0 g (P < 0.05).

***10 g different from 2 g (P < 0.05).

^10 g at 45-min and 60-min different from 10 g at 120-min (P < 0.05).

^^10 g at 45-min and 60-min different from 10 g at 0-min (P < 0.05).

No significant differences in insulin levels were noted at differing doses of DR. Insulin levels peaked at 15 minutes with a corresponding decline in serum glucose values following DR ingestion. However, the mean insulin concentrations in the 40-50 year age group (2.9 ± 0.1 uIU/ml) was statistically greater than the mean level observed in the 20-30 year age group (2.5 ± 0.1 uIU/ml) ($p<0.05$). (Figure 2)

Figure 2

Figure 2: Treatment Differences on Insulin Over Time (n=10)
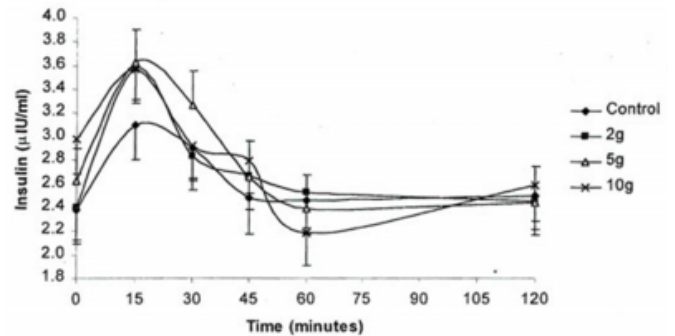
Normal uric acid levels significantly increased with varying doses of DR ($p<0.05$). Lactate levels demonstrated differences between the age groups, measured time points, and age/time measurements. The 24-30 year old subjects demonstrated elevated lactate levels at 45 minutes post consumption of 5 and 10 grams of DR; however the 40-50 year old individuals exhibited a decrease with higher doses of DR. Comparing age groups at 60 and 120 minutes revealed significantly higher lactate levels in the 24-30 age group. (Figure 3) The placebo dose (0 grams) reflected a similar decrease in lactate.

Figure 3

Figure 3: Lactic Acid Differences Between Age Groups
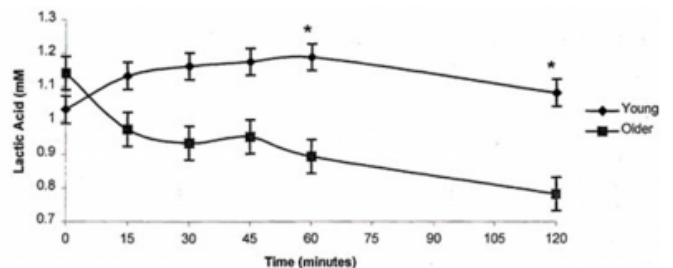
DISCUSSION

This study provided additional insight into differences in glucose and purine metabolites with varying doses of oral DR. As expected, higher doses of DR resulted in a greater decline in blood glucose levels, supporting previous reported studies.[3,4,5,6,7] Both 5 and 10 gram oral doses of DR produced a transient, asymptomatic state of hypoglycemia before rebounding to baseline values at 120 min post ingestion. This observed state of hypoglycemia is not entirely due to changes in insulin secretion. We observed an initial spike in insulin levels at 15-30 minutes post consumption without a sustained elevation. Further, we found no escalation in insulin levels with increasing doses of

DR, as reported by other researchers.[4,8] Even at our maximal dose of 10 grams of DR, we did not observe a greater level of insulin.

An initial spike in insulin could account for this drop in glucose concentrations; however, the persistence in hypoglycemia is probably multi-factorial. Many have proposed an up regulation of the enzyme, phosphoglucomutase, for the persistence of hypoglycemia with others proposing an increased rate of fatty acid synthesis, increased amino acid synthesis, greater conversion to glycogen, enzyme alterations, or an increase in peripheral utilization of glucose.[4,9]

An end product of glycolysis is lactate.[10,11] Theoretically, if the state of hypoglycemia resulted from increased glycolysis, an accompanying increase in lactate production should be present. We found no significant changes in lactate, concurring with others.[4,9,12] However, we did observe differences in lactate levels between age groups. The younger subjects demonstrated increased levels with older individuals reflecting decrease concentrations.

Contrary to other researchers, we found increased uric acid levels with DR consumption.[4,9,13] When DR binds to adenine, adenosine is produced and the catabolism of adenosine could increase uric acid levels. Therefore, excess DR could potentially produce higher adenosine concentrations, and the catabolism of adenosine could ultimately produce an elevation in measured uric acid levels.

CONCLUSIONS

We conclude that the oral tested doses of DR are well tolerated and have minimal sequelae. We found a state of hypoglycemia following DR consumption with higher doses producing a more marked transient effect without long lasting insulin level correlations. Ten grams of DR produced an increase in uric acid concentration, not appreciated at lower doses. Varying doses of DR did not influence lactate production. D-ribose appears to be safe with acceptable laboratory parameters in healthy individuals.

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