The Effects of Bovine Colostrum on the Stress-Hyperglycemia Ratio and the Triglyceride-Glucose Index in Exercise-Trained Healthy Subjects: A Double-Blind, Placebo-Controlled Clinical Study

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Abstract

Bovine colostrum (BC) is a natural substance that has been shown of benefits for exercising, and reducing the blood glucose levels in type 2 diabetes. Stress hyperglycemia is a brief rise in blood glucose levels caused by physiological stress. This placebo-controlled clinical study aimed to investigate the effects of BC on stress hyperglycemia and the triglyceride-glucose index in healthy subjects who trained in resistance exercise. This research was carried out at Al-Kut University College from April 30th to November 30th, 2022. Fifty healthy young men were randomly assigned: Group I (n = 24) received a placebo, whereas Group II (n = 26) received a 500mg single oral dosage of BC nutraceutical pill. During the treatment period, both groups of volunteers engaged in resistance exercise training. Body mass index (BMI), waist circumference (WC), stress blood glucose levels, Triglyceride glucose index (TyGI), and rate pressure product (as a hemodynamic response) were all measured at the start and end of the eight-week study. Stress blood glucose levels were considerably higher in Group II following resistance training (89.0±6.5 vs 102.1±11.5mg/dL, p<0.001), whereas stress HbA1c% did not alter (4.70±0.25 vs 4.66±0.29, p=0.608). Bovine colostrum significantly increases the SGR from 1.01±0.03 to 1.18±0.13, p<0.001. The TyGI at the stress glucose level was increased by 2.7%. We conclude that bovine colostrum significantly elevates the stress hyperglycemic ratio without inducing significant changes in the TyGI following exercise. This impact is accompanied by a stabilizing hemodynamic response.

Keywords: Bovine colostrum, Stress glucose level, Triglyceride-glucose index, Rate pressure product.

تأثير اللبأ البقري على نسبة فرط السكرالأجهادي و مؤشر الشحوم الثلاثية-الكلكوز عند الأشخاص

ال研究成果: دراسة سريرية مزدوجة - هemiديموت موسومة - مؤديتة

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الخلاصة

اللباي البقري مادة طبيعية ذات فائدة للمتمرنين الرياضيين كما يعمل على تخفيض مستويات سكر الدم عند مرضى السكري نمط 2. يعرض فرط السكر الأجهادي علي أنه ارتفاع غير متوقع في مستويات سكر الدم عند التعرض إلى اجهاد وتحديي. هذه الدراسة للنصح على أثر تناول كبسولة اللبأ البقري على فرط السكرالأجهادي و مؤشر الشحوم الثلاثية. الكلوزك ضد الأسلاك Disconnect مع ملاحظة ان تأثير لبأ البقري الصيدلانية. تشير هذه الدراسة إلى أن تناول كبسولة اللبأ البقري الصيدلانية يقلل من ارتفاع سكر الدم عند التعرض إلى اجهاد وتحديي. تكونت الشحوم الثلاثية و مؤشر الشحوم الثلاثية بشكل ملحوظ، حيث دخلت خلال الفترة من تشرين الثاني 2022 إلى تشرين ثاني 2023. تم تعيين 50 شخص بالغ من ذكور من سوري عربونا وتشير إلى مجموعة مختلطة في كلية الكوت الجامعة للفرقة من 20 إلى 30 سنة. تم قياس مستويات سكر الدم،BMI،WC، مؤشر الشحوم الثلاثية، مؤشر الكبد، مؤشر الشحوم الثلاثية، مؤشر الضغط والدواء في جميع المشاركين.

بحثت هذه الدراسة أن تناول كبسولة اللبأ البقري الصيدلانية يقلل من ارتفاع سكر الدم عند التعرض إلى اجهاد وتحديي، وتقليل محتوى الشحوم الثلاثية، ونسبة الكبد، ومراعاة ضغط الدم. ويمكن القول بذلك أن تناول كبسولة اللبأ البقري الصيدلانية يقلل من ارتفاع سكر الدم عند التعرض إلى اجهاد وتحديي، وتقليل محتوى الشحوم الثلاثية، ونسبة الكبد، ومراعاة ضغط الدم.

#المؤلفون العلمي الثاني لطيفة الدروات العلي
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Introduction

A blood glucose level of equal to or greater than 180 mg/dL that occurred during stress in healthy subjects without diabetes mellitus (DM) is termed stress hyperglycemia (SH) (1). The stress hyperglycemia ratio (SHR) is defined as the fasting blood glucose divided by the blood glucose level that is calculated from the glycosylated hemoglobin (HbA1c) value on admission (2) [Mi et al., 2022]. A significantly higher SHR is associated with worse prognostic biomarkers in diabetic patients with complications (2). Exercise has a positive impact on blood glucose levels in diabetic patients. Aerobic exercise in the form of walking for ≥2.5 hr, 5 times a week for 8 weeks reduced glucose levels and HbA1c in type 2 diabetes (T2D) (3). Resistance exercise significantly reduced the glucose levels (1.33±1.78 reduction) in T1D, greater than the corresponding value that was induced by aerobic exercise (3.94±2.67 mmol/L) (4). Exercise per se can induce hyperglycemia, particularly when practiced in a hot environment, due to brisk elevations of hormones involved in glucose kinetics, including catecholamine, cortisol, glucagon, and growth hormones (5). The effect of exercise on the reduction of the blood glucose level in patients with T1D was significantly greater than that in healthy subjects, which accounted for a range of 81–155% versus 10–40% reduction, respectively (6). The triglyceride-glucose index (TyGI) is a useful biomarker for assessing insulin resistance and inflammation in T2D. A higher value of TyGI is significantly associated with increased risk for the development of T2D (7). In non-diabetic people with a low skeletal muscle index, the TyGI is paradoxically and significantly increased (8). Bovine colostrum (BC) is a nutritional supplement support that has been used in sport and exercise for more than a quarter of a century. It exerts a favorable effect on gut permeability and improves immune function, especially during resistance exercise (9). Therefore, the rationale of this study is to fill the gap in the research by testing the hypothesis that the changes in glucose kinetics can be attenuated by using nutraceuticals, which are commonly used by people who train and exercise. This double-blind, placebo-controlled study was aimed at investigating the effects of BC on stress-induced hyperglycemia and the triglyceride-glucose index in healthy subjects who trained in resistance exercise as during exercise the glucose homeostasis was altered.

Materials and Methods

Ethical approval

The Institutional Scientific Committee at the Al-Farabi Kazakh National University, Almaty, Kazakhstan, approved this study as part of a candidate postgraduate research project (No. 4-3672). This study was conducted according to the Helsinki guidelines. Each subject signed a consent form before being included in the study.

Design and Setting

This double-blind, randomized-controlled clinical study was conducted in the Department of Pharmacy at Al-Kut College University in Wasit, Iraq, in cooperation with Al-Farabi Kazakh National University, Almaty, Kazakhstan, from April 30th to November 30th, 2022.

Participants

Apparent healthy men were recruited from the college undergraduate students by using random tables extracted from the Excel-10 software utility. The eligible participants were young males aged 18–25 years. The criteria for inclusion included apparently healthy subjects. Subjects with current acute illnesses, a history of hereditary or congenital diseases, or drug intake within the past 2 weeks were excluded from the study. All the participants were instructed not to take any tonics, nutraceuticals, or herbal medicines during the period of the study, and they were free to withdraw from the study at any time. The appropriate sample size was calculated using the G*Power 3.1 program, and the sample size was determined at a type I error probability of 0.05 and a type II error probability (the power) of 0.95. The participants were divided into two groups:

Group I (n = 24): The participants received a placebo substance at an equivalent dose of 500 mg/day, and they were considered the control group. They had been doing resistance exercise in the gym hall for 2 hours per cycle, three cycles per week, for 8 weeks.

Group II (n = 26): The participants were treated with 500mg of colostrum as a capsule, a single oral dosage daily, and by practicing resistance exercise for 8 weeks as mentioned above. The following measurements were determined at the time of entry into the study and after 8 weeks of treatment and exercise.

Anthropometric measurements

The subjects’ weight (kg), height (m), and waist circumference (cm) were measured. The weight and height were measured using a stadiometer, and the waist and hip circumferences were measured at the level of the umbilicus and at the largest parts of the hip, respectively, using metallic tape measurements. The body mass index (BMI) was calculated by dividing the body weight (kg) as a numerator by the squared height (m) as a denominator.
**Rate pressure product (RPP) measurement**

The heart rate (beat.min⁻¹) and the blood pressure (mmHg) were measured in a sitting position after three minutes of rest. The rate-pressure product as a determinant of cardiac rate is simply calculated by using the following formula:

\[ \text{RPP (beat.min}^{-1}\text{. mmHg)} = \text{Heart rate} \times \text{systolic blood pressure} \times 10^{-2} \]

**Hematological and glycemic indexes**

Blood samples (before and after treatments) were obtained from the participants of both groups after overnight fasting and immediately sent to the private laboratories for determination of fasting blood glucose (FBG), glycosylated hemoglobin (HbA1c%), and triglycerides. The FBS and HbA1c% values represented the acute or current levels. The stress or admission blood glucose level (mg/dL) was equal to \((28.7\times \text{current HbA1c}%-46.7)\). The stress, or in-admission, % of HbA1c is equal to \(\frac{\text{stress FBG}-46.7}{28.7}\) \((11, 12)\).

The current triglyceride-glucose index (TyGI) \((13)\):

\[ \text{TyGI} = \ln \left( \frac{\text{Current FBG} \times \text{Triglycerides}}{2} \right) \]

The stress or in admission: \[ \text{TyGI} = \ln \left( \frac{\text{Stress FBG} \times \text{Triglycerides}}{2} \right) \]

**Statistical analysis**

The results are presented as a number, a percentage, and a mean with SD. Microsoft Excel 10 for Windows (Microsoft Cooperation, One Microsoft Way, Redmond, Washington, USA) was used to statistically analyze the results. Differences between means before and after treatment for both groups were analyzed using a paired t-test and an independent two-sample (two-tailed) t-test to compare the baseline data between groups. Fisher's exact probability test was used for categorized data. P-values of \(\leq 0.05\) indicated significant differences.

**Results**

Table 1 shows the baseline data of the healthy subjects at the time of entry into the study. Significant differences between the two groups were observed in the WC, RPP, and TyGI values, which were greater in Group II compared with Group I. Neither the placebo nor the BC induced changes in the BMI and WC, while both treatments showed significant reductions in the MCV values (Table 2). In Group I, the mean RPP was significantly elevated by 13.0%, while the mean Hb level was elevated by 2.8% in Group II (Table 2).

Table 3 showed the effects of BC versus placebo on the changes in glucose indices following 8 weeks of resistance exercise. Table 3 showed non-significant differences in the current FBS, HbA1c (%), and TyGI observed in participants in Group I. These changes were represented by a decline of the mean FBS by 1% and an elevation of the mean values of HbA1c% and TyGI by 4.3% and 1.2%, respectively. Subjects treated with BC showed a non-significant decline of FBS (1.1%) and a significantly (\(p<0.001\)) elevated mean value of HbA1c by 10.6%. The calculated FBG, which represented stress hyperglycemia, was significantly elevated by 5.3% and 14.7 in Groups I and II, respectively. The differences in the calculated HbA1c in both groups were non-significant. Significantly higher values of SHR and TyGI were observed in Group II compared with the corresponding values of Group I.

**Table 1. Baseline data of the participants enrolled in the study**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group I (n=24)</th>
<th>Group II (n=26)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>24.2±4.9</td>
<td>25.5±6.8</td>
<td>0.451</td>
</tr>
<tr>
<td>Residency (Urban: Rural)</td>
<td>23:1</td>
<td>25:1</td>
<td>1.000</td>
</tr>
<tr>
<td>Smoking</td>
<td>9</td>
<td>14</td>
<td>0.272</td>
</tr>
<tr>
<td>Body mass index (kg/m2)</td>
<td>28.6±8.4</td>
<td>29.6±3.8</td>
<td>0.584</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>86.2±7.6</td>
<td>91.6±9.6</td>
<td>0.033</td>
</tr>
<tr>
<td>Rate pressure product</td>
<td>95.8±19.9</td>
<td>119.8±36.3</td>
<td>0.006</td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>14.9±0.9</td>
<td>14.5±1.4</td>
<td>0.246</td>
</tr>
<tr>
<td>Mean cell volume (fL)</td>
<td>85.2±6.4</td>
<td>83.8±4.3</td>
<td>0.367</td>
</tr>
<tr>
<td>Fasting blood glucose (mg/dL)</td>
<td>87.7±9.2</td>
<td>88.1±7.1</td>
<td>0.847</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>4.7±0.3</td>
<td>4.7±0.2</td>
<td>0.659</td>
</tr>
</tbody>
</table>

The results are expressed as mean ±SD for continuous data and number for categorized data. P-value was calculated using independent two sample t-test (two-tailed) with assumed equal variance, and Chi square test for categorized data. Group I: placebo-treated group, and Group II: bovine colostrum-treated group.
Table 2. Effects of placebo (Group I) and bovine colostrum (Group II) on the anthropometric, cardiac and hematological indices in participants training resistant exercise

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group I (n=24)</th>
<th>Group II (n=26)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before</td>
<td>After</td>
</tr>
<tr>
<td>BMI</td>
<td>28.6±8.4</td>
<td>27.1±4.0</td>
</tr>
<tr>
<td>WC</td>
<td>86.2±7.6</td>
<td>86.7±7.8</td>
</tr>
<tr>
<td>RPP</td>
<td>95.8±19.9</td>
<td>108.3±20.7</td>
</tr>
<tr>
<td>HB</td>
<td>14.9±0.9</td>
<td>14.7±1.1</td>
</tr>
<tr>
<td>MCV</td>
<td>85.2±6.4</td>
<td>84.2±6.7</td>
</tr>
</tbody>
</table>

The results are expressed as mean ±SD, p-value was calculated using paired t-test (two-tailed) for continuous data. BMI: body mass index, WC: waist circumference, RPP: rate pressure product, HB: hemoglobin, and MCV: mean cell volume.

Table 3. Effects of placebo (Group I) and bovine colostrum (Group II) on the glycemic indices in participants training resistant exercise

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group I (n=24)</th>
<th>Group II (n=26)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before</td>
<td>After</td>
</tr>
<tr>
<td>FBG (mg/dL)</td>
<td>87.7±9.2</td>
<td>86.8±8.1</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>4.7±0.33</td>
<td>4.9±0.49</td>
</tr>
<tr>
<td>TyGI</td>
<td>8.4±0.42</td>
<td>8.5±0.4</td>
</tr>
<tr>
<td>Calculated FBG</td>
<td>88.0±9.4</td>
<td>92.7±13.9</td>
</tr>
<tr>
<td>Calculated HbA1c</td>
<td>4.7±0.32</td>
<td>4.7±0.28</td>
</tr>
<tr>
<td>Calculated TyGI</td>
<td>8.4±0.43</td>
<td>8.6±0.47</td>
</tr>
<tr>
<td>SHR</td>
<td>0.998±0.020</td>
<td>0.956±0.164</td>
</tr>
</tbody>
</table>

The results are expressed as mean ±SD, p-value was calculated using paired t-test (two-tailed) for continuous data. FBG: fasting blood glucose, HBA1c: glycosylated hemoglobin, TyGI: triglyceride-glucose index and SHR: stress hyperglycemia ratio. Calculated values indicate an assumption stress values.

Discussion

The results of this study show that BC has a positive effect on the changes in the blood indices of participants exercising resistance exercise. The results of this study showed non-significant reductions in BMI in both treated groups. These results are in agreement with other studies that showed that 8 weeks of aerobic exercise reduced the body weight by 1 kg (14). Other studies clarified the benefits of using BC on the health of athletes. In Group I, the hemodynamic response assessed by the determination of RPP was significantly increased, which indicated that the cardiac work was increased following resistance exercise.

These results are in agreement with others who showed that a temporary elevation of heart rate and blood pressure is increased following the exercise as a result of physiological hemodynamic responses (15). In Group II, the non-significant changes in the RPP indicate that BC stabilized the hemodynamic responses and maintained the cardiac work. These results confirmed previous studies that BC supplementation improved the performance of road cyclists who carried out high-intensity training (16). A significant decrease in the mean value of MCV following the exercise in both groups is an interesting observation. Previous studies demonstrated that exercise induced a significant increase in red distribution width (17), while others (18) found non-significant changes in the MCV value in people who trained many types of exercises. The significant increment in the HB level in Group II is due to using BC rather than being related to the exercise, as BC impacts positively on HB (19). The other interesting findings in this study are the effects of exercise and BC on glucose levels. In both groups, the FBG levels were non-significantly decreased after an 8-week training program of resistance exercise, indicating that exercise enhanced the utilization of the glucose molecule (20).

A significantly higher HbA1c% in Group II indicates that BC is effective in the mobilization of glucose into the circulation and then utilization by skeletal muscle. There is evidence that BC stimulates the intestinal absorption of glucose in the neonatal calves, and this explained the significantly higher HbA1c% in Group II (21). During exercise, there is an activation of the autonomic nervous system and the release of catecholamines, which stimulate the gluconeogenesis and glycolysis processes, leading to elevation of FBG, and this explained the higher levels of stress or in-admission FBG in both groups, which reached a significant value in Group II (22).
The changes in the FBG and HbA1c%, which are measured acutely or calculated to express the changes during the physical examination, lead to a significantly higher level of SHR, which exceeds 1.0 in Group II compared with Group I. It is expected to have FBG levels less than 180 mg/dL because the participants were healthy, there is no evidence of sepsis or trauma that leads to stress hyperglycemia, and the exercise per se reduced the FBG \(^{(23, 24)}\). The non-significant changes in the TyGI in both groups are attributed to the health status of the participants, and TyGI is considered a prognostic biomarker in diseased people, e.g., diabetes and hypertension \(^{(25, 26)}\).

There is evidence that hyperimmune bovine colostrum supplementation reduced the serum level of triglycerides in patients with non-alcoholic steatohepatitis, but there is no evidence that BC altered serum triglycerides in healthy subjects \(^{(27)}\). Limitations of the study included a small sample size, and there are significant differences in the baseline characteristics between groups.

**Conclusion**

Bovine colostrum is useful in resistance exercise because it considerably raises stress glucose levels without causing changes in glycosylated hemoglobin, indicating that it supplies glucose to the muscle as a vital component for physical activity. The increased TYGI during exercise is related to a large rise in stress glucose. This impact is also accompanied by a sustained hemodynamic effect.

**Funding**

The authors did not receive any funds.

**Ethics Statements**

The Institutional Scientific Committee at the Al-Farabi Kazakh National University, Almaty, Kazakhstan, approved this study as part of a candidate postgraduate research project (No. 4-3672).

**Conflict of Interest**

The authors declare no conflicts of interest.

**Author contributions:**

Concept: M. Al-N; Design: M. Al-N; Supervision: D.S.; U.D; Fundings: A. Al-B; Materials: A. Al-B; Data Collection and/or Processing: A. Al-B; Analysis and/or Interpretation: M. Al-N; Literature: M. Al-N; Review: M. Al-N; A. Al-B; Writing: M. Al-N; Critical Review: M. Al-N; A. Al-B; D.S.; U.D.

**References**


