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Acute effect of ketogenic diet on metabolic flexibility during exercise in adults

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A ketogenic diet (KD) has shown positive effects on metabolic improvement in individuals with chronic diseases; however, we found that 3-days of KD causes impaired exercise efficiency (EE) by 11% during the graded exercise testing (GXT) when compared to 3-days of mixed diet (MD). To explain potential mechanism(s) responsible for impaired EE by KD, we hypothesized that metabolic flexibility (ability to adjust substrate use in response to a physiological stimulus) will be blunted during the GXT after KD vs. MD. **PURPOSE:** We aimed to compare acute effects of KD vs. MD on metabolic flexibility during the GXT in adults. **METHODS:** Fourteen adults (age 26.3 ± 3.1 [SD] years; BMI 23.6 ± 4.2 kg/m²) completed the following procedures: 3-days of MD (15% fat, 25% protein, 60% carbohydrate), 3-days of wash-out, and 3-days of KD (75% fat, 20% protein, 5% carbohydrate). Upon completion of each diet arm, all participants completed the GXT on treadmill with low- (LIE; 40% of VO₂max), moderate- (MIE; 55%), and high-intensity exercise (HIE; 70%). Metabolic flexibility was estimated by the changes in respiratory quotient (DRQ) from resting to LIE to MIE to HIE to recovery period in both diet arms. Repeated measures ANOVA with Bonferroni's post-hoc tests were used to examine DRQ over the GXT by two diet arms (i.e., interaction). Pearson correlation was used to examine bivariate relationship between metabolic flexibility and EE (%). Statistical significance was set at $p < 0.05$. **RESULTS:** Baseline RQ was lower in KD vs. MD (0.75 ± 0.1 vs. 0.84 ± 0.1 , $p < 0.01$), and fat oxidation was higher in KD vs. MD (1.1 ± 0.3 vs. 0.6 ± 0.3 kcal/min, $p < 0.01$). Significant interactive effects were observed for the group by time on DRQ ($F = 3.58$; $df = 2, 1$; $p < 0.01$), indicating that (after the KD vs. MD), DRQ was blunted (a) from resting to LIE (-0.013 ± 0.01 vs. -0.076 ± 0.01) and (b) from MIE to HIE (0.116 ± 0.02 vs. 0.163 ± 0.01), all $p < 0.01$. DRQ correlated positively with EE ($r = 0.437$; $p < 0.05$). **CONCLUSION:** Our data suggest that 3-days of ketogenic diet could cause metabolic inflexibility during the GXT, potentially explaining the relationship between KD and exercise inefficiency. Our positive correlation between metabolic flexibility and EE further supports our hypothesis/speculation. Combined effects of KD and exercise training on metabolic flexibility should be uncovered.

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