Proceedings of the British Pharmacological Society at http://www.pA2online.org/abstracts/Vol13Issue3abst249P.pdf

A ketone ester drink results in nutritional ketosiswith low within and between subject variability when fed or fasted

Introduction: Ketone bodies (KB) are oxidative fuel substrates and metabolic signals produced in response to starvation or a high fat low carbohydrate diet. Recently, we developed a ketone ester (KE) that, when consumed as a drink, rapidly increased circulating KB [1]. However, the effects of concomitant meal ingestion on the KEabsorption and variability of the resulting ketosis have not been described. Theaim of this study was to characterize the kinetics of blood KB following KE consumption with a standard meal and on an empty stomach and to determine the degree of within and between subject variability in each state.

Methods: Healthy, non-obese participants (n = 16) completed a 4-visit, randomized, cross over study that was ethically approved by an NHS REC and adhered to the Declaration of Helsinki. Following an overnight fast, subjects consumed 395 mg/kg KE, on two occasions when fasted (CON) and on two occasions following a standard meal (FED). Blood samples were obtained via an intravenous catheter at baseline (BL) andat regular intervals post-drink/meal and analyzed for β-hydroxybutyrate (BHB). Peak BHB concentration (BHB C_{max}) was calculated from the raw data; BHB AUC (area under the curve) was calculated using the trapezoidal method. Values are means ± SEM.A linear fixed effects model was constructed to examine the effect of feeding(FED vs. CON) and visit order (within-subject variability in each condition) on BHB kinetics. A paired t-test was used and significance taken at $p<0.05$.

Results: BHB C_{max} was significantly lower in FED vs. CON (2.2 mM ± 0.1 mM vs. 3.3 mM ± 0.1 mM). BHB AUC was ~ 40% lower in FED vs. CON ($p<0.05$). There was no significant effect of visit order (i.e: within subject variability) on AUC or C_{max}($p = 0.88$). The coefficient of variation (CV) of both the BHB C_{max} and AUC was approximately constant at ~25% when computed through the method of Vangel[2]. This indicates that the variability of both methods of quantifying ketone metabolism is approximately equal.

The adjusted generalized R^2 metric [3] was calculated to partition variance in the complete data set between visit order (<1%), between-subject variability (16%), residual variability (24%) and feeding condition (61%), showing that within and between individual variability in BHB kinetics was low.

Conclusions: BHB kinetics are significantly altered by prior consumption of a meal, which may be due to lower gut absorption [4] or increased metabolic disposal mediated by higher insulin levels [5] in the FED vs. CON state. The within and between subject variance in BHB kinetics following KE consumptionwas low regardless of feeding state. These resultsdemonstrate the importance of meal ingestion when planning to induce or maintain ketosis using theKEdrink and that ketosis following a KE drink is reproducible in either the fed and fasted state.

References:

1. Clarke, K., et al. Regulatory Toxicology and Pharmacology, 2012. **63**(3): p. 401-8.
2. Vangel, M.G. The American Statistician, 1996. **50**(1): p. 21-26.
3. Nakagawa, S. and H. Schielzeth, Methods in Ecology and Evolution, 2013. **4**(2): p. 133-142.
4. Riley, S.A., et al. British Journal of Clinical Pharmacology, 1992. **34**(1): p. 32-39.
5. Keller, U., M. Lustenberger, and W. Stauffacher, Diabetologia, 1988. **31**(1): p. 24-9.