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DEEPPDIVE SUMMARIES

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Are Hunger Levels Higher in PCOS?

Japur CC, Diez-Garcia RW, de Oliveira Penaforte FR, das Graças Pena G, de Araújo LB, de Sá MFS. Insulin, ghrelin and early return of hunger in women with obesity and polycystic ovary syndrome. *Physiol Behav.* 2019;206:252-258.

Background

- Women with PCOS have been shown to have lower levels of gastrointestinal appetite-regulating hormones in response to food intake.
- Some experimental research has suggested that in women with PCOS, improving insulin sensitivity may enhance appetite regulation mediated by the hunger hormone, ghrelin.
- No research had examined the associations between pre and post-meal ghrelin and insulin levels, subjective hunger, and energy intake in response to a test meal.

The Study

- A cross-sectional analysis of women with PCOS [$n = 30$] and non-PCOS women for comparison [$n = 23$], comparing the associations between insulin, ghrelin, and subjective hunger in response to an *ad libitum* test meal.

Findings, Strengths & Limitations

- Both groups consumed similar *ad libitum* energy intake during the test meal. Insulin levels were 36% higher while ghrelin levels were 8% lower and blood glucose levels 5% lower, in the PCOS group.
- Hunger levels were significantly higher across the 2 h postprandial period in the PCOS group compared to the non-PCOS group.
- Strengths include the *ad libitum* test meal which allowed for a more “real world” test of how ghrelin, insulin, and appetite, may interact to influence energy intake in women with PCOS. Limitations include the non-randomised, cross-sectional design.

Context

- The main finding of the present study is also its most interesting result, namely the earlier return to hunger in the PCOS group compared to the non-PCOS group, which was independent of differences in ghrelin or insulin.
- As there was only a negligible difference in energy consumed during the *ad libitum* test meal, the inference is that the earlier return to hunger in women with PCOS compared to non-PCOS controls may be evident despite similar levels of energy intake.
- Perhaps the lower satiety and higher hunger levels in women with PCOS are independent of ghrelin, however, better designed, and larger trials will be required to get a more definitive answer on this question.

Application

- If we assume that the finding that women with PCOS do exhibit greater hunger and less satiety is a real effect, there is evidence that higher protein, moderate carbohydrate intakes, and frontloading energy intake in the early period of the day, may improve appetite control.
- The combination of higher – up to 30% energy – protein intakes, in combination and moderate [~40-45%] carbohydrate intakes, and low GL carbohydrate sources, may be useful in women with PCOS.

Can a Ketogenic Diet Outperform a Mediterranean Diet for Diabetes Control?

Gardner CD, Landry MJ, Perelman D, et al. Effect of a ketogenic diet versus Mediterranean diet on glycated hemoglobin in individuals with prediabetes and type 2 diabetes mellitus: The interventional Keto-Med randomized crossover trial. *Am J Clin Nutr.* 2022;116(3):640-652.

Background

- Low-carbohydrate diets lead to reductions in haemoglobin A1c, a marker of longer term [2-3 months] blood glucose regulation, however these effects of low-carb diets appear to be short-term and observed primarily over 6 to 12-months.
- Mediterranean diets have shown benefits for reductions in HbA1c and fasting blood glucose compared to control diets, but these effects may also be short-term/ .
- The “Keto-Med study” optimised a ketogenic diet and compared it with a Mediterranean diet for glycaemic control in adults with type-2 diabetes [T2D].

The Study

- The study was a randomised crossover trial comparing a “Well-Formulated Ketogenic Diet” [WFKD] to a “Mediterranean-Plus Diet” [MPD].
- Both diets had three characteristics in common: maximise non-starchy vegetable intakes, and avoidance of refined grains and added sugars.
- The primary outcome was change in HbA1c over 12-weeks between the diets. Secondary outcomes included changes in fasting glucose and insulin, blood lipids, and weight.

Findings, Strengths & Limitations

- There was no significant difference between diets; both diets improved glycaemic control with the WFKD lowering HbA1c by 9% and the MPD by 7%. Weight loss explained the improvement in HbA1c, not the type of diet.
- At the end of the first diet phase, participants who began with the WFKD lost an average of 7.5kg compared to 5.1kg on the MPD. The WFKD led to significant increases in LDL-C, HDL-C, and decrease in triglycerides.
- Strengths include randomised, crossover design of the trial and provision of foods for a third of the study duration. The main limitation is the small sample size and the lack of washout period between diets.

Context

- The lack of effect of diet type, rather than weight loss, adds to a body of evidence indicating no particularly unique effect of diet independent of weight loss.
- The data tells us nothing beyond what we already knew; that improvements in HbA1c will be proportional to the magnitude of weight loss, and the type of diet is secondary.
- In effect, participants started out in a high-risk HbA1c range and ended up at the lower end of the risk range. This is unlikely to have any meaningful impact on progressive deterioration of disease severity over the longer term.

Application

- From the perspective of T2D management, at least the Keto-Med trial provides further evidence that the composition of the diet is a secondary consideration to weight loss.
- Diets that may have an effect in the short-term over 3-6-months, like low-carb/ketogenic diets or even Mediterranean diets, tend to washout in effect over 1-year.

“Compared to What”? Artificial Sweeteners and Cardio-Metabolic Risk

McGlynn ND, Khan TA, Wang L, et al. Association of Low- and No-Calorie Sweetened Beverages as a Replacement for Sugar-Sweetened Beverages With Body Weight and Cardiometabolic Risk: A Systematic Review and Meta-analysis. *JAMA Netw Open*. 2022;5(3):e222092.

Background

- 2022 has been a good year for keeping the artificial sweetener controversy evergreen, with the French NutriNet-Santé cohort suggesting increased risk of cardiovascular disease.
- For RCTs, however, whether artificial sweeteners are compared to another non-calorie control [i.e., water], or are compared to a calorie-containing control [i.e., sugar-sweetened beverages (SSB)] is an important factor that may influence the outcomes.
- The present study was a meta-analysis to investigate these different comparisons for artificial sweeteners on cardio-metabolic risk.

The Study

- The study conducted a meta-analysis of the effect of artificial sweeteners [AS] on cardio-metabolic risk factors based on three comparative interventions: AS replacing sugar-sweetened beverages [SSB; i.e., calorie displacement]; AS replacing water [i.e., no calorie displacement]; Water replacing SSB [i.e., calorie displacement].

Findings, Strengths & Limitations

- Substituting SSB for AS was associated with a 1.06kg decrease in bodyweight, a 0.32kg/m² decrease in BMI, and a 0.60% decrease in body fat. Liver fat was also significantly decreased.
- Substituting water for AS was associated with a 1.07kg decrease in bodyweight, and a 2.63mmHg decrease in systolic blood pressure. Compared to AS, water was associated with a 0.21% [95% CI 0.02 to 0.40%] decrease in HbA1c.
- Strengths include the clearly defined inclusion criteria and comparison of three exposures. Limitations include the small sample size of some comparisons, and the lack of subgroup analyses were conducted to determine the influence of factors like sex, study duration, or funding source.

Context

- The present study demonstrated the replacement of SSB with AS are associated with improved body composition and decreases in liver fat, albeit these differences are modest.
- The direction of effect for blood lipids and blood pressure tends to be lower comparing AS to SSB.
- The findings in relation to water as the comparator need to be considered as relative, i.e., both AS and water show improved risk factors in weight loss trials, however, the magnitude of the change may differ – and look in a meta-analysis as if AS are less favourable.

Application

- AS can certainly be an effective substitution for calorie-containing foods and beverages, provided those calories are not compensated for elsewhere in the diet.
- Where this substitution effect is achieved, AS may be useful in facilitating reductions in energy intake, but the wider diet is crucial for improving cardio-metabolic risk factors