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Introduction: Time-restricted eating (TRE) or time-restricted feeding (TRF), a form of intermittent fasting (IF) when food consumption is restricted to a 4–12 hour window, poses unique possible health benefits that allow the nutrient to work in harmony with circadian rhythm. Whether TRF is effective in weight loss and cardiometabolic profile compare to usual diet is controversial. We conducted a meta-analysis of randomized control trials to investigate the weight and metabolic effects of TRF in humans.
Methods: The systematic review was conducted according to the PRISMA guidelines. The literature search was conducted in MEDLINE, EMBASE, and CENTRAL from database inception to November 30, 2020. The search terms included time restricting feeding, time-restricted eating, periodic fasting, intermittent fasting, and periodic fasting. The eligibility criteria included a randomized controlled trial (RCT) comparing the effect of TRF as an intervention and control diet on weight and cardiometabolic risks in individuals with overweight (BMI 23–26.9 kg/m^2 in Asian and 25–29.9 kg/m^2 in others) or obesity (BMI≥27 kg/m^2 in Asian and ≥30 kg/m^2 in others) with study duration of at least 8 weeks. The primary outcome is the change in body weight between preintervention and postintervention. The secondary outcome is the change in total fat mass and lean mass, HDL, LDL, and triglycerides. Pool mean differences (MD) with 95% confidence interval (CI) were calculated for each outcome.
Results: Four articles met the inclusion criteria and were included in this systematic review and meta-analysis. There were 511 participants with BMI 24 kg/m^2 and above and aged between 18 and 65. TRF was defined as a 4–8 hours ad-lib unrestricted eating in 24 hours. The control diet was defined as ad-lib eating per usual habits. There was a significant improvement in weight and body composition in the TRF group. The mean weight loss was -2.08 kg (95% CI: -3.49 to -0.68) greater among TRF group. There was a significant total fat mass and lean mass loss in the TRF group with the MD of -1.29 kg (95% CI: -2.04 to -0.54) and -0.59 kg (95% CI: -1.15 to -0.03), respectively. There was no significant change in HDL, LDL, or triglycerides comparing between TRF and control diet.
Conclusion: This systematic review and meta-analysis of RCT showed that TRF with no calories restriction resulted in significant decreased in weight, fat mass, and a slight decreased in total lean mass compared with control diet. Our findings support TRF as an effective lifestyle intervention for weight loss.

Adipose Tissue, Appetite, and Obesity

INTEGRATED PHYSIOLOGY OF OBESITY AND METABOLIC DISEASE

Effects of Colchicine on Measures of Lipolysis in Adults With Obesity

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Background: Obesity-associated inflammation promotes adipose tissue (AT) dysfunction and contributes to the progression of type 2 diabetes and cardiovascular disease. Recent clinical studies have demonstrated that colchicine may improve metabolic and cardiovascular outcomes; however, colchicine's effects on metabolic and inflammatory measures within AT remain unclear. **Methods:** The aim of this study was to examine if colchicine's anti-inflammatory effects would improve measures of lipolysis and immune cell populations in subcutaneous AT (SAT). This is a secondary analysis of a double-blind, randomized, placebo-controlled pilot study in which 40 nondiabetic adults with obesity and metabolic syndrome (MetS) were randomized to colchicine 0.6mg or placebo twice daily for 3 months. Blood samples for insulin, glucose, and free fatty acids were collected in the fasted state and during a frequently-sampled intravenous glucose tolerance test. Noninsulin-suppressible (l_0), insulin-suppressible (l_2), and maximal (l_0+l_2) lipolysis rates were calculated by minimal model analysis. Body composition was determined by DXA. SAT immune cell populations were characterized by flow cytometry fluorescence-activated single cell sorting of the stromovascular fractions obtained after collagenase digestion of SAT samples obtained using a mini-liposuction technique pre- and post-intervention. **Results:** Data from 18 subjects in the colchicine group (Mean ± SD: age 48.4 ± 13.5 y; BMI 39.3 ± 6.3 kg/m2; sex: female 72.2%) and 18 subjects in the placebo group (age 44.7 ± 10.2 y; BMI 41.8 ± 8.2 kg/m2; sex: female 77.8%) were available for this study. Colchicine treatment significantly reduced l_2 ($p = 0.04$) and l_0+l_2 ($p = 0.04$) versus placebo. These changes were significantly associated with reductions in systemic inflammation, including the changes in high-sensitivity C-reactive protein concentrations, white blood cell count, circulating monocyte and neutrophil populations, and the neutrophil-lymphocyte ratio (p's < 0.015). Colchicine did not significantly alter SAT immune cell population distributions (p's > 0.05). **Conclusions:** In adults with obesity and MetS, colchicine may improve insulin action at the level of AT. These improvements were positively associated with the suppression of systemic inflammation. However, no local AT inflammatory cell populations were significantly affected by

colchicine use in our study, suggesting that colchicine's systemic, rather than local, anti-inflammatory effects may be more consequential in ameliorating AT metabolic pathways in MetS. Further studies are warranted to elucidate the biological mechanisms underlying colchicine's effects in AT, as these investigations could potentially shed light on treatments to improve metabolic outcomes in human obesity.

Adipose Tissue, Appetite, and Obesity

INTEGRATED PHYSIOLOGY OF OBESITY AND METABOLIC DISEASE

Efficacy and Safety of Once-Weekly Subcutaneous Semaglutide 2.4 MG in Adults With Overweight or Obesity (STEP 1)

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Background: Despite the increasing global adverse health impact of obesity, there are few pharmacological options for effective weight management. STEP 1 investigated the efficacy and safety of the glucagon-like peptide-1 analogue, subcutaneous (s.c.) semaglutide, for weight management in adults with overweight or obesity.

Methods: This randomized, double-blind, placebo-controlled, phase 3 trial was conducted at 129 sites across 16 countries (NCT03548935). Adults aged ≥18 years with either body mass index (BMI) ≥30 kg/m^2 or BMI ≥27 kg/m^2 with ≥1 weight-related comorbidity, without type 2 diabetes, were randomized 2:1 to 68 weeks' treatment with once-weekly s.c. semaglutide 2.4 mg or placebo, both as adjunct to lifestyle intervention. The co-primary endpoints were percentage change in body weight and achievement of weight loss ≥5%. Cardiometabolic risk factors, patient-reported outcomes, and safety/tolerability were also assessed. Two estimands were defined: treatment policy (effect regardless of treatment adherence and use of rescue intervention) and trial product (effect assuming treatment adherence and without rescue intervention); results are presented for the treatment policy estimand, unless stated otherwise. P values for parameters marked with # were not controlled for multiplicity.

Results: 1961 randomized participants (mean age 46 years, body weight 105.3 kg, BMI 37.9 kg/m^2; 74.1% female) were included. Mean body weight change from baseline to week 68 was −14.9% in the semaglutide group vs −2.4% with placebo (estimated treatment difference [ETD]: −12.4%; 95% confidence interval (CI): −13.4, −11.5; p<0.0001). Similar results were obtained with the trial product estimand: mean body weight change# was -16.9% for semaglutide vs -2.4% for placebo (ETD: -14.4%; 95% CI: -15.3, -13.6; p<0.0001). Participants were more likely to achieve weight loss ≥5%, ≥10%, ≥15%, and ≥20%# with semaglutide vs placebo (86.4% vs 31.5%, 69.1% vs 12.0%, 50.5% vs 4.9%, and 32.0% vs 1.7%, respectively; p<0.0001 for all). Greater improvements were seen with semaglutide vs placebo in waist circumference, BMI#, systolic and diastolic# blood pressure, glycated hemoglobin#, fasting plasma glucose#, C-reactive protein#, fasting lipid profile#, and self-reported physical functioning (p<0.05 for all). No new safety signals with semaglutide were observed. The most frequent adverse events with semaglutide were gastrointestinal disorders (typically transient and mild-to-moderate).

Conclusion: In adults with overweight or obesity, once-weekly s.c. semaglutide 2.4 mg plus lifestyle intervention induced a mean weight loss of approximately 15% by week 68. Clinically beneficial weight loss of ≥10% was achieved by over two-thirds of participants and ≥20% by one-third of participants, along with associated improvements in cardiometabolic risk factors and physical functioning.

Adipose Tissue, Appetite, and Obesity

INTEGRATED PHYSIOLOGY OF OBESITY AND METABOLIC DISEASE

Efficacy and Safety of Semaglutide 2.4 MG Once-Weekly in Adults With Overweight or Obesity and Type 2 Diabetes (STEP 2)

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