Crimson Publishers
Wings to the Research

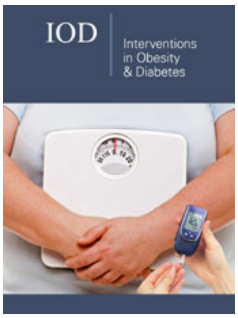
Mini Review

The Incretin Response to Exercise and Dietary Interventions in Individuals with Obesity

Jared Rosenberg and Joon Young Kim*

Department of Exercise Science, David B Falk College of Sport and Human Dynamics, Syracuse University, USA

ISSN: 2578-0263



***Corresponding authors:** Joon Young Kim, Assistant Professor, Department of Exercise Science, David B Falk College of Sport and Human Dynamics, Syracuse University, 430H White Hall, Syracuse, New York 13244, USA

Submission: January 29, 2024
Published: February 15, 2024

Volume 6 - Issue 4

How to cite this article: Jared Rosenberg and Joon Young Kim*. The Incretin Response to Exercise and Dietary Interventions in Individuals with Obesity. Interventions Obes Diabetes. 6(4). IOD. 000641. 2024. DOI: 10.31031/IOD.2024.06.000641

Abstract

Recently, much attention has been focused on pharmacological agents that target the incretin axis due to the efficacy in reducing body weight and glycemia in adults and youth with overweight and obesity. However, much less focus has been placed on the endogenous secretion of the incretin hormones. In the present mini review, we examine studies that assessed the incretin changes in response to either diet or exercise intervention, in adults and youth with overweight and/or obesity. The types of intervention could differently impact on changes in incretin hormones as exercise studies consistently showed increase in incretin hormones while the findings from the diet studies were controversial.

Keywords: Lifestyle; Incretin; GLP-1; GIP; Obesity

Abbreviations: AUC: Area Under the Curve; GIP: Gastric Inhibitory Polypeptide; GLP-1: Glucagon-Like Peptide-One; MMT: Mixed Meal Tolerance Test; OGTT: Oral Glucose Tolerance Test; T2D: Type 2 Diabetes

Introduction

Gastric Inhibitory Polypeptide (GIP) and Glucagon-Like Peptide-One (GLP-1), the two known incretin hormones, are secreted in the presence of lipids and glucose, and act on the β-cells via specific receptors stimulating insulin secretion [1]. Pharmacological agents that act on these β-cells specific receptors have been efficacious in reducing glycated Hemoglobin (HbA1c) and body weight in both adults and adolescents [2,3]. Despite the efficacy of these pharmacological agents in reducing HbA1c and body weight, lifestyle interventions are still the first-line intervention for individuals at heighten risk for Type 2 Diabetes (T2D) [4]. Currently, only a limited number of studies have assessed the changes in incretin concentrations in response to either a dietary or an exercise intervention. A better understanding of the incretin response to lifestyle changes could help physicians/researchers prescribe specific interventions to reduce the risk of T2D development in individuals who are disproportionally impacted by obesity, insulin resistance and T2D. Therefore, our current mini review discussed previous studies evaluating changes in incretin concentrations in both adults and youth, with overweight and/or obesity, undergoing a diet or an exercise intervention.

The Incretin Response to Dietary Interventions

Due to both GLP-1 and GIP being stimulated by nutrient intake, it is postulated that improvements in dietary habits could improve incretin concentrations, thereby improving cardiometabolic health [1]. Otten et al. [5] assessed changes in the incretin concentrations after 2 years of a paleolithic diet, in 26 postmenopausal women with obesity. Participants underwent a 2-hr Oral Glucose Tolerance Test (OGTT) and Dual Energy X-Ray Absorptiometry (DEXA) scan to measure postprandial total GLP-1 & GIP concentrations, and fat mass, respectively, before and after the intervention. When compared to the baseline, GLP-1 and GIP concentrations were increased by 45 and 23%, as measured by the mean incremental Area Under the Curve (iAUC), respectively. Furthermore, a 13.8% decrease in fat mass (kg) was observed after the intervention. These findings are not limited to female adults, as

a previous study by Lespen et al. [6] including both males and females had similar results. Twenty adults with obesity underwent an 8-week very low-calorie diet (800kcal/day) and were evaluated their changes in total incretin concentrations measured by a 3-hr mixed Meal Tolerance Test (MMT) and fat mass measured by DEXA. GLP-1 and GIP responses (estimated by iAUC) were increased by 44 and 36%, respectively, and a 6.5% reduction in percent body fat was observed after the intervention. Both studies, showing that dietary interventions can increase total incretin response, together with fat loss, signifying potential reduction in T2D risk in adults with obesity. However, some other studies were not in agreement on their incretin findings. Coutinho et al. [7] examined the changes in GLP-1 concentrations after a 12-week calorie restriction (33%) diet in 17 adults with obesity. Active GLP-1 was measured during an MMT, and total fat mass was assessed via a BodPod before and after the intervention.

A reduction in basal active GLP-1 concentrations was observed along with a 24% reduction in total fat mass. Potential explanations for the discrepancies in incretin findings between Coutinho et al. [7] vs. the former two studies [5,6] would be the participants with varying degree of adiposity and diet intervention components. Weiss et al. [8] evaluated the changes in total incretin concentrations in 17 adults who were overweight, that underwent 19-weeks of caloric restriction (~20%). Total incretin concentrations were measured during a 2-hr OGTT. Both total GLP-1 and GIP concentrations (expressed by the total AUC) were reduced by 13.8 and 9.3%, respectively, after the intervention. These findings suggest that total incretin response to the OGTT is reduced by caloric restriction, which is in line with the findings from the Coutinho et al. [7]. Taken together, changes in absolute concentrations of incretin hormone in response to any types of dietary intervention can be bidirectional based on physiological (measurement types of incretins), physical (degrees of adiposity), and environmental (compositions of diet) factors. To our knowledge, there is no such data in pediatric populations.

The Incretin Response to Exercise Interventions

In contrast to the findings from previous dietary interventions, relatively consistent findings were observed in the exercise interventions in both adults and youth. Eshghi et al. [9] examined the incretin response to an exercise intervention compared to the rest intervention, in 12 adult males with and without T2D, in a randomized crossover study. The exercise intervention had participants perform two 90-min bouts of treadmill exercise at 80% of the ventilatory threshold on the same day, with fasting blood samples were collected. The following day participants underwent a 4-hr OGTT after the fasting. The rest intervention had same protocol of blood draw without exercise components. Fasting GIP and active GLP-1 were higher during the OGTT day following exercise, than compared to the OGTT following the rest intervention, for both adults with and without T2D. Furthermore, both plasma insulin and glucagon concentrations were lower during the OGTT following the exercise intervention vs. the OGTT after the rest intervention. These findings suggest that short term exercise can influence incretin concentrations in adults with and without T2D, thereby potentially contributing to better glycemic control. Further, Chanoine et al. [10] observed a significant increase in the acute GLP-1 response (0-30 mins) during a MMT after five consecutive days of aerobic training (designed for no weight loss) in 17 young males with obesity and normal weight. After the exercise training, significant elevations of acute GLP-1 response were observed both in youth with obesity and normal weight. Kahle et al. [11] examined the GIP response to a 5-month exercise intervention (performed three times per week, which included a variety of aerobic exercise at 70% of age predicted heart rate max) in 13 youths with obesity. A significant increase in the GIP AUC during the MMT, together with improvements of insulin dynamics (decrease in insulin concentrations at 30 and 60 minutes during the test), was found after the intervention in youth with obesity. Taken together, limited data suggest that exercise could improve incretin hormone profile (i.e., amplified secretion) in both adults and youth, thereby potentially reducing T2D risk.

Additional Considerations

Sirtuin 1 (SIRT 1), a protein that is encoded by the SIRT 1 gene, has been noted for its role in overall health [12-14]. Recent evidence suggests that SIRT 1 may be influenced by incretin biology. Like the incretins, SIRT 1 is associated with insulin release and is dysregulated by obesity [12,15]. In addition to dietary and exercise interventions influencing incretin concentrations, caloric restriction and aerobic exercise have both been shown to increase SIRT 1 activity [16,17]. Further evidence linking SIRT 1 to incretin biology comes from recent pharmacological studies of metformin and incretin mimetics. Metformin has been shown to activate the SIRT 1 pathway and cause an increase of GLP-1 secretion [17,18]. It is possible that the incretins and SIRT 1 create a synergistic effect on the β-cell, thus lowering T2D risk. Therefore, the synergist effect on the β-cell may explain why individuals taking metformin vs. individuals not taking metformin were more likely to lose more than 15% of baseline body weight, when undergoing tirzepatide (a glp-1 and GIP dual receptor agonist) treatment [19]. Further research should examine the relationship between incretin concentrations and SIRT 1 activity during a nutrition or exercise intervention.

Conclusion

Despite the efficacy of lifestyle interventions for reducing T2D risk for adults and youth at heighten risk (i.e., obesity), the incretin response to such interventions remains unclear. Furthermore, whether an increase or decrease of incretin concentrations, before and after any interventions, is associated with metabolic improvements also remains unknown. Additional studies in large cohorts in adults and youth are warranted to evaluate whether incretin hormone could be an interventional target for preventing T2D or a criterion for evaluating exercise/diet effectiveness.

References

1. Campbell JE, Drucker DJ (2013) Pharmacology, physiology, and mechanisms of incretin hormone action. Cell Metab 17(6): 819-837.
2. Tamborlane WV, Barrientos-Pérez M, Fainberg U, Frimer-Larsen H, Hafez M, et al. (2019) Liraglutide in children and adolescents with type 2 diabetes. N Engl J Med 381(7): 637-646.

3. Lovshin JA (2017) Glucagon-like peptide-1 receptor agonists: a class update for treating type 2 diabetes. Can J Diabetes 41(5): 524-535.
4. American Diabetes Association (2016) Obesity management for the treatment of type 2 diabetes. Diabetes Care 39(1): S47-S51.
5. Otten J, Ryberg M, Mellberg C, Andersson T, Chorell E, et al. (2019) Postprandial levels of GLP-1, GIP and glucagon after 2 years of weight loss with a Paleolithic diet: A randomised controlled trial in healthy obese women. European Journal of Endocrinology 180(6): 417-427.
6. Lepsen EW, Lundgren J, Holst JJ, Madsbad S, Torekov SS (2016) Successful weight loss maintenance includes long-term increased meal responses of GLP-1 and PYY_{3-36}. Eur J Endocrinol 174(6): 775-784.
7. Coutinho SR, Halset EH, Gåsbakk S, Rehfeld JF, Kulseng B, et al. (2018) Compensatory mechanisms activated with intermittent energy restriction: A randomized control trial. Clinical Nutrition (Edinburgh, Scotland) 37(3): 815-823.
8. Weiss EP, Albert SG, Reeds DN, Kress KS, Ezekiel UR, et al. (2015) Calorie restriction and matched weight loss from exercise: Independent and additive effects on glucoregulation and the incretin system in overweight women and men. Diabetes Care 38(7): 1253-1262.
9. Eshghi SR, Fletcher K, Myette-Côté É, Durrer C, Gabr RQ, et al. (2017) Glycemic and metabolic effects of two long bouts of moderate-intensity exercise in men with normal glucose tolerance or type 2 diabetes. Frontiers in Endocrinology 8: 154.
10. Chanoine JP, Mackelvie KJ, Barr SI, Wong AC, Meneilly GS, et al. (2008) GLP-1 and appetite responses to a meal in lean and overweight adolescents following exercise. Obesity (Silver Spring)16(1):202-204.
11. Kahle EB, O'Dorisio TM, Walker RB, Eisenman PA, Reiser S, et al. (1986) Exercise adaptation responses for gastric inhibitory polypeptide (GIP) and insulin in obese children. Possible extra-pancreatic effects. Diabetes 35(5): 579-582.
12. Martins IJ (2016) Anti-aging genes improve appetite regulation and reverse cell senescence and apoptosis in global populations. Advances in Ageing 5: 9-26.
13. Martins IJ (2013) Appetite dysregulation and obesity in Western Countries. Ebook Project. In: Ian Martins (Author), Emma Jones (Ed.), Acquisition Editor LAP LAMBERT Academic Publishing is a trademark of: AV Akademikerverlag GmbH & Co. KG, Germany.
14. Martins IJ (2018) Sirtuin 1, a diagnostic protein marker and its relevance to chronic disease and therapeutic drug interventions. EC Pharmacology and Toxicology 6(4): 209-215.
15. Lingappa N, Mayrovitz HN (2022) Role of sirtuins in diabetes and age-related processes. Cureus 14(9): e28774.
16. Radak Z, Suzuki K, Posa A, Petrovszky Z, Koltai E, et al. (2020) The systemic role of SIRT1 in exercise mediated adaptation. Redox Biology 35: 101467.
17. Song YM, Lee YH, Kim JW, Ham DS, Kang ES, et al. (2015). Metformin alleviates hepatosteatosis by restoring SIRT1-mediated autophagy induction via an AMP-activated protein kinase-independent pathway. Autophagy 11(1): 46-59.
18. Mannucci E, Tesi F, Bardini G, Ognibene A, Petracca MG, et al. (2004) Effects of metformin on glucagon-like peptide-1 levels in obese patients with and without Type 2 diabetes. Diabetes, Nutrition & Metabolism 17(6): 336-342.
19. Małecki MT, Batterham RL, Sattar N, Levine JA, Rodríguez Á, et al. (2023) Predictors of ≥15% weight reduction and associated changes in cardiometabolic risk factors with tirzepatide in adults with type 2 diabetes in SURPASS 1-4. Diabetes Care 46(12): 2292-2299.