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PERSPECTIVE

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Physical activity in the new era of antiobesity medications

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Abstract

Contemporary antiobesity medications (AOMs) are highly efficacious for the treatment of obesity and obesity-related comorbidities. Given this effectiveness, lifestyle factors within the context of AOM treatments need to refocus and move away from efforts to enhance weight loss. Rather, lifestyle considerations should pivot to being complementary to the benefits realized with AOM treatment and be redirected to enhancing holistic patient health and well-being. Physical activity is an important lifestyle behavior that contributes to many health benefits both in conjunction with, and in the absence of, weight loss. Physical activity improves cardiorespiratory fitness, muscle strength, and physical function. Physical activity may attenuate the loss of lean mass that is observed with AOM treatments and may enhance the quality and function of muscle. Physical activity is a key behavior for holistic health within this era of contemporary AOMs that warrants appropriate attention within the clinical care of patients.

Excess weight and adiposity and the related chronic health conditions continue to be significant public health concerns. Contemporary incretin-based antiobesity medications (AOMs) are efficacious for the treatment of obesity and obesity-related comorbidities [1] and on average result in greater weight loss than lifestyle interventions of similar duration alone. However, despite the demonstrated effectiveness of these AOMs, there is a need for continued long-term evaluation of their effectiveness and safety.

Given the current effectiveness of contemporary AOMs, we posit that lifestyle factors within the context of AOM treatments need to refocus and pivot to being complementary to the benefits realized with AOM treatment and also be redirected to enhancing holistic patient health and well-being. A key lifestyle behavior is physical activity, and there is extensive evidence of its health benefits, with many of these benefits realized both in conjunction with, and in the absence of, weight loss.

Physical activity has the potential for reducing weight and adiposity beyond what is achieved with energy restriction alone. However, given the effectiveness of contemporary AOMs for reducing weight and adiposity, physical activity may have importance for other reasons. A shift to holistic health of the patient includes enhancing the benefits achieved with weight loss and using treatments that enhance health in ways that are not optimally achieved with weight loss alone. We posit that physical activity is particularly important in this context for patients receiving AOM treatments. Low cardiorespiratory fitness is a powerful risk factor for cardiovascular disease and all-cause mortality, and higher levels of cardiorespiratory fitness are associated with other health benefits across the life-span that are independent or additive to the effects of lower body weight, lower adiposity, or weight loss [2]. Within the context of weight-loss treatment, cardiorespiratory fitness is improved with inclusion of a sufficient dose of physical activity [3]. A similar pattern has been observed in a study of AOMs that showed that exercise needed to be added to liraglutide to elicit an improvement in cardiorespiratory fitness [4]. Muscle strength is also improved with the inclusion of resistance exercise in the weight-loss treatment plan, but strength is not improved with weight loss alone [3]. Although there are limited data on understanding how AOMs may impact cardiorespiratory fitness, muscle strength, or physical function [1], best practices would support that these benefits will occur with the appropriate dose and mode of physical activity in patients with excess weight and adiposity that may be coupled with additional comorbidities.

There is a loss of lean mass observed with contemporary AOMs [1]. When resistance exercise alone or in combination with aerobic

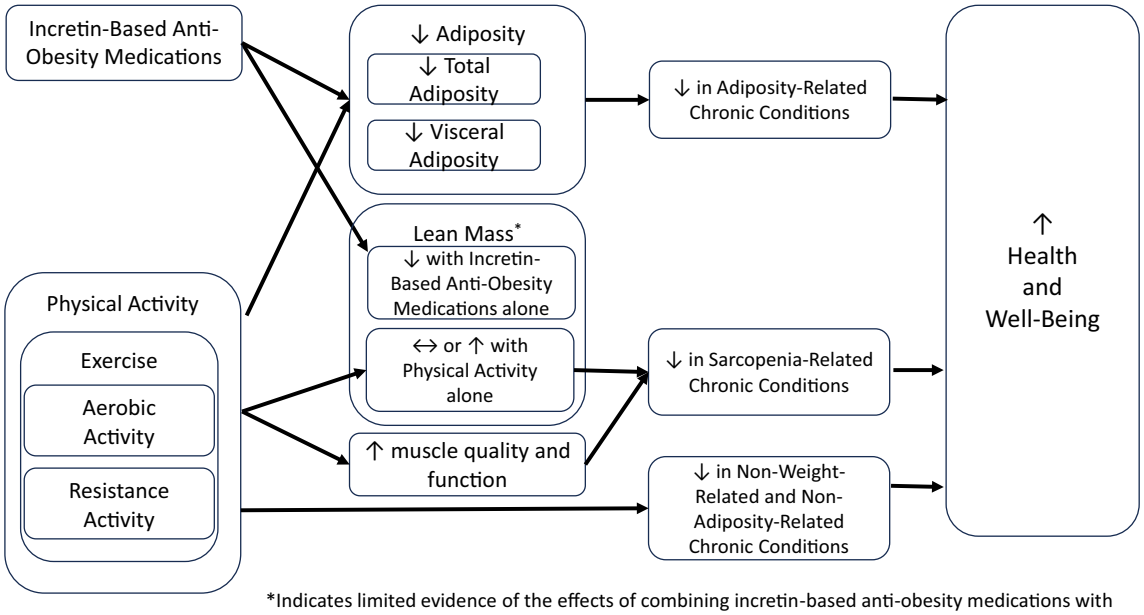

FIGURE 1 Body composition and health benefits of physical activity within the context of glucagon-like peptide-1 (GLP-1) antiobesity medications.

exercise is implemented in adults with obesity, without an accompanying reduced energy intake diet, no loss or a modest increase in lean mass are observed [5]. Moreover, exercise can increase muscle volume and cross-sectional area even in the presence of weight loss, and this can occur with aerobic modes of exercise [6]. However, there are limited data currently available to support that physical activity, whether aerobic or resistance exercise, will partially or completely eliminate the reduction in lean mass in the context of an AOM. Thus, until sufficient data are available within the context of AOMs, we propose applying what has been learned in other medical approaches for obesity treatment. Metabolic/bariatric surgery or very-low energy diets have shown that physical activity has very modest effects on enhancing weight loss or blunting the loss of lean mass [3, 7]. In the presence of diets that reduce energy intake by >500 kcal/day, even resistance exercise may not result in gains in lean mass [8]. As an alternative, we suggest that the focus should shift to lean tissue (muscle) quality, as muscle quality is enhanced with physical activity, even in the presence of reductions in total body weight and lean mass [9] and even when these reductions are induced by medical treatments such as metabolic/bariatric surgery [10]. This is illustrated in Figure 1. This approach would also support the need for clinical evaluations and research studies to include measures of muscle tissue quality and function, in addition to total body composition, to assess the potential influence on health.

Clinical guidelines recommend physical activity to be at a dose of 200 to 300 min per week of moderate-to-vigorous intensity to facilitate enhanced and sustainable weight loss [11]. However, given the efficacy of contemporary AOMs, this dose of physical activity may not be clinically indicated. Rather, an initial physical activity target should be consistent with public health recommendations to reduce sedentary behavior and to appropriately progress to at least 150 min per week of moderate-intensity physical activity (equivalent to a brisk walk) that also includes at least 2 days per week of muscle strengthening activities [12]. Particularly applicable to persons with excess weight and adiposity, health benefits are realized at thresholds of activity below these desired public health targets [12], which may be even more effective when implemented in combination with AOM therapies.

Clinical approaches should go beyond simply prescribing physical activity and need to engage appropriately trained and certified clinical exercise professionals to address the complex needs of patients in collaboration with others on the clinical care team. Approaches need to consider the challenges patients with excess weight and adiposity experience to physical activity engagement, which may include considerations that are unique to patients receiving AOM treatment.

For patients treated with AOMs to realize the benefits of physical activity that contribute to holistic and sustainable health, appropriate systems and approaches need to be in place and implemented. Health care providers prescribing AOMs should consider physical activity within the context of comprehensive care for patients. Health care payers need to facilitate support for the appropriate exercise professionals to be included within clinical patient care and to support resources that promote engagement and sustainability of physical activity. This includes providing equitable and inclusive access to appropriate physical activity programs and treatments. Professional organizations and universities/colleges need to provide appropriate training and certification programs that address the specific physical activity needs of patients treated with AOMs. Pharmaceutical companies have a responsibility to consider how physical activity fits within AOM treatments to enhance effectiveness to optimize holistic patient care. Collectively, holistic patient care should be the priority, with

weight loss just one component of treatment for patients with excess weight and adiposity. We posit that physical activity is a key behavior for holistic health within this era of contemporary AOMs that warrants appropriate attention within the clinical care of patients. We also recognize the importance of dietary considerations within the context of weight-loss treatments with AOMs. Therefore, we recommend that there be a dietary parallel to the perspective provided for physical activity to ensure that patients are prescribed, have access to, and follow a health-promoting diet while receiving treatment with an AOM.

CONFLICT OF INTEREST STATEMENT

John M. Jakicic is a Scientific Advisor for Wondr Health, Inc., and the Principal Investigator for a research grant from Epitomee Medical, Inc., awarded to the University of Kansas Medical Center, and he was a consultant for Education Initiatives, Inc. Renee J. Rogers is a consultant for Wondr Health, Inc. Timothy S. Church declared no conflict of interest.

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