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DERLEME MAKALESİ / REVIEW ARTICLE

EFFECTS OF CHRONOTYPE-BASED NUTRITIONAL MODELS ON CARDIOMETABOLIC RISK FACTORS-CHRONO NUTRITIONAL APPROACHES

KRONOTİPE DAYALI BESLENME MODELLERİNİN KARDİYOMETABOLİK SAĞLIK ÇIKTILARI ÜZERİNE ETKİLERİ-KRONO BESLENME YAKLAŞIMLARI

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ABSTRACT

Cardiovascular diseases (CVD) continue to be a worldwide public health problem. Since it causes multiple comorbid and chronic medical conditions, a versatile approach should be taken in the nutrition therapy of metabolic disorders such as CVD. Meal timing is an important aspect of nutrition therapy as well as meal content. Chrono-nutrition is defined as meal timing. Chrono-nutrition, which is a relatively new field of nutrition science, is thought to be effective in the management of cardiometabolic risk markers such as obesity and metabolic syndrome. In the control of these markers, chronotype and nutritional models based on chronotype are very important. Although there are many studies in the literature investigating the effects of meal timing on health outcomes, the number of studies investigating the effects of nutritional models arranged according to chronotype is insufficient. New studies on this subject are needed.

Keywords: Chrono-nutrition, Circadian Rhythm, Cardiometabolic Risk

ÖZET

Kardiyovasküler hastalıklar (KVH), dünya çapında bir halk sağlığı sorunu olmaya devam etmektedir. Birden fazla komorbid ve kronik tıbbi duruma neden olduğu için KVH gibi metabolik bozuklukların beslenme tedavisinde çok yönlü bir yaklaşıma sahip olunmalıdır. Öğün içeriği kadar öğün zamanlaması da beslenme tedavisinin önemli bir boyutudur. Krono-beslenme ise öğün zamanlaması olarak tanımlanmaktadır. Nispeten yeni bir beslenme bilimi alanı olan krono-beslenmenin, obezite ve metabolik sendrom gibi kardiyometabolik risk belirteçlerinin yönetiminde etkili olacağı düşünülmektedir. Bu belirteçlerin kontrolünde kronotip ve kronotipe dayalı beslenme modelleri oldukça önemlidir. Literatürde öğün zamanlamasının sağlık çıktıları üzerine etkilerini araştıran çok sayıda çalışma bulunmasına rağmen kronotipe göre düzenlenmiş beslenme modellerinin etkilerini araştıran çalışma sayısı yetersizdir. Bu konuda yapılacak yeni çalışmalara gereksinim duyulmaktadır.

Anahtar Kelimeler: Krono-Beslenme, Sirkadiyen Ritim, Kardiyometabolik Risk

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1. INTRODUCTION

The circadian clock system that expresses these rhythms is common in many species, from prokaryotes to mammals. "Circadian" means "about a day" in Latin, and therefore "circadian rhythm" refers to a cycle of approximately 24 hours. This system responds to daily environmental changes such as the light-dark cycle and food consumption (Tahara & Shibata, 2014, p. 320). The circadian timing system consists of numerous cellular oscillators found in the hypothalamic suprachiasmatic nucleus (SCN), non-SCN brain structures, and other peripheral tissues. The SCN is synchronized by photoreceptors and environmental light-dark cycles (Rosenwasser & Turek, 2015, p. 409).

The chronotype is defined as the circadian typology. It is closely related to nutrition and health outcomes. Due to the possible effects of the chronotype on metabolism, the most appropriate dietary models for the timing, frequency, and order of meals suitable for the chronotype are studied (Almoosawi et al., 2019, p. 30). This new field of research examining the impact of meal timing on health outcomes is called chrono-nutrition and links nutrition research with chrono-biology. Chrono-nutrition; explains the interaction between sleep, nutrition, and urbanization (Pot, 2018, p. 189).

Skipping meals and frequent snacking habits are more common today due to the increasing disorders in nutritional habits. Meal timing is a very effective factor in physiological rhythms such as glucose rhythm. It has been reported that there is a significant relationship between the late meal pattern and the delay in plasma glucose rhythm (Wehrens et al., 2017, p. 1771). Skipping meals and later eating habits are associated with various cardiometabolic risk factors such as obesity, metabolic syndrome, insulin resistance, inflammation, hypercholesterolemia, hypertension, diabetes, and higher body mass index (BMI) (St-Onge et al., 2017, p. 96). Chrono-nutrition, a new discipline investigating the this relationship between circadian rhythm, nutrition, and metabolism, has attracted attention in recent years (Kessler & Pivovarova-Ramich, 2019, p. 1911). Although there are many studies examining the effects of meal timings and energy density in meals on health outcomes, the number of studies investigating the effects of chronotype-based nutritional approaches is insufficient. The aim of this review is to elucidate the effects of chronotype-based nutrition models on cardiometabolic risk markers and to explain in detail the chrono-nutrition approaches with circadian rhythm. This review was created by searching the literature using keywords such as "Circadian rhythm, clock genes, chronotype, cardiometabolic risk, health outcomes, and chrono-nutrition" from databases such as Pub-Med, Cochrane, and Google Scholar.

1.1. Circadian Rhythm

The circadian rhythm is a biological clock designed for the healthy functioning of individuals' daily rhythms for 24 hours. Thus, it has become a self-controlled system of the human body to regulate eating habits, activities, and body functions (Senthilnathan & Sathiyasegar, 2019). The main regulator of the circadian rhythm in our body is the suprachiasmatic nucleus of the anterior hypothalamus. The SCN is synchronized by environmental light-dark cycles through different photoreceptors and neural pathways that mediate visual perception. The circadian rhythm is regulated not only by the SCN but also by various oscillator/clock genes found in peripheral tissues and organs. SCN also includes peripheral circadian clocks via neural and neuroendocrine pathways (Rosenwasser & Turek, 2015, p. 403).

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Clarifying the relationship between circadian rhythm and cellular biology is very important for understanding the physiological and pathological mechanisms underlying diseases. Positive and negative molecular feedback loops regulate circadian rhythm expressions. There are several clock genes such as Brain and Muscle Arnt-Like protein-1/2 (BMAL1/BMAL2), Circadian Loco motor Output Cycles Kaput (CLOCK), Cryptochrome (CRY1/CRY2), and Period (PER1/PER2/PER3) genes that regulate and control transcription and translation (Reddy et al., 2021). There are 3 main helix-loop-helix (HLH)/PAS domains in the primary feedback loop, such as CLOCK, BMAL1, and Neuronal PAS domain protein 2 (Npas2), which contain positive transcription factors (Kelleher et al., 2014, p. 11). The CLOCK and BMAL1 genes form a heterodimer and initiate heterodimerization and transcription of the PER1, PER2, PER3, CRY1, and CRY2 genes containing E-box cis-regulatory sequences (Ko & Takahashi, 2006, p. 272). They activate the transcription of PER1, PER2, CRY1, and CRY2 by binding the cis-elements of E-boxes within the promoters of genes. In the negative feedback loop, the clock-controlled genes PER and CRY accumulate in the cytosol and become multimerized. This complex, which is transferred to the nucleus, binds to the BMAL1 promoter, blocks BMAL1/CLOCK activity, and terminates the transcription of its genes. PER-CRY complexes are degraded by phosphorylation with casein kinase-1 (CK1) and F-box/LRR-repeat protein-3, thus ending the inhibition of CLOCK-BMAL1 and closing the negative feedback loop (Potter et al., 2016, p. 588).

1.2. Chrono-Nutrition Patterns and Their Effects

Nutritional patterns regulate peripheral circadian clocks. Peripheral clock systems also control the absorption, digestion, and metabolism of nutrients. This shows that there is a bidirectional interaction between the circadian rhythm and nutrition. These interactions are termed "chrono-nutrition" (Shibata et al., 2013, p. 2194). Chrono-nutrition is an emerging field that explains the relationship between circadian rhythm and metabolic health. While circadian rhythm disorder creates negative metabolic results, optimizing circadian rhythm according to feeding times can be effective for improving metabolic health (Flanagan et al., 2021, p. 54).

In the nutritional sciences, chrono-nutrition combines nutritional research with chrono-biology. Chrono-nutrition can mediate the effects between sleep, nutrition, and urbanization (Pot, 2018). At present, the term "chrono-nutrition" is used to describe the relationship between food and the circadian clock system (Tahara & Shibata, 2014, p. 189).

Chrono-nutrition is influenced by the "chronotype" of individuals. Meal timing has an impact on the postprandial glucose response to a meal. The circadian patterns of postprandial glycemia in similar meals consumed in the evening or the morning differ. Not only the type and amount of food consumed but also the timing of meals closely affect health outcomes. Meal timing and dietary components play an important role in regulating circadian clocks and improving metabolic health. Circadian rhythm synchronization is essential for optimal health. When this synchronization is disrupted, the risk of obesity increases (Henry et al., 2020, p. 4). Both foods and meal timing can affect the circadian rhythm. So chrono-nutrition has two aspects: 1) Effects of nutrients on circadian rhythm 2) Meal timing influences circadian rhythm outputs (Oike et al., 2014, p. 206). In addition, circadian rhythm and intrinsic clock also affects food intake and eating habits. Besides these two factors, sleep is an important determinant of the intrinsic clock (Pot, 2018, p. 195). Time-restricted feeding patterns synchronize circadian rhythms. However, unhealthy eating habits cause circadian asynchrony and weaken circadian rhythms (Oike et al., 2014, p. 206).

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Xiao et al. (Xiao et al., 2019, p. 1703) 4 intervals were defined according to sleep time in order to investigate the relationship between meal timing and BMI depending on chronotype; morning (within 2 hours of waking up), night (within 2 hours before going to sleep), and two midday periods (midpoint of awake time and sleep time). It was found that energy consumption during the morning window was associated with lower BMI and this relationship was stronger in people with morning chronotype. Energy expenditure during the night window is associated with a higher probability of BMI, especially in people with the later chronotype (Xiao et al., 2019, p. 1703). In another study investigating the effect of sleep and meal timing on insulin sensitivity in overweight adults under the same sleep duration and nutritional conditions, participants were given normal meal patterns (1, 5, 11, and 12.5 hours after waking up) and late meal patterns (4.5, 8.5, 14.5, 12.5, and 16 hours later) intervention was applied. It was seen that it did not affect the acute insulin response. Besides glucose tolerance test was found to be lower in normal meal order. Sleep-meal interaction and meal times were found to be effective on glucose and insulin throughout the night (Pizinger et al., 2018, p. 35).

Long periods of fasting sensitize the leptin response to the next meal. It also eliminates the leptin increase caused by Dexamethasone. Meal timing is an important factor in determining the daily rhythm of leptin. However, the leptin response to a standard meal taken in the evening is higher than the same meal taken in the morning (Elimam & Marcus, 2002, p. 147). A high-carb and protein breakfast can prevent weight regain by reducing the suppression of fasting ghrelin. Meal timing and macronutrient composition should be regulated to achieve long-term weight loss (Jakubowicz et al., 2012, p. 327).

1.3. Effects of Nutritional Models Based on Chronotype on Cardiometabolic Risk Factors

Evening chronotype, sleep disorders, and social jetlag are important risk factors for chronic diseases such as obesity, metabolic syndrome, and cardiovascular disease (McMahon et al., 2019, p. 500). This effect is also mediated by the microbiota. The gut microbiota also has a circadian rhythm. This rhythm is largely regulated by meal timing. Due to this relationship between circadian rhythm and microbiota, probiotics and prebiotic treatments are of interest to improve the effects of impaired circadian homeostasis (Voigt et al., 2016, p. 193). Mice without intestinal bacterial colonization had impaired hepatic and central clock gene expression. In vitro, microbial metabolite (acetate and butyrate) administration was found to affect PER2 and BMAL1 gene expression in the liver. In vivo, exogenous butyrate administration in bacteria-free mice increased the PER2:BMAL1 ratio in hepatic and mediobasal hypothalamic cells (Matenchuk et al., 2020). Papadopoulou et al. (Papadopoulou et al., 2020, p. 322) investigated the effect of timing of main meal consumption on the microbiome and cardiometabolic biomarkers in healthy adults (>18 years of age). Two different dietary interventions (lunch or evening energy intensity) were used in the study. The results of the study showed that meal timing had no significant effect on stool short-chain fatty acids concentration, stool energy loss, microbial profile, and relative abundance of bacterial species, but Escherichia coli concentration was significantly higher during afternoon energy-dense diet intervention (Papadopoulou et al., 2020, p. 322).

Obesity and unhealthy eating habits are associated with the evening chronotype. In addition, it was determined that the physical activity levels of the evening types, their compliance with the Mediterranean Diet were lower, and their cigarette consumption was higher (Muscogiuri et al., 2020, p. 1360). It has been determined that the evening types exhibit a more unhealthy lifestyle, perform less physical activity, smoke more frequently, are more likely to have Type 2 diabetes, and thus have a higher risk of cardiovascular disease compared to other chronotypes (Muscogiuri et al., 2021, p. 895). Similarly, Wong et al. (Wong et al., 2015, p. 4616) found that social jetlag was associated with lower high-density lipoprotein-cholesterol (High-Density Lipoprotein-HDL), triglyceride, fasting plasma insulin levels, insulin resistance, and adiposity. Thus, social jetlag was found to be associated with metabolic risk factors that predispose to atherosclerotic cardiovascular disease (Wong et al., 2015, p. 4616). Rodríguez-Muñoz et al. (Rodríguez-Muñoz et al., 2020, p. 1906) reported that the evening types had significantly lower consumption of fruit, vegetables, legumes, cereals, and olive oil, and their breakfast skipping habits were higher (Rodríguez-Muñoz et al., 2020, p. 1906). When examining the relationship between chronotype and diet quality in pregnant women, it was found that morning chronotype was associated with longer eating times, earlier first meals, more meals, and better diet quality in the first trimester of pregnancy (Gontijo et al., 2019, p. 79). In addition, the evening chronotype was associated with more severe obesity and lower weight loss after bariatric surgery in extremely obese individuals (Ruiz-Lozano et al., 2016, p. 1553).

Energy density in meals is an important factor, and it is known that higher energy density in the evening meal may adversely affect cardiovascular health (Zuraikat et al., 2021, p. 1155). It is reported that consuming more of the daily energy in the morning has positive effects on weight loss and weight control. Versteeg et al. (Versteeg et al., 2018, p. 160) applied a hypocaloric diet intervention based on consuming 50% of daily energy in the morning or evening for 4 weeks in 12 obese individuals with insulin resistance. There was no difference in meal macronutrient composition and weight loss, but endogenous glucose production and hepatic and peripheral insulin sensitivity were significantly improved with weight loss. However, no difference was found between the morning and evening types (Versteeg et al., 2018, p. 160).

Meal timing influences health outcomes through metabolic and circadian markers. St-Onge et al. (St-Onge et al., 2019, p. 80) investigated the effects of delaying sleep and meal times for 3.5 hours on appetite and satiety indicators and determined that there was a significant sleep-eating interaction on ghrelin concentrations. Additionally, it has been found that lower ghrelin concentrations are seen under normal sleep and normal meal timing conditions (St-Onge et al., 2019, p. 80). Bandín et al. (Bandín et al., 2015, p. 831) reported that individuals with late lunch consumption had a lower respiratory coefficient, a higher postprandial glucose level, a lower cortisol level, and a lower postprandial wrist temperature (Bandín et al., 2015, p. 831).

Papadopoulou et al. (Papadopoulou et al., 2020, p. 327) investigated the effect of timing of main meal consumption on the microbiome and cardiometabolic biomarkers in healthy adults (>18 years of age). Two different dietary interventions (lunch or evening energy intensity) were used in the study. The results of the study showed that meal timing had no significant effect on stool short-chain fatty acids concentration, stool energy loss, microbial profile, and relative abundance of bacterial species, but Escherichia coli concentration was significantly higher during afternoon energy-dense diet intervention (Papadopoulou et al., 2020, p. 327). It was also found that morning energy-dense diet consumption significantly improved endogenous glucose production, hepatic and peripheral insulin sensitivity, and intrahepatic triglyceride content with weight loss (Versteeg et al., 2018, p. 160), with a higher metabolic intermediate response to the morning meal (Takahashi et al., 2018, p. 1770). Evening meal consumption is associated with an increase in BMI, resting heart rate, and HDL cholesterol (Lucassen et al., 2013, p. 5).

As discussed above, although there are many studies examining the effects of meal timings and energy density in meals on health outcomes, the number of studies investigating the effects of chronotype-based nutritional approaches is insufficient. The first and the only study to our knowledge in this context was conducted by Muñoz et al. (Galindo Muñoz et al., 2020, p. 1045) in 2020. In this study, it was investigated whether a diet model adjusted according to the chronotype of the person was more effective than the standard diet models, and the participants were divided into 2 groups control (standard hypocaloric diet) and chrono-group (diet adjusted according to chronotype). In conclusion, although both groups improved anthropometric parameters at the end of the 12-week dietary intervention, a higher reduction in percent total body weight loss (%TWL), BMI, and waist circumference was obtained in the chronotype-adjusted diet group compared to the control group treated with the ordinary hypocaloric diet (Galindo Muñoz et al., 2020, p. 1045).

2. CONCLUSION

In conclusion, the evidence to date indicates that chrono-nutrition may be beneficial not only for improving the metabolic health of the general population but also for improving the health of certain groups (for example, shift workers and transmeridian travelers with jet lag) and for the treatment of chronic metabolic diseases such as cardiovascular diseases. Since the pathogenesis of cardiovascular disease is multifactorial, up-to-date approaches and measures are needed for effective prevention and treatment. In this context, the harmony of the circadian rhythm has gained particular importance. Circadian rhythm harmony is provided by regulating sleep, meal order, and physical activity times. For this reason, chronotype and chronotype-based nutritional models are important in the control of cardiometabolic risk markers. Although there are many studies in the literature investigating the effects of meal timing on health outcomes, the number of studies investigating the effects of diet models arranged according to chronotype is insufficient. Randomized-controlled intervention studies are needed in this content.

DECLARATION OF THE AUTHORS

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