The Effect of Photobiomodulation Therapy in Obese Mice: A Review

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ABSTRACT
Obesity involves genetic, epigenetic and environmental factors such as physical inactivity and hypercaloric diets. The obesity associated with cardiovascular disease leads to hypertension. The main site where the mechanism of obesity present is Adipose Tissue. Brown Adipose Tissue and White Adipose Tissues plays a key role in the obesity. Photobiomodulation therapy (PBMT) is also known as low-level therapy which is suggested for the treatment of wound healing, tissue regeneration, increase circulation and acute inflammation. Photobiomodulation therapy is painless treatment which triggers at various sites without side effects. PBMT can reduce both adiposity and inflammatory infiltrate in adipose tissue. The free fatty acid generation and insulin resistant adipose tissues will be reduced by photobiomodulation therapy. The presence of excess glucose is also ameliorated by the photobiomodulation therapy. Through this photobiomodulation therapy either initiate or help excess weight loss as well as ameliorating inflammation. Uses of Low-level therapy for localized fat reduction do not affect lipid serum levels. This review discusses about how the photobiomodulation therapy involves in the treatment of obesity in both mice and rat models

Introduction

The term obesity is defined as normal or excessive fat accumulation that presents a risk to health. Developing countries like in United States, obesity is rapidly growing epidemic and affects the lots of citizens including children worldwide (Seidell et al., 2015) (Bluher et al., 2019) (Karpe et al., 2015). Diets high in trans fat are associated with increased risk of overweight and obesity in prospective studies (He et al., 2014).The main site is Adipose tissue where the physical and functional changes of obesity occur (Junior et al., 2017) (Croghan et al., 2020).Obesity is a polygenic disease that involves genetic, epigenetic and environmental factors (such as physical inactivity and hypercaloric diets)(Gold et al., 2011).This disease which has different methods that could promote treatment and control of this disease are being constantly investigated. Some data indicates that low-level laser therapy can help with cellulite, manage lipids, and offer non-invasive body contouring (Heymsfield SB et al., 2017) (Jackson et al., 2009).

Research in rodent models of dietary and genetic obesity has explored the causes of obesity-induced inflammation, but the exact cause for triggers is still unclear. Obesity enhances intestinal permeability, leading to higher levels of lipopolysaccharides (LPS) from Gram-positive bacteria in the blood stream (Amar et al., 2009). Photobiomodulation (PBM) therapy is a non-invasive treatment that employs a low- intensity light source to produce therapeutic effects (Braverman et al., 1989). Thus, photo biomodulation (PBM) therapy uses low-intensity light sources like laser or light-emitting diodes (LEDs) to help alleviate cellular stress. It works by boosting the activity of anti-inflammatory enzymes (Liang et al., 2006) and decreasing the activation of inflammation-promoting pathways (Begum et al., 2013). PBMT is thought to influence enzyme activity and cell cycle progression, thereby impacting the redox-sensitive transcription factors in cells. This therapy boosts the production of antioxidants through enzymatic processes, which are crucial for the wound healing process (Duan et al., 2018).

Recently, excessive calorie intake, particularly from high-fat diets, has been identified as major controllable risk factor for elevated blood glucose levels and the onset of type-2 diabetes (Rachek et al., 2014). Type-2 diabetes and obesity are marked by insulin resistance, which results in decreased insulin sensitivity in peripheral tissues. Free fatty acids (FFAs) play a crucial role in causing this insulin resistance (Samuel et al., 2016). The exact mechanism behind insulin resistance associated with obesity is not yet completely understood. However, evidence indicates that the buildup of intracellular fat and the subsequent rise in fatty acid metabolites contribute to the development of insulin resistance (Mitu et al., 2013).

Thus, obesity-particularly when involving central and visceral fat- and insulin resistance have been closely linked to the onset of metabolic syndrome and cardiovascular diseases (Padwal et al., 2014). Dietary interventions such as reducing calorie intake, following a low-carb diet, or increasing protein consumption can effectively aid in weight loss and decrease visceral fat by creating a state of negative energy balance (Sackner-Bernstein et al., 2015) (Astrup et al., 2000) (Verheggen et al., 2016) (Karkada et al., 2022) (Oishi et al., 2024).

Mechanism of PBM on obesity

When they treat with PBM appears to decrease the body mass and visceral adipose tissue. After few weeks the high fat diet led to a significant increase and PBM started at the moment the blood pressure increased. Experimental animals from the high fat diet group showed a significant decrease in blood NO concentration. To verify the endothelial function, they performed the vascular reactivity experiments in isolated aortic rings

Repeated exposure to low-dose ultraviolet radiation (UVR) in mice helped prevent glucose intolerance and fat build up in the liver through the release of nitric oxide from the skin, and it also lowered levels of the inflammatory marker IL-6. However, this effect was not replicated by dietary nitrate supplementation. A single low dose of UVR significantly increased UCP-1levels in the brown adipose tissue of mice on a low-fat diet within 24 hours, but did not affectUCP-1expressioninmiceonahigh-fatdietovera12-weekperiod.Extensivestudies on circadian rhythms showed no major changes in UCP-1 expression due to UVR did lower skin temperature (Dhamrait et al., 2020).

The studies are done on the Antioxidant enzymes activity in obesity as follows:

Total-SOD [Superoxide dismutase activity]

Sedentary groups including both normal group with photobiomodulation sedentary normal diet plus laser [SNL] and sedentary high fat diet exhibited lower total -SOD activity compared to the normal sedentary group [SN]. No significant changes occur among the other groups.

CAT Activity [catalase assay]

Catalase activity was significantly reduced in the sedentary normal diet laser, sedentary high fat diet and normal aerobic training groups compared to the sedentary normal diet group.

Glutathione peroxidase [GPx]

Aerobic training resulted in a decrease in glutathione peroxidase activity in the normal group compared to sedentary normal diet. Combining photobiomodulation with aerobic raining in obese animals lead to increase in GPx activity (Aquino et al., 2017).

Mechanism of PBM (Photo biomodulation) on insulin resistance

Insulin resistance is when the body cells don't respond effectively to insulin, which impairs the ability to clear glucose from the bloodstream and properly absorb it. This affects various tissues like fat, liver and muscle making it harder for the body to regulate blood sugar levels (Yao et al., 2016).

To improve blood glucose levels and insulin sensitivity in diet-induced diabetes, photo biomodulation could potentially be used to manage obesity. PBM also prevented liver fat accumulation and insulin resistance. Additionally, PBM led to increased activation of AMP-activated protein kinase, reduced the activity of a key protein involved in lipogenesis (sterol regulatory element binding protein 1), and improved insulin sensitivity in the liver. The study also observed activation of Ca^{2+}/calmodulin-dependent protein kinase β, suggesting that PBM could have broad, positive effects on various tissues and systems related to obesity (Bicknell et al., 2019).

PBMT enhanced glucose tolerance, insulin sensitivity, and reduced fasting insulin levels. It also decreased fat accumulation and inflammation in adipose tissue. PBMT improved phosphorylation of Akt in both adipose and muscle tissues, reversed reduced AS160 phosphorylation and Glut4 content in fat, and corrected mitochondrial and β-oxidation protein changes in muscle caused by a high-fat diet. Overall, PBMT effectively improved insulin resistance and glucose metabolism in mice on a high-fat diet (Silva et al., 2020).

PBM therapy reduces free fatty acid production and release in insulin-resistant fat cells by targeting free radicals and activating fat-cell-destroying pathways. It also helps lower excess glucose in diabetic mice. When combined with exercise, PBMT enhances body composition, reduces inflammation, and may promote the browning of adipose tissue (Gong et al., 2020).

Impact of laser therapy on reducing obesity in individuals with high body weights may vary depending on how often the laser is applied. Additionally, the effectiveness of the therapy could be influenced by factors such as the person's age, pain levels,inflammation, degree of insulin resistance, overall health, and both the duration and severity of their obesity, as well as the specifics of their laser treatment (Croghan et al., 2020).

Conclusion

To our best knowledge, the present study is the first to investigate the effects of PBM therapy on HFD-induced obesity and insulin resistance and cellular signaling in mice. This review shows that photobiomodulation therapy (PBMT) could be a new, painless way to treat obesity and related problems like insulin resistance. These findings suggest that PBMT can help reduce body fat, lower inflammation, and improve metabolic health in mice fed a high-fat diet. The therapy was effective in reducing body weight and fat around the organs and also helped improve blood vessel function and antioxidant enzyme activity. More researchers needed to fully understand how it works. Overall Photobio modulation therapy appears to be a promising additional treatment for obesity and its related issues.

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