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The Effects of Intermittent Fasting on Type 2 Diabetes

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Abstract

Type 2 diabetes occurs when a body does not use insulin properly: either the body begins to resist insulin or the pancreas does not produce enough insulin. The exact cause of type 2 diabetes is unknown, but genetic and environmental factors appear to be key contributors to its development. Because the prevalence of this condition is increasing, it is important to find new ways to manage it. One such way is intermittent fasting. Intermittent fasting is a cycle that requires a specific eating time followed by a voluntary fasting time. This repeating cycle is known to provide many benefits including weight loss, increased energy, mental focus, cardiovascular health, and reversal of diabetes. There have been few studies on the effects of intermittent fasting on type 2 diabetes. Many of these studies were completed on rodents, while a few focused on human subjects suffering from type 2 diabetes. All studies described in this review have found benefits of intermittent fasting relating to type 2 diabetes, but the mechanisms the researchers found vary. The aim of this review is to present the research established on intermittent fasting and type 2 diabetes while acknowledging the differences in results and the need for further study. The sections of this review will explore the effects of intermittent fasting on insulin, the mechanisms that improve insulin sensitivity, as well as the feasibility of intermittent fasting as a treatment strategy for type 2 diabetes.

Introduction

The prevalence of type 2 diabetes has been steadily increasing over the years. It is predicted that by the year 2035 592 million people will be diagnosed with this type of diabetes (Baumeier et al. 2015). Type 2 diabetes is a metabolic condition where a person's body does not use insulin properly, meaning that the body resists insulin or the pancreas no longer produces a sufficient amount of insulin. The result of improper insulin usage is hyperglycemia, elevated levels of glucose in the blood. Hyperglycemia can cause drastic effects on the body such as excessive thirst, increased hunger, fatigue, blurred vision, slow-healing sores, dark spots on the skin, and frequent infections if not treated properly (Mayo Clinic Staff 2020). Diabetes is also linked to more serious conditions such as cardiovascular disease, neuropathy, and kidney failure (Arnason et al. 2017). The exact cause of type 2 diabetes still remains unknown; however, environmental and genetic factors appear to contribute to its onset. Current treatment strategies for type 2 diabetes include lifestyle changes in exercise and diet, medications, and sometimes a combination of the two.

One such lifestyle change is intermittent fasting, an eating plan in which an individual has designated eating periods and designated fasting periods which can range from sixteen hours to even several days. Fasting is defined as abstaining from all calories; therefore, when fasting, an individual may consume water, black coffee, and even some teas (Furmli et al. 2018). People engage in fasting periods because such periods can have numerous benefits including improved mental clarity, heart health, memory, and tissue health. Additionally, intermittent fasting can aid in diabetes management (Johns Hopkins Medicine 2020). This review will focus on the last of these listed benefits, diabetes management.

Research on the effects of intermittent fasting on type 2 diabetes began with rodents. Results from these studies showed increased insulin sensitivity, increased beta cell mass, and reduced fat cells in the liver (Anson et al. 2003; Wei et al. 2018; Kim et al. 2017; Baumeier, et al. 2015; Belkacemi et al. 2011). Further research was completed on humans–some diagnosed with diabetes, some prediabetics, and some healthy (Furmli et al. 2018; Larson-Meyer et al. 2006; Arnason et al. 2017; Lim et al. 2011). These studies reported the same benefits as the rodent studies. However, a study on rodents by Lui (2017) found the opposite of these results. With these conflicting results, intermittent fasting has not yet been popularized by clinicians as a treatment plan for type 2 diabetes because more research on the long-term effects and efficacy of fasting humans is necessary before such action can become a reliable treatment option for type 2 diabetes (Grajower and Horne 2019). Discussing the effect of intermittent fasting on insulin sensitivity, the mechanisms by which intermittent fasting improves glycemic control, and the feasibility of intermittent fasting for those who practice it, this review illustrates the promise of intermittent fasting as a treatment for type 2 diabetes.

Intermittant Fasting and Diabetes

One of the major factors in the development of type 2 diabetes is insulin resistance as it is linked to obesity, a causative environmental factor of type 2 diabetes. The work of Larson-Meyer (2006) demonstrates that insulin resistance is due to an increase in fat cell size, but it is not related to increased fat cell deposition. Instead, the fat cells that contribute to insulin resistance are thought to be found in visceral and hepatic tissues (Baumeier et al. 2015; Wei et al. 2018; Kim et al. 2017). Other research suggests increased fat cells in muscle tissue contribute to insulin resistance. For example, Baumeier's (2015) study on diabetic mice showed reduced fat cells in muscle tissue contributing to decreased insulin resistance, but a similar study on humans showed no significant change in lipids in muscle tissue (Larson-Meyer et al. 2006).

Current research on intermittent fasting and diabetes suggests there may be a decrease in overall insulin levels in participants who engage in fasting. A study completed on diabetic sand rats found that the levels of insulin following alternate day intermittent fasting of fifteen hours were always lower than the non-fasting control sand rats (Belkacemi et al. 2011). Similarly, a study by Anson and colleagues (2003) also found lower levels of insulin in mice who completed an alternate day intermittent fast of twenty-four hours. Furthermore, a study on prediabetic men agreed with these results, showing a lower level of insulin (Sutton et al. 2018). In this trial the insulin levels were reduced

most significantly in the participants who had a greater incidence of hyperinsulinemia at the baseline testing before beginning intermittent fasting. The reduced insulin levels persisted in seven out of eight participants for the seven monitored weeks following the five week fasting phase (Sutton et al. 2018).

There is no absolute answer for how intermittent fasting affects insulin resistance since much of the research has had conflicting results. One study on mice found no significant reduction of insulin resistance (Liu, 2017). However, two other studies on mice found that intermittent fasting does reduce insulin resistance (Baumeier et al. 2015; Wei et al. 2018), though both mentioned the need for further study on human subjects regarding intermittent fasting. One such study on humans with type 2 diabetes was completed by Arnason and colleagues (2017). All participants in this study were given a fasting goal of eighteen-twenty hours per day; however, Arnason et al. found no significant reduction in insulin resistance. Other studies on adults with type 2 diabetes and with prediabetic men resulted in a reduction of insulin resistance and an increase in insulin sensitivity following fasting periods (Sutton et al. 2018; Lim 2011). The varying results found by these researchers illustrate the research that still needs to be done on the effect of intermittent fasting on insulin resistance and sensitivity.

One particular study relating intermittent fasting and insulin is worth mentioning. In this study focusing on patients with type 2 diabetes, the patients successfully discontinued using insulin to manage their diabetes (Furmli et al. 2018). With participants fasting for twenty-four hours three times a week, the researchers reported that participants were able to wean off of their insulin safely until they no longer needed it. Two of the three participants were also able to discontinue the oral medications they were taking to manage the condition. This study suggests the reduction of insulin resistance reported by Baumeier (2015), Wei et al. (2018), Sutton (2018), and Lim (2011).

Mechanisms for Improved Insulin Sensitivity

Increased Beta Cells

It is widely agreed upon that intermittent fasting strengthens beta cell functioning (Liu et al. 2007; Anson et al. 2003; Wei et al. 2018; Sutton et al. 2018; Baumeier et al. 2015). However, researchers have described various mechanisms by which strengthened beta cell functioning is accomplished. One such mechanism is the fasting-induced stimulation of a progenitor signal called NEUROG3 (Liu et al. 2017; Wei, 2018). Liu et al. (2017) examined the pancreas of a fasting mouse and found an increased number of NEUROG3 cells, cells that stimulate the regeneration of beta cells (Liu et al. 2017). The same results were confirmed by Wei et al. (2018). These findings suggest that intermittent fasting improves insulin sensitivity by increasing the mass of beta cells and therefore increasing insulin secretion. Baumeier (2015) suggests that PSMD9, a regulator protein, is responsible for increased beta cell functioning, reporting that levels of PSMD9 were elevated in intermittent fasting mice. The function of this regulator protein is to protect beta cells. This insinuates that intermittent fasting improves insulin sensitivity by preventing beta cell loss.

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Activation of Autophagy-Lysosome Pathway

Recent research has considered the role of the autophagy-lysosome pathway in the functioning of insulin production. This pathway is a key player in maintaining beta cells and in insulin secretion (Liu et al. 2017; Wei et al. 2018). TFEB, a coding protein, is stimulated by intermittent fasting. It functions in regulating autophagic flux in pancreatic beta cells. Liu (2017) found that a decrease in autophagic flux was accompanied by a decrease in TFEB in mice with diabetes. Liu's team took their study one step further by eliminating the function of TFEB in one group and stimulating its function in another. Results supported the theory that TFEB induces the autophagy-lysosome pathway. This pathway is important because it degrades cells with malfunctioning mitochondria and harmful white adipose cells in diabetics (Liu et al. 2017; Wei et al., 2018). Overall the autophagy-lysosome pathway contributes to beta cell survival and thus, heightened insulin production.

Reduced triacylglycerol levels in liver and pancreatic tissue

There is a common consensus among researchers that intermittent fasting lowers triacylglycerol levels (Larson-Meyer et al. 2006; Lim et al. 2011; Belkacemi et al. 2011; Kim et al. 2017). Such lowered levels might be significant because Lim et al. (2011) have found that just before the onset of type 2 diabetes, triacylglycerol levels are elevated; as such elevated levels are a common indicator of type 2 diabetes. One study on forty-eight humans suggested that a decrease in triacylglycerol levels in the liver and pancreas stimulates the return of beta cells (Larson-Meyer et al. 2006). Another reported similar findings in rats, stating that lower levels of triacylglycerol in the liver prevents the transport of these lipids to the pancreas where they can damage beta cells (Lim et al. 2011); such aversion of lipids to the pancreas is important in preserving beta cell health and ultimately preventing insulin resistance. Additionally, Belkacemi et al.'s study with rats (2011) observes this inverse relationship between triacylglycerol levels in the liver and insulin sensitivity. Results showed that the triacylglycerol levels in the liver of fasting rats was half as much as the triacylglycerol levels of non-fasting rats. Research by Kim and colleagues (2017) revealed a lower overall weight of the liver in intermittent fasting mice than in the non-fasting control group. They attributed this to lower levels of lipid accumulation in the fasting mice. While these four studies all agree that intermittent fasting results in lower triacylglycerol levels in the liver and pancreas, Sutton (2018) reports an increase in triacylglycerol levels in fasting subjects. This finding was acknowledged as contradictory and was explained by possible re-esterification of the triacylglycerides. The researchers believed this was a possibility because the measurements were taken in the morning following the long fasting time of 12-18 hours. This result warrants further research to ensure the accuracy of the data collected. The majority of research agrees that one mechanism by which intermittent fasting ameliorates type two diabetes is the lowering of triacylglycerol levels in the liver and furthermore in the pancreas.

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Feasibility of Intermittent Fasting as a Treatment Option

Effective Without Increased Exercise

There is limited research on intermittent fasting and exercise. Larson-Meyer et al.'s study (2006) comparing the effect of intermittent fasting with the effect of intermittent fasting combined with increased exercise showed no difference in weight loss, insulin sensitivity, or fat mass in liver and visceral tissues between the two groups. A second study reported unclear results on how exercise affected the benefits of intermittent fasting. Participants in this study self-reported their exercise levels each day, so there was no way to determine any patterns (Arnason et al. 2017).

Effective Without Caloric Restriction and Weight Loss

In these studies, it is evident that intermittent fasting, not caloric restriction, is the cause of most benefits observed. One study found that caloric restriction alone did not improve insulin sensitivity while intermittent fasting alone did (Baumeier et al. 2015), demonstrating the importance of the intermittent fasting regimen in achieving results. Two other studies provided their subjects with food and enough calories to maintain their weight in order to observe the effects of intermittent fasting independent of weight loss. Both of these studies found that participants still experienced increased insulin sensitivity even without weight loss (Anson et al. 2013; Sutton et al. 2018). Another study showed that intermittent fasting combined with caloric restriction enhanced the benefits of intermittent fasting (Klempel et al. 2012). In this study, weight loss, decreased waist circumference, increased insulin sensitivity, and lower lipid levels were among the enhanced benefits. Such findings suggest that intermittent fasting is effective without weight loss.

Participant Experiences

One reason intermittent fasting seems a promising treatment is that it creates positive participant experiences. In many studies involving such fasting, researchers asked participants of their experiences throughout the study. For example, Furmli et al. (2018) found that three out of three diabetic patients reported a positive experience from intermittent fasting. In Arnason's (2017) two week trial, six out of ten participants reported that they would consider continuing practicing intermittent fasting following the study. Seven out of ten of these participants also reported that fasting was tolerable. Participants in Sutton's (2018) described that it took twelve±ten days to adjust to the six hour eating period and eighteen hour fast. Seven out of eight of them also reported that fasting was not difficult and that they would consider continuing. These positive experiences attest to the feasibility of intermittent fasting.

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Conclusion

Despite the limited amount of research on the effects of intermittent fasting on type 2 diabetes, it is clear that intermittent fasting is beneficial for those with this diagnosis. The progression of research from rodent studies to human studies shows the efficacy of intermittent fasting as a treatment strategy for type 2 diabetes; however, the research is not without limitations that affect the integrity of the results. For example, most studies were completed on a small group of human subjects (Furmli et al. 2018; Arnason et al. 2017; Sutton et al. 2018). A larger study group would strengthen the validity of the results found in some of these studies. Additionally, the studies all had varying definitions of intermittent fasting. For example, some had the subjects fast for twenty-four hours and eat for twenty-four hours, one had a six hour eating period and an eighteen hour fasting period, and another let the participants choose how long they wanted to fast and self-report their fasting hours. The varying methods of fasting make it difficult to draw conclusions from the group of research as a whole. Similarly, there is a lack of research comparing the different methods side by side. Each method has shown benefits, but not always to the same extent. Differences in weight, age, and gender of test subjects could have also played a role. Additional controlled research to determine which method is best is necessary for the future of intermittent fasting as a treatment for type 2 diabetes.

It is already known that intermittent fasting creates benefits such as increased insulin sensitivity, decreased fat cells, and increased glycemic control. However, the mechanisms by which these benefits are achieved are still a mystery. Researchers have found that beta cells, the autophagy-lysosome pathway, and triacylglycerol levels do play a role. More in-depth studies on these mechanisms could help determine the best method of fasting to maximize the results and potentially reverse the effects of type 2 diabetes. The long-term effects of intermittent fasting on diabetes are also still unknown. Researchers should conduct longer studies and monitor participants for long periods following the study to determine if the benefits are sustainable. The effect of intermittent fasting on insulin resistance and sensitivity also deserves more attention. The studies discussed in this review did not agree on whether insulin resistance was increased or decreased due to intermittent fasting. This piece of information is important because insulin resistance is a major contributor for the progression of type 2 diabetes. Therefore, these inconclusive findings warrant future research.

The current research presented in this review offers a solid base for the encouragement of intermittent fasting to treat type 2 diabetes. Closing the gaps in this research may offer clinicians a new treatment option to present to their patients with type 2 diabetes. Researchers in this field should continue to explore the benefits of intermittent fasting on type 2 diabetes to find the best possible way to utilize this treatment strategy.

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