



3-27-2019

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Effect of Intermittent Fasting in Patients with Type 2 Diabetes

NURS 997 Independent Study

Family Nurse Practitioner Program

University of North Dakota

Paul Reynolds, FNP Student

PERMISSION

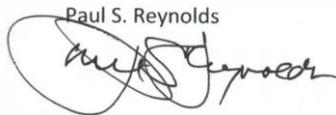
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Department Nursing

Degree Master of Science

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Date: March 21, 2019

Abstract

Avoiding hypoglycemia is an important health and safety priority for all Type 2 diabetes mellitus (T2DM) patients. However, many diabetic patients do not adhere to a typical, American diet regimen. These individuals may consume fewer calories during religious, diet-restrictive activity or as they participate in weight-loss practices via a variety of popularized diets, including those that promote caloric restriction for varying periods. The modality for these diets is commonly referred to as “intermittent fasting” (IF). This case study concerns an obese woman with chronic diabetes with recent weight gain and who states she abstains from eating for “long periods of time.” Her lab indicators show poor blood glucose control over the past six months. She currently takes a sulfonylurea, which lowers blood glucose by increasing insulin release from pancreatic beta cells. Additionally, long-acting exogenous insulin is to be initiated. Given medically-sustained levels of insulin during periods of unknown, reduced caloric intake, serious concern arises that she may experience periods of hypoglycemia. In order to better understand how to best control blood glucose levels for this and other T2DM patients during periods of IF, a review of the literature was conducted. MEDLINE, CINAHL, PubMed and Cochrane databases were searched, and 21 articles were chosen for study inclusion. Popular literature was considered, as well. This research allows for a much clearer understanding of the effects of IF for general clinical application in T2DM and notes important measures for monitoring blood glucose levels during periods of IF and avoiding hypoglycemic episodes.

Background

This case concerns a 65-year-old woman who has presented in the clinic for a six-month follow-up to monitor her diabetes, diagnosed 10 years prior. Her BMI is 36.5, and she has gained weight since her last visit. She checks her blood sugars infrequently with no consistent blood sugar log available. She is unconcerned that her a.m. blood sugars are elevated. She currently takes a biguanide/dipeptyl peptidase-IV inhibitor and a sulfonylurea. Lab parameters today are within normal limits aside from an abnormally high blood glucose level of 324, an HbA1c of 9.5 and a minimally abnormal lipid panel.

During the course of the patient interview, the patient indicated that she eats infrequently and that she may abstain from eating for “long periods of time.” During these periods, she noted she does not consume sufficient carbohydrates, proteins and fats in spite of maintaining her diabetic medication regimen. These events, of course, raised concern for hypoglycemic episodes during periods of low caloric intake, especially given her use of a sulfonylurea (Ibrahim et al., 2010). Additionally, given the decision to start this patient on long-acting insulin, the likelihood of hypoglycemic episodes could be further increased during calorie-restricted periods (American Diabetes Association, 2016). It is, therefore, critical that nurse practitioners have a clear understanding of IF and its effects in order to proactively manage patient health.

IF has been a functional reality for most of human history and currently presents in a variety of forms. Fung (2019) reminds us that IF has existed for many thousands of years in that our ancestors did not always have reliable access to food sources. IF has also been used in the last few millennia for religious purposes and, most recently, for its proposed health benefits. It is currently popularized as a diet form, which typically consists of minimal/restricted caloric intake

on one or more days per week or during a specific period of fasting each day (Leonard, 2018). It is, of course, important to understand how this type of diet may affect our diabetic patients.

In order to properly educate this patient concerning her diet and possible medication adjustments during periods of low caloric intake, it was necessary to undertake a review of the literature to understand more clearly how various types of fasting may affect glycemic levels in patients, especially in those patients prescribed a variety of oral and injected anti-hyperglycemic medications. This report addresses the effect of IF in patients with T2DM and discusses reasonable methods for patients to monitor blood sugar levels and avoid hypoglycemic episodes.

Case Report

History of Present Illness:

Mrs. Jones is a 65-year-old patient here for a 6-month follow-up regarding her diabetes. No complaints, states she is compliant with medications. Does no regular exercise, works in the shop some during the week. Weight has gone up 5-10lbs, blames it on “winter, too cold to do much”. Checks blood sugars 2-3x per week, randomly, sometimes fasting, sometimes after eating. Denies any low blood sugars. Thinks the morning readings are in the 170-220 range. She saw ophthalmology 3 months ago for diabetic eye exam.

Current medications:

Glipizide 10 mg daily
Lisinopril 10 mg daily
Toprol XL 50 mg daily
Zocor 20 mg daily
Janumet 50-1000 BID
Aspirin 81 mg daily
Multivitamin

Allergies: None

Social: Retired school teacher, retired last year, lives at home with spouse. 2 adult children, no grandchildren

Past Medical History: Obesity, Hyperlipidemia, DM Type 2 (diagnosed 10 years ago), Actinic Keratosis

Past Surgical History: Cataract bilateral 2016, Colon polyp removal 2005, Right Carpal Tunnel 2006

Tobacco Use: None

Alcohol Use: Socially, 1-2 beers on the weekends

Immunizations/screening:

Influenza: 10/2018

PPSV23 - None

PSV13 - None

Tetanus- 2/2003

Last colonoscopy: 2003

Review of Systems: Head-to-toe review completed. Negative except as noted in HPI.

Physical Exam:

Vital Signs: 138/80, P – 72, R- 18. Wt: 122 kg (269 lb), BMI: 36.5

General examination, pertinent items: Obese, well-nourished in NAD, PERRLA, EOMI, RRR, no murmur, gallops/rubs; clear breath sounds; abd soft, non-tender, kidneys negative to percussion; no acanthosis nigricans noted; DTRs are symmetric and brisk; diabetic foot exam negative, pulses 2+. Exam negative unless otherwise noted.

Labs:

Creatinine Urine	30.00 - 259.00 mg/dL	101.82
Microalbumin mg/L	mg/L	22.17
Microalbumin/Creatinine Ratio	0 - 30 mg/g	22

Cholesterol	0 - 200 mg/dL	133
Triglyceride	30 - 150 mg/dL	167 Abnormally high
HDL	40 - 60 mg/dL	39 Abnormally low
LDL	0 - 129 mg/dL	61
Fasting	Yes, No, Unknown	Yes

Hgb A1C – 9.5, 6 months ago – 8.1

CMP:

Glucose	70 - 100 mg/dL	324 Abnormally high
BUN	7 - 18 mg/dL	16
Creatinine	0.70 - 1.30 mg/dL	0.92
BUN/Creatinine Ratio	15.0 - 20.0	17.4
Sodium	136 - 145 meq/L	139
Potassium	3.5 - 5.1 meq/L	4.3
Chloride	98 - 107 meq/L	102

CO2	21 - 32 meq/L	28
Anion Gap with K	6 - 20 meq/L	13
Calcium	8.5 - 10.1 mg/dL	9.0
Protein Total	6.4 - 8.2 g/dL	7.8
Albumin	3.5 - 5.0 g/dL	4.7
Alkaline Phosphatase	46 - 116 U/L	84
AST - SGOT	15 - 37 U/L	19
ALT - SGPT	12 - 78 U/L	30
Bilirubin Total	0.2 - 1.0 mg/dL	1.1

Assessment and Plan:

E66.0 Obesity

E78.5 Hyperlipidemia

E11 DM Type 2

Obesity: We reminded Mrs. Jones today of the need for diet modification and increased activity levels and that her obesity will continue to become more of a problem as time goes on. She agrees that she will increase her activity levels by taking over responsibilities for the family pet by walking the dog on a daily basis, morning and evening. She also agrees to visit with the dietitian for six visits over the next three months. We will follow up with her in three months to see if she feels that this is an effective strategy for her and to reassess her progress. She understands that her lipids and blood sugar levels will be positively affected if she is able to establish new dietary habits and lifestyle.

Hyperlipidemia: Although her triglyceride levels are slightly elevated and her HDL is just below range, we will wait until she has tried the dietary/lifestyle intervention, and, if she is having success in the program, we will recheck labs in six months. We will continue the Zocor as ordered until that time. Refill ordered today. Should she feel the program is ineffective for her, we will recheck labs at that time and discuss possible changes in medication.

DM Type 2: Given Mrs. Jones' abnormally elevated blood sugar today and the change of her HbA1c to 9.5 from 8.1 six months ago, we agree it would be wise for her to start long acting insulin to better control her blood sugar levels. We will start with Lantus 10mg nightly and titrate up every three days by 2 units until her morning fasting blood sugar is <120. She states she is aware of low blood sugar symptoms and is able to use her glucose tabs or juices in the event of hypoglycemic episodes. We will follow up with a phone call in two weeks to monitor progress. Am placing a referral to the diabetic educator today for instructions on use of pen, injection sites, and lifestyle changes. She is also concerned about cost, so we are providing her information about resources available and will coordinate with DM educator with further questions. Our plan is to reduce diabetic medications, as possible.

Immunizations/Screenings: Mrs. Jones is advised that she now meets the criteria for the pneumococcal vaccines. We will give PSV13 today, and she understands she will receive PPSV23 in one year. Tetanus booster also given today. Mrs. Jones continues to refuse follow-up

colonoscopy after discovering her polyp in 2005. She is, however, willing to complete a Cologuard test. We will order that today.

Follow-up: She will continue to follow up with eye doctor for diabetic care. Next appointment in 9 months. She will return to our clinic in three months for follow-up visit or sooner as needed.

Literature Review

Types and Number of Sources Reviewed

A search was conducted in MEDLINE, CINAHL, PubMed and the Cochrane Library for high-quality, original research articles via the Harley French Library at the University of North Dakota in order to gather information concerning the application of intermittent fasting in persons with T2DM. Search terms included “intermittent fasting,” “calorie restriction,” “diabetes mellitus type 2,” or “type 2 diabetes.” Results were limited to English and publish dates after 2014 for recency and relevance. Searches were limited to clinical trials with good results, where possible. This search resulted in a total of 116 articles, initially. 21 articles were retained based on a review of the respective abstracts and their ability to answer the clinical question of how intermittent fasting might affect patients with T2DM. These articles included one randomized controlled trial and three systematic reviews. Public opinion pieces were also researched in order to understand public perception of IF and to understand how it was being defined in layman's terms and within the diabetic community.

Introduction to the Case

In that our patient was most likely engaging in various types of IF, whether intentional or not, she was placing herself at risk of dangerous hypoglycemic episodes in the context of two medications she was taking that increase the amount of insulin in her blood stream while she was simultaneously reducing dietary calories/glucose available for uptake into the cells. This case, therefore, reminds the provider of the unpredictability of individuals' eating schedules as well as

the need to prepare for cases in which patients intentionally choose to reduce caloric intake for religious or weight-loss purposes. It is important to understand IF as presented in the literature and in the common vernacular, its typical effects in Type 2 diabetics, and how these patients can safely integrate this activity into their lifestyles while avoiding hypoglycemic episodes.

Intermittent Fasting: Promising Results

Findings concerning IF diets are promising but are currently limited. Leonard (2018) describes several different commonly-used fasting diets: 12 to 16-hour fasts, fasting two days per week or on alternate days, one 24-hour fast per week, skipping specific meals, and limiting intake to primarily one meal per day. Mattson, Longo, and Harvie (2017) conclude that this type of intermittent and periodic fasting likely provides many beneficial effects on human health and disease, to include improvement in insulin resistance in diabetics. Arnason, Bowen, and Mansell (2017) agreed that IF may be a safe, tolerable dietary intervention that does improve key outcomes, including body weight, fasting glucose and postprandial variability. Additionally, from a financial perspective, Croppi and Tutt (2017) suggest that routine periodic fasting is essentially a no-cost therapy to both the patient and healthcare system. It can be seen then that IF has been found to provide a number of well-known health and economic benefits in several studies. However, when studying dietary patterns in general and the management of T2DM, Papamichou, Panagiotakos, and Itsiopoulos (2019) concluded that, while promising, IF lacked adequate research. In addition, Zubrzycki, Cierpka-Kmiec, Kmiec, and Wronska (2018) concluded that while caloric restriction did result in reductions in body fat mass and metabolic parameter improvements, they encountered a paucity of large scale RCTs on low calorie diets and IF. Therefore, while several studies do support IF practices, the current lack of data suggests

it might be valuable to understand similarities between IF and daily caloric restriction, which is a more standard means of diet management (Zuo et al., 2016).

Comparing IF to Continuous Energy Restriction

By way of comparison, several authors studied intermittent energy restriction versus continuous (daily) energy restriction groups, both in terms of specific effects on HbA1c levels and, generally, in terms of sustained weight loss. Carter, Clifton, and Keogh (2016b; 2018) concluded that both groups offered a suitable treatment strategy causing significant reductions in HbA1c levels, which allowed for reduced medication dosages. Davis et al. (2016), Harris et al. (2018), and Zuo et al. (2016) all concluded that both groups experienced significant sustained weight loss. Zuo et al. (2016) also noted that an IF diet minimized weight regain and enhanced arterial compliance after one year. These findings could lead nurse practitioners to expect patients to accept and adopt IF dietary models as they prove more beneficial and effective over time.

Nonetheless, opinion does exist that standard, daily caloric restriction may be a preferred method of weight loss. In Doheny (2019), three endocrinologists expressed opinions that a standard low-calorie meal plan is probably safer and easier than IF. Additionally, it should be noted that even in popular literature (Diabetes Community UK, 2018), contributors state that while it is similar to other calorie restricted diets in terms of benefits, no long-term studies have been performed concerning IF and that individuals on medication could have significantly increased hypoglycemic episodes. Opinions, however, do not negate data gathered thus far, and, while continuous calorie restriction remains the typical means of dieting in the United States, important developments concerning IF are now occurring.

A Small but Important Case Study

Of specific interest in understanding IF is a small case study that gained recent attention due to its dramatic results. Furmli, Elmasry, Ramos, and Fung (2018) studied three adult males with chronic T2DM, multiple comorbidities, and who used at least 70 units of insulin daily. They were placed on an IF diet, and, over the course of 12 months, insulin resistance and HbA1c levels improved as they all lost weight. Importantly, they were all able to cease insulin therapy within 5 to 18 days of starting the program, and authors concluded that IF may aid in the remission of T2DM.

In spite of the study parameters which required the three patients to be followed by the treating physician every two weeks on average, the leaders of two academic diabetic centers and one dietitian disagreed with the results as a safe option and encouraged medical consultation in addition to further research (Pratt, 2018). Scher (2018) and Tucker (2018) were supportive of the research conclusions, and Townley (2018) found the results encouraging. These disagreements remind nurse practitioners to remain aware of the potential for ideological differences due to conflicts of interest and encourage providers to seek unbiased data that points them in the direction of improving patient health. The status quo will require revision as our understanding evolves, and nurse practitioners must gather best data as it exists.

To that end, on a tangential but relevant note, two murine studies also showed interesting results applicable to the work of Furmli et al. (2018). Liu et al. (2017) showed that IF restored glucose tolerance, enhanced insulin secretion and beta cell survival and caused pancreatic regeneration in mice. In addition, Wei et al. (2018) showed that IF effectively intervenes in the progression of diabetes in mice. These results add useful data to the body of knowledge in this

area and could potentially lead to human studies that will reinforce the results of Furmli et al. (2018). The healthcare community awaits those studies.

As discussed, IF will require continued study, but early results are promising. Given the potential cost savings in medications due to a simple lifestyle change, the implications of Furmli et al. (2018) are enormous. As new research is conducted, providers are likely to continue to encounter both diabetic and non-diabetic patients who will engage in IF. However, in order to properly make use of the case at hand, specific clinical parameters must be evaluated as they are affected by IF. In this case, the critical parameter is hypoglycemia.

Likelihood of Low Blood Sugar during Fasting Periods

A key clinical question one must ask is “how frequently will intermittent fasting cause significant hypoglycemia in most patients?” To that end, Corley et al. (2018) determined that fasting on either consecutive or nonconsecutive days increased the mean hypoglycemia rate from 1.4 events in 12 weeks to 3.52 events in 12 weeks, which is significantly less than the mean rate of 1.74 events in five days as determined by Gehlout et al. (2015) for most non-fasting Type 2 diabetics. Additionally, Babineaux et al. (2015) determined that patients were able to fast for a greater number of days without acute complications by adjusting treatment regimens and following diet and blood glucose self-monitoring recommendations during Ramadan fasting. As an added benefit, Alharbi et al. (2017) concluded that Ramadan fasting did decrease fat mass in Type 2 diabetics. These studies point out that hypoglycemia occurs less frequently in most patients during intentional fasting periods when patients are closely monitoring blood sugars, medications, and caloric intake. Therefore, in that caloric restriction obviously necessitates careful monitoring of the above parameters, guidelines are useful for successful application of those monitoring tools.

Guidelines for Monitoring and Controlling Blood Sugars During Fasting

On days when patients engage in intermittent energy restriction (IER) (consuming 400 to 800 kcal per day) Carter, Clifton, and Keogh (2016a) recommend taking oral medications as ordered, other than sulfonylureas. On IER days, they recommend discontinuation of sulfonylureas as well as insulin if baseline HbA1c is <10%. If HbA1c is >10%, the two medications are not adjusted. Also, in her article concerning daily fasting between dawn and sundown during Ramadan, Olansky (2017) notes, “Long-acting basal insulin should not require adjustment during fasting if the dose is not excessive” (p.1). The author writes that short-acting insulin analogues may still be taken with meals per anticipated carbohydrate intake, while insulin mixes should be avoided, and sulfonylureas should be reduced or eliminated during fasting hours. Lastly, she notes that blood glucose level should be monitored carefully during a fasting period, and patients are advised to break the fast if dangerously low glycemic levels occur. As providers learn and educate patients using these guidelines, they will assist patients in improving the likelihood of maintaining normoglycemic levels during fasting and non-fasting periods.

Learning Points

In summarizing the main ideas of this case study, some key points that should be taken away from this discussion are as follows:

- Low blood sugars occur rarely on intermittent fasting days.
- In spite of infrequent hypoglycemia during fasting, blood sugars and dietary intake should be carefully monitored during these times.
- Follow guidelines during fasting to minimize episodes of hypoglycemia.
- Only sulfonylureas and short-acting insulin need to be reduced during periods of very low caloric intake.

While intermittent dietary restrictions may cause initial concern for hypoglycemia in Type 2 diabetics, research suggests that hypoglycemic events may be readily controlled via careful monitoring of physical parameters and medication dosing per guideline. Educating patients using these guidelines will allow them to more safely engage in IF as described and proactively avoid hypoglycemic episodes as they maintain a healthier lifestyle as T2DM patients.

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