The Effects of Blood Sugar (Glucose) Metabolism on the Sleep and Memory in Ahwaz Diabetic Patients

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Abstract: This study was aimed to examine the effects of blood sugar (glucose) metabolism on the sleep and memory in diabetic patients from Ahwaz metropolitan. The sample subsumed 90 diabetic patients from Ahwaz metropolitan whom were selected via two procedures: a systematic random sampling and incidental sampling procedure (within reach clients). The patients were allocated to three groups (two experimental and one control groups); the medical treatment or medicine therapy group (Hospitals clients), diet therapy group and the control group (from Diabetic Patients Association of Khouzestan Province registered patient members). The experimental groups' blood sugar (glucose) metabolisms (the independent variable) were manipulated by insulin treatment (insulin injection) in medical therapy group and in diet therapy group through diet treatment training. Kimkarad Visual Memory Test, Immediate Auditory Memory Test and Groningen Sleep Quality Scale were implemented to collect data. Based on Multivariate Analysis of Variance (MANOVA) as applied statistical method the outcome results revealed that: devious management of the blood glucose level through insulin injection and diet therapy improved sleep and auditeal and visual short term memory, mid term and long term memories in diabetic patients.

Key words: Blood sugar (glucose) metabolism, medicine therapy (insulin injection), diet therapy, sleep, memory

INTRODUCTION

Most of the food we eat is turned into glucose, or sugar, for our bodies to use for energy. The pancreas, an organ that lies near the stomach, makes a hormone called insulin to help glucose get into the cells of our bodies. When you have diabetes, your body either doesn't make enough insulin or can't use its own insulin as well as it should. This causes sugars to build up in your blood. Diabetes can cause serious health complications including heart disease, blindness, kidney failure and lower-extremity amputations.

People who think they might have diabetes must visit a physician for diagnosis. They might have SOME or NONE of the following symptoms: Frequent urination; Excessive thirst; Unexplained weight loss; Extreme hunger; Sudden vision changes; Tingling or numbness in hands or feet; Feeling very tired much of the time; Very dry skin; Sores that are slow to heal; More infections than usual AND Nausea, vomiting, or stomach pains may accompany some of these symptoms in the abrupt onset of insulin-dependent diabetes, now called type 1 diabetes.

Type 1 diabetes occurs when the body's immune system attacks insulin-producing beta cells in the pancreas and destroys them. This results in the pancreas producing little or no insulin, forcing an individual to take insulin through injections or an insulin pump. Approximately 5-10% of diabetics have type 1 diabetes. It usually occurs in children or young adults, though it can also develop in older adults. This disorder increases the risk of Cardiovascular Disease, blindness (retinopathy), nerve damage (neuropathy) and kidney damage (nephropathy).

Pre-diabetes, type 2 diabetes and gestational diabetes are among various forms of a disease, which is already one of the major health crises of the 21st century. The number of cases of diabetes in its different variations is almost triple what it was 50 years ago, with 150 million people now affected throughout the world. Diabetes is basically a disorder in which the body either fails to produce enough insulin or does not use insulin properly to convert sugar, or glucose, in the blood stream into energy. Pre-Diabetes is a condition that occurs when a person's blood glucose levels are higher than normal but are not in the range of type 2 diabetes. Gestational diabetes is a glucose and insulin disorder than often strikes pregnant women.

The major goal in treating diabetes is to minimize any elevation of blood sugar (glucose) without causing abnormally low levels of blood sugar. Type 1 diabetes is

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treated with insulin, exercise and a diabetic diet. Type 2 diabetes is treated first with weight reduction, a diabetic diet and exercise. When these measures fail to control the elevated blood sugars, oral medications are used. If oral medications are still insufficient, treatment with insulin is considered. Adherence to a diabetic diet is an important aspect of controlling elevated blood sugar in patients with diabetes. The American Diabetes Association (ADA) has provided guidelines for a diabetic diet. The ADA diet is a balanced, nutritious diet that is low in fat, cholesterol and simple sugars. The total daily calories are evenly divided into three meals. In the past two years, the ADA has lifted the absolute ban on simple sugars. Small amounts of simple sugars are allowed when consumed with a complex meal. Weight reduction and exercise are important treatments for diabetes. Weight reduction and exercise increase the body's sensitivity to insulin, thus helping to control blood sugar elevations.

Insulin/insulin receptor plays diverse roles in brain functions including learning and memory. Cognition-enhancing effects of insulin have been reported in both human and animal experiments (Kern et al., 1999, 2001; Park et al., 2000), whereas impairments in insulin and the brain Insulin Receptor (IR) have been linked to development of aging-associated brain degenerative disorders such as Alzheimer’s disease (Craft et al., 1996; Frolich et al., 1998; Gasparini and Xu, 2003; Watson and Craft, 2003). Unlike its peripheral counterpart, insulin/insulin receptor in the brain does not appear to exert a direct effect on neuronal glucose metabolism, but most likely plays a modulatory role, via activating specific signal transduction cascades, in synaptic activities involved in memory formation. Evidence has shown that insulin/insulin receptor is involved in regulation of neurotransmitter release (Blattacharya and Saraswati, 1991; Figlewicz and Szot, 1991), receptor conductance and trafficking (Wan et al., 1997; Beattie et al., 2000; Lin et al., 2000; Man et al., 2000; Skeberdis et al., 2001) and intracellular Ca$^+$ release and neuropeptide secretion (Jonas et al., 1997). As a receptor tyrosine kinase, the insulin receptor in the hippocampus was shown to respond to learning experiences by alterations in its gene expression and activation of downstream molecules such as Shc/Erk1/2 in an early stage of memory formation (Zhao et al., 1999). Despite the accumulated evidence, contradictory results appear to exist regarding roles of insulin/insulin receptor in learning. On the one hand, specific deletion of the brain insulin receptor did not seem to affect animals' ability to form a spatial memory following water maze learning (Schubert et al., 2004). On the other hand, pharmacological disruption of the blood insulin supply by acute administrations of streptozotocin (STZ) that induced experimental Diabetes Mellitus (DM) resulted in spatial learning deficits and impaired Long-Term Potentiation (LTP) (Biessels et al., 1996, 1998). Thus, the precise role of insulin/insulin receptor in learning and memory remains to be clarified.

This research was purposed to examine the effects of blood sugar (glucose) metabolism on the sleep and memory in diabetic patients from Ahwaz metropolitan.

Questions: The research investigated conclusive answers for the next coming questions.

Q1: Has devious management of blood sugar (glucose) metabolism a positive impact on the sleep in diabetic patients via the two treatment methods: medical therapy and diet therapy?

Q2: Does the practice of blood sugar (glucose) metabolism manipulating positively impact the memory in diabetic patients through the two treatment methods: medical therapy and diet therapy?

Q3: Is there any difference between the two treatment methods: medical therapy and diet therapy?

The research proposed three hypotheses. The main triple hypotheses of the current research suggested:

H1: Blood sugar (glucose) metabolism has positive impact on the sleep in diabetic patients through medical therapy (insulin injection) and diet therapy (diet treatment training).

H2: Blood sugar (glucose) metabolism positively impacts the memory in diabetic patients through medical therapy (insulin injection) and diet therapy (diet treatment training).

H3: There is difference between the two treatment methods: medical therapy and diet therapy.

MATERIALS AND METHODS

The universal population included all the diabetic patients from Diabetic Patients Association of Khouzestan Province registered patient members and patients diagnosed with diabetes referred to Ahwaz metropolitan hospitals for therapeutic procedure during July-August 2007.

The sample subsumed 90 diabetic patients from Ahwaz metropolitan whom were selected via two procedures: a systematic random sampling and incidental sampling procedure (within reach clients). The patients
were allocated to three groups (two experimental and one control groups); the medical treatment or medicine therapy group (Hospitals clients), diet therapy group and the control group (from Diabetic Patients Association of Khosestan Province registered patient members). The experimental groups’ blood sugar (glucose) metabolisms (the independent variable) were manipulated by insulin treatment/insulin injection in medical therapy group and in diet therapy group through diet treatment training.

First group referred to as medicine therapy group embraced 30 inpatients of Golastan Hospital and Imam Hospital. All the subjects in this group were selected via incidental sampling procedure (within reach hospitalized patients). Insulin injection was processed as devious management of blood sugar (glucose) metabolism prescribed therapeutics procedure in this group.

The second group or diet therapy group bracketed 30 diabetics by a systematic random sampling procedure from Diabetic Patients Association of Khosestan Province registered patient members. Diet treatment training tutored by nutrition expert was applied as blood sugar (glucose) metabolism manipulating for this group.

The third group mentioned as control group received no any practice of blood sugar (glucose) metabolism manipulating therapeutics (independent variable). All the 30 diabetics of the control group were selected randomly by systematic sampling procedure from Diabetic Patients Association of Khosestan Province registered patient members.

To collect data Oral Glucose Tolerance Test (OGTT), Kimkaraad Visual Memory Test, Immediate Auditory Memory Test and Groningen Sleep Quality Scale were administrated for all the subjects.

**Oral Glucose Tolerance Test (OGTT):** There are two tests determine whether an individual has Pre-Diabetes or type 2 diabetes. One is called a Fasting Plasma Glucose Test (FPG), the other an Oral Glucose Tolerance Test (OGTT).

With the FPG test, a fasting blood glucose level between 100 and 125 mg per deciliter (mg dL⁻¹) signals Pre-Diabetes. A person with fasting blood glucose level of 126 mg dL⁻¹ or higher has type 2 diabetes. In the OGTT procedure, one’s blood glucose level is measured after fasting and two hours after drinking a glucose-rich beverage. If the 2-h blood glucose level is between 140 and 199 mg dL⁻¹, the person tested has Pre-Diabetes. If the two-hour blood glucose level is at 200 mg dL⁻¹ or higher, the person tested has type 2 diabetes. The normal range is 70 to 110 mg dL⁻¹.

**Groningen Sleep Quality Scale (GSQS):** Groningen Sleep Quality Scale is a self-report inventory with the maximum score of 14 that symptomatize a total insomnia and the minimum score of 0 which indicates a normal sleep. It obtained a validity of 0.82 in our research and a reliability of 0.65 and 0.60 via Coefficient alpha (Cronbach’s α) and halving (split-half) methods, respectively.

The first outcome measure was quality of sleep, assessed using the 14-item Groningen Sleep Quality Scale (GSQS) (Mulder-Hajonides van der Meulen et al., 1980). GSQS score ranges from 0 to 14, a higher score indicating lower subjective quality of sleep. The scale was originally constructed to study sleeping problems of depressed patients. In a validation study with 80 depressed inpatients, the mean (SD) score on the scale was 6.0 (4.2) and Cronbach’s alpha for internal consistency 0.88 (Mulder-Hajonides van der Meulen et al., unpublished data). The GSQS has been previously used in a study 27 SAD patients (Meesters et al., 1993) and 70 shift-workers (Meijman et al., 1990). In general, if sleep is unrestricted and undisturbed, subjects score 0 to 2 points. A higher score (6 to 7) indicates a disturbed sleep. The Groningen Sleep Quality Scale seems a promising and reliable method of measuring sleep quality even in the general population.

In future it should, however, be validated against more established questionnaires, e.g., The Pittsburgh Sleep Quality Index (Buysse et al., 1989). All items are scored true/false. The first question does not count for the total score. One point if answer is true: questions 2, 3, 4, 5, 6, 7, 9, 11, 13, 14 and 15. One point if answer is false: questions 8, 10 and 12. Maximum score 14 points, indicating poor sleep the night before.

**Kimkaraad Visual Memory Test (KVMT):** Kimkaraad Visual Memory Test is one of the most valid tests for measuring visual memory that is worldwide implemented in the research of visual memory issues.

**Immediate Auditory Memory Test (IAMT):** Immediate Auditory Memory Test was utilized to scale audible short-term memory in the current research.

To put the research into practice for both experimental groups and the sole control group the following details followed on:

**Medicine therapy group:** To proceed the research, Oral Glucose Tolerance Test (OGTT), Kimkaraad Visual Memory Test, Immediate Auditory Memory Test and Groningen Sleep Quality Scale; were administrated for all the included in the sample clientele patients to General Hospital diagnosed for diabetes as pre test at the beginning of their hospitalizing process. While sustaining normal range blood glucose level through receiving insulin injection as prescribed therapeutics procedure for devious management of the blood sugar (glucose)
metabolism all the subjects of medicine therapy group post tested by Kimkarad Visual Memory Test, Immediate Auditory Memory Test and Groningen Sleep Quality Scale.

**Diet therapy group:** All the selected patients from Diabetic Patients Association of Khouzastan Province registered patient members were pre tested by means of Oral Glucose Tolerance Test (OGTT), Kimkarad Visual Memory Test, Immediate Auditory Memory Test and Groningen Sleep Quality Scale for their sleep and memory. Diet therapy group received tutor on cooking method, food consumption quantity, calculating the amount of foods calorie, glucose controlling edibles and diabetes products by nutrition expert and under MD physician supervision for two training sessions and two follow up sessions. After three weeks diet therapy group post tested by utilizing Oral Glucose Tolerance Test (OGTT), Kimkarad Visual Memory Test, Immediate Auditory Memory Test and Groningen Sleep Quality Scale for their sleep and memory.

**Control group:** Oral Glucose Tolerance Test (OGTT), Kimkarad Visual Memory Test, Immediate Auditory Memory Test and Groningen Sleep Quality Scale were implemented for all the selected patients as pretest. Then the group was post tested for sleep and memory after three weeks period at the same time with the diet therapy group.

**RESULTS**

As the results show (Table 1), the experimental groups and the control group significantly differ with respect to sleep (F = 13 and p<0.0001). So the first hypothesis was confirmed. That means devious management of blood sugar (glucose) metabolism as dependent variable reduces insomnia and improves the sleeping of the patients subjects.

Once you have determined that differences exist among the means, post hoc can determine which means differ. Hence, Tukey's Post Hoc Test was implied for comparisons of means differences (Table 2).

So it could be concluded that Blood sugar (glucose) metabolism has positive impact on the sleep in diabetic patients through medical therapy (insulin injection) and diet therapy (diet treatment training).

There is also statistically significant difference between experimental groups (groups included subjects received blood glucose metabolism manipulating) and control group refer to all types of inquired memories (Table 1). Therefore the second hypothesis was reconsolidated too. In another words blood sugar metabolism manipulating positively impact the memory in diabetic patients through the two treatment methods; medical therapy and diet therapy.

To determine which means differ for each type of the inquired memories, post hoc test was applied. The finding indicated that experimental groups and control group were significantly different in all kinds (audible short term memory, mid term memory and long term memory) of memories except visual short-term memory (Table 3).

There exist significant differences between the two experimental groups with regard to sleep and the all examined types of memories. The results exceeded for the medical therapy method compare to diet therapy. Thus the
third hypothesis was affirmed too. That means: There is
difference between the two treatment methods: medical
therapy and diet therapy.

**DISCUSSION**

**H1:** Blood sugar (glucose) metabolism has positive impact
on the sleep in diabetic patients through medical therapy
(insulin injection) and diet therapy (diet treatment
training).

Serotonin is a neurotransmitter (nervous) mediator that
extends the sleeping. Research also has shown that
acetylcholine increases RAM sleeping. On the otherhand,
according to Zhou *et al.* (2001) Insulin cause the
increase of serotonin and acetylcholine. As a result it
may be concluded that via either insulin injection or
insulin increment after receiving carbohydrate foods, the
amount of serotonin and acetylcholine grow up in the
brain and ultimately serotonin extends the sleeping and
acetylcholine increases RAM sleeping.

The other explanation that may be taken into
consideration is that: as various researches made clear
receiving edible carbohydrate such as amylaceous, bread,
grains and etc. results the insulin level increment (in type
2 diabetic patients). The insulin compels the serotonin to
be more active in the brain, since it causes the amino acids
decrease that compete serotonin to move into the brain.
Consequently the brain receives more serotonin, which it
extends the sleeping. So carbohydrate foods are one of
the variables, which effect the sleeping improvement.

It may generally be discussed that any of glucose
metabolism regulating process such as normal insulin
secretion, insulin injection, glycogenesis (the formation or
synthesis of glycogen) and glycolysis (converting
glucose to lactic acid) drive the organism to either
compensate the consumed energy or storage glucose
which may be metabolized by the body to satisfy its
energy needs in coming activities. In such condition it
appears that the organism initiates a sleepy mood to
counterbalance and resume the lost energy. This may be
why we experience sleepiness after either daily work
exhaustion or an intensive mental effort or after having
heavy foods and glucose controlling edibles such as
dairy and meat.

**H2:** Blood sugar (glucose) metabolism positively impacts
the memory in diabetic patients through medical therapy
(insulin injection) and diet therapy (diet treatment
training).

Blood sugar metabolism manipulating positively
impact the memory in diabetic patients through the two
treatment methods; medical therapy and diet therapy.

The finding indicated that experimental groups and
control group were significantly different in all kinds
(auditory short term memory, mid term memory and long term
memory) of memories except visual short-term memory.

To offer reasons for signficateness of the findings
and expound the impact of blood sugar metabolism
manipulating on short term, mid term and long-term
memory respectively, details are followed and represented
in three epoques:

To explain the impact of blood sugar metabolism
manipulating on short term memory we may notify the
most important feature of the short term memory that is
the attention and on the other hand the salient diabetes'
patient's characteristcs such as impatience and
inattention while undertaking imbalance in insulin and
blood sugar. Receiving insulin via insulin injection and
balancing blood sugar by diet therapy decrease the
impatience and inattention in diabetic patients and
consequently improve the short-term memory in the
patients.

To expound details of the effects of blood sugar
metabolism on mid term memory, the influence of insulin
on the serotonin should be taken into account. Insulin
enlarges the serotonin influence in the brain since it
decrease amino acids being rivalries to serotonin. So with
regard to serotonin increment caused by the insulin level
and the existence of serotonin as most important
facilitative mediator for the mid term memory we may come
to such conclusion that: insulin via its influence upon the
brain serotonin and increasing the impacts of this
mediator could raised the diabetics patients midterm
memory in the current research.

To explicate the influence minuta of blood sugar
metabolism on long term memory we must draw our
attention to hippocampus as most significant part of the
brain that plays an important role in long term memory.
According to Guyton and Hall (2000) the long term
memory become a component of the brain structure and
make changes to the number of dendrites' branches
pre-synaptic terminals and the mediators. The brain and the
hippocampus that is responsible for the long term memory
utilize and metabolize glucose as the principle source to
perform coding, storage and retrieval. While the blood
sugar exceeds the normal level, the diabetic patients avoid
consumption and take diet of the edible carbohydrate to
rebalance the blood sugar level. So the organism
experiences glucose decrement and the brain under
metabolize because of the glucose shortage and lose. As
a result diabetic patients encounter long-term memory
deficiency.

One more explanation that may be discussed with
respect to our findings is that: In a poor carbohydrate
diet, patients lose a great amount of sodium and are not able to prevent protein tissue degeneration and histolysis. Dehydration, fatigue and energy losing also are observed in such patients. On the other hand protein histogenesis plays a very significant role in long-term memory reconsolidation.

The results reconfirmed findings in the increment of serotonin that extends the sleeping, in regulation of neurotransmitter release, neuropeptide secretion, the cognition-enhancing effects of insulin and learning experiences on early stage of memory formation reported by Zhou et al. (2001), Bhattacharya and Saraswati (1991), Figlewicz and Szot (1991), Jonas et al. (1997), Kern et al. (1999, 2001), Park et al. (2000) and Zhao et al. (1999), respectively.

**H3:** There is difference between the two treatment methods: medical therapy and diet therapy.

There exist significant differences between the two experimental groups with regard to sleep and the all examined types of memories. The result exceeded for the medical therapy method compare to diet therapy. Thus the third hypothesis was affirmed too.

To explain the significant differences between the medical therapy method and the diet therapy, we may point out to the circumstances that must be considered in the both procedures. In the first treatment procedure, devious management of the blood glucose level (as independent variable) through insulin injection supervised and processed by MD prudent specialist physician and according to a routine schedule based on accurate medical treatment principles. As a result blood sugar (glucose) metabolisms were manipulated in a precise manner and under exact in vitro conditions. While in the diet therapy which was basically emerged and resulted from diet treatment training sessions, serving as a starting point, many of the variables such as forgetting and lapse, non accurate and incorrect learning because of low education of many of the patients, misperformance of the directions and the given instructions by the patients, in spite of proceeding follow up sessions to reduce suppressor, moderator and disturbing variables; were less controlled. Consequently it may be concluded that the reason for advancing and the exceeding results of the medicine therapy treatment and the comparative preference of the medical therapy method as devious management of the blood glucose level through insulin injection compare to diet therapy was due to a beneficial factor or combination of factors of more accurately controlling and reducing the suppressor, moderator and disturbing variables.

**CONCLUSION**

The research concluded that: devious management of the blood glucose level through insulin injection and diet therapy improved sleep, auditory and visual short term memory, mid term and long term memories in diabetic patients. The result also exceeded for the medical therapy method compare to diet therapy. So the revealed result recommend and suggest, based on the history of each individual patient and the diagnosis of the physician; that medical therapy should be prescribed for diabetic patients who are involved in traditional style of life, in circumstances that many of the disturbing and confounding variables such as forgetting and lapse, non accurate and incorrect learning because of low education of many of the patients, misperformance of the directions and the given instructions by the patients are less controlled.

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