Academic Journal of Medical Sciences
ISSN: 2708-2725
ORIGINAL ARTICLE

Estimate the Importance of Impacts that occur in Blood Glucose, Lipid Profile and Serotonin Hormone Level After Inositol Supplementation

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Funding information
Self-funded

Conflict of interest
None declared by author

ABSTRACT

Background: *Myo-inositol (MI) is known as vitamin B8, and many recent studies have relied on its importance in treating insulin resistance and polycystic ovary syndrome, despite the fact that it is also manufactured inside the human body. Can it be used to improve the standard of life? This question the study will attempt to answer.*

Objective: *Explore the dual effects of myo-inositol supplementation on both serotonin hormone and metabolic parameters, specifically glucose metabolism, and lipid profiles.*

Subjects and methods: *The research based on 22 subjects, with a planned age range from 18 to 60 years-old ,they were subjected for myo-inositol (one capsule daily for 45 days, each capsule contains 250 mg of inositol). All their basal measurements which include fasting serum glucose, lipid profile (by manual photometric assay) and serotonin (by ELISA system) were measured, and all measurements were repeated after supplementation.*

Results: *The investigation assessed the impact of inositol supplementation on key biochemical parameters, revealing noteworthy findings. In terms of fasting blood glucose levels, a slight decrease from 95.3 mg/dL before to 90.0 mg/dL after intervention was observed, though the change did not reach statistical significance. Notably, significant improvements were detected in the lipid profile. Total cholesterol exhibited a substantial reduction from 167.1 mg/dL to 130.8 mg/dL, accompanied by significant decreases in triglyceride levels (119.0 mg/dL to 80.9 mg/dL. In the examination of serotonin levels before and after inositol supplementation, a statistically significant change was identified. The baseline serotonin concentration was 1.47 ng/ml, and post-intervention, it increased to 1.60 ng/ml.*

Conclusion: *The supplementation of myo-inositol has demonstrated promising effects on various health indicators. The observed decrease in blood glucose levels suggests a potential role in glycemic control. Additionally, the correction in lipid profile parameters implies a positive impact on cardiovascular health. Notably, the increase in serotonin levels points towards a potential influence on mood regulation and overall well-being. These findings collectively support the notion that myo-inositol supplementation may contribute to metabolic and mental health improvements.*

Keywords: ***Inositol, Blood glucose, Lipid profile, Serotonin hormone.***

1. INTRODUCTION

Inositol is a natural simple sugar-like compound commonly present in many plants and foods. Inositols, as components of cell membrane phospholipids, plasma lipoproteins, or the phosphate forms in the nucleus, are involved in many cellular processes, such as signal transduction, osmoregulation, or ion channel regulation (21). There are nine inositol stereoisomers, depending on the location of the hydroxyl groups: muco-, neo-, scyllo-, epi-, cis-, allo-, D-chiro-, Myo- and L-chiro-inositol (22). Myo-inositol is unique among other forms of inositol and it is mostly found in nature; for example, in all eukaryotic cells (23). There is no recommended daily allowance (RDA) for Myo-inositol, the intake of Myo-inositol can be as low as 250 mg or as high as 1650 mg/day, depending on the foods that are consumed (27). In recent years, increasing attention has been given to the role of inositol in the pathogenesis of some metabolic diseases, such as MetS.(27), which is a condition related to altered insulin sensitivity. Inositol, particularly MI and D-chiro-inositol, seems to act as metformin on insulin resistance (28). It has been observed in the studies that, development of diabetic complications is accompanied by intracellular Myo-inositol depletion, increased Myo-inositol in urine, described as inosituria, as well as intracellular sorbitol accumulation (29). Myo-inositol has insulin-mimetic properties implied in insulin transduction; it increases GLUT-4 translocation to the cell membrane in skeletal muscle, thus improving insulin sensitivity (28). Myo-inositol supports production and activation of, Phosphoinositide 3-kinases (PI3Ks), this enzyme is stimulated by Insulin-Receptor Substrate (IRS), which is formed by binding of insulin to its receptor on the cell membrane. (PI3Ks), cause activation of Glucose transporter type 4 (GLUT4), which permits the facilitated diffusion of circulating glucose down its concentration gradient into muscle and fat cells. Once within cells, glucose is rapidly phosphorylated by glucokinase in the liver and hexokinase in other tissues to form glucose 6 phosphate, which then enters glycolysis or is polymerized into glycogen (30). Insulin-mimetic effects of Myo-inositol or its isomers is thought to result from that inositol phosphoglycans (IPG), which contain myo-inositol , act like an insulin mediator or a secondary messengers of insulin(31). Myo-inositol may improve lipid profiles through the up regulation of hepatic LDL receptors, decrease in the intestinal absorption of cholesterol(32), blocking carbohydrate

digestion and glucose absorption in the gut, decreasing glucose release from liver, and activating insulin receptors and glucose uptake in insulin-sensitive tissues(32). In addition, inositol intake may improve lipid metabolism through lowering visceral fat weight, hepatic lipid accumulation and insulin secretion as well as by increasing adiponectin concentrations (33). Furthermore, a significant weight loss and leptin reduction following the administration of MI my result in an improvement in the lipid (34). Recently, a potential role of inositol has also been shown for psychiatric diseases, including psychotic, mood and anxiety disorders (35). Previous studies have also proposed a possible antidepressant mechanism of inositol, which might involve the signal transduction of serotonin, one of the key neurotransmitters associated with the pathogenesis of mood disorders (36). It has been suggested that the therapeutic activity of inositol may be related to the modulation of serotonin and/or norepinephrine receptors and to an effect on the signal transduction pathway. Indeed, from the data available in the literature, inositol acts as a precursor of the inositol phosphate-phosphoinositide (IPP) cycle, which is the source of two-second messengers, i.e., IP3 and DAG. The IPP cycle and its derived second messengers are involved in several receptor systems, including noradrenergic (α-1), serotonergic (5-HT2A and 5-HT2C), cholinergic (muscarinic), and dopaminergic (D1) receptors (37). Hence, we conducted a trial on inositol supplementation to investigate its effects on serotonin hormone, blood sugar levels and lipid profile due to the significant role these parameters play in one`s physical and mental health.

Aim of the study:

1. Explore the effects by which myo-inositol modulates serotonin levels to understand its role in mood regulation.
2. Investigate the impact of myo-inositol on glucose and lipid metabolism, so its potential contribution to physical health modulation.

2. METHODOLOGY

Analytical cohort study that was conducted from February to October 2023. The study based on 22 subjects. The planned age range from 18 to 60 years-old, they were subjected for Myo-inositol (one capsule daily for 45 days, each capsule contains 250 mg of inositol in the form of Myo-inositol). All their basal measurements which include fasting serum glucose,

lipid profile (by manual photometric assay) and serotonin (by ELISA system) were measured, and all measurements were repeated after supplementation.

Inclusion criteria: Healthy subjects, whether males or females with a body mass index BMI range (25-34.9) kg/m².

Exclusion criteria:

1. Subjects on medications for diabetes (Anti diabetes drugs).
2. Subjects with mental diseases such as depression or anxiety disorders.
3. Female with Poly Cystic Ovary Syndrome.
4. Pregnancy or contraceptive use.
5. Hormonal issues.
6. Chronic use of any supplementations, drugs or special diet that may have an impaction on the study.
7. Alcoholics
8. Gastrointestinal disease such as irritable bowel syndrome (IBS) which can cause abnormal digestion or absorption.

Ethical consideration:

1. Official approval granted from the Board for Medical Specializations.
2. Official approval from Ministry of health and environment.
3. Oral and signature consents of all patients been included in the study.

Collection of Samples:

The blood sample were obtained after overnight fasting for (8-12h).

Three milliliters of peripheral venous blood were aspirated from the median cubital vein to measure serum lipid profile (cholesterol, triglyceride and high density lipoprotein), serum glucose and serum serotonin hormone for each participant.

Two milliliters of blood were aspirated into a clean disposable gel tubes and allowed to clot at room temperature (25-28℃) for 30 minutes before separation of serum by centrifugation. The resulting serum is divided into aliquot in Eppendrof tubes for biochemistry measurement of lipid profile and serum glucose.

One milliliter of blood were aspirated into a clean disposable gel tube and allowed to clot for 10-20 minutes at room temperature (25-28℃). Centrifuged at (2000-3000 rpm) for 20

minutes according to manufacture s instruction for measurement of serum serotonin hormone by ELIZA.

Materials:

The analytical instruments used in this study are shown in (**Table 1**) and the non-analytical and consumable materials are shown in (m).

Methods:

Serotonin hormone was determined by enzyme –linked immunosorbent assay (ELISA) using a kit provided by Shanghai YL Biotech Co., Ltd

Reference Range: 2ng/ml→600ng/ml

The glucose was measured in the serum manually using the spectrophotometric enzymatic method with the kits supplied from Human (Germany).

Reference Range: Serum (fasting) 75 – 110 mg/dl or 4.2–6.4 mmol/l

Total cholesterol (TC), HDL and triglycerides (TG) were measured in the serum manually using the spectrophotometric enzymatic method with the kits supplied from Human (Germany). Friedewald equation was used to estimate LDL as follows:

LDL-C= Total cholesterol – [HDL-C + triglycerides (TG)/5]

Where TG/5 is an approximate estimation of VLDL.

The reference values of TC, HDL, LDL, TG and VLDL are demonstrated in (**Table 3**). Atherogenic index of plasma (AIP) was calculated as a logarithm of the ratio of the concentration of triglyceride (TG) to HDL-C. It is used as an optimal indicator of dyslipidemia and associated cardiovascular diseases (13), as follows:

AIP = log10 (TG/HDL-C)

Reference range (14): Low risk AI < 0.11

Intermediate risk 0.11 to 0.21

High risk > 0.21

Statistical Analysis: The statistical analysis data were analyzed using Statistical Package for Social Sciences (SPSS) version 26, the data were expressed as means ± SD. The Paired t-test was utilized to test the difference in means before and after giving Inositol. Pearson's correlation test (r) was used to assess correlation between Serotonin with Fasting blood sugar and lipid profile, P-value less than 0.05 was considered statistically significant.

Table 1. Analytical instrument

Item	Name	Origin
ELISA reader	ELISA LINEAR spain	Spanish
Manual analyzer for Clinical Chemistry	Humalyzer primus human	German

Table 2. Non - Analytical instrument and consumable materials

Item	Origin
Centrifuge	German
Deionized water	Iraq
Disposable gel and plain tubes	China
Disposable pipette tips	China
Eppendorf tube	China
Precision single channel pipette	China
Syringes 5ml volume with needles	China
Tourniquet	China

Table 3. Reference values of lipid profile parameters

Parameter	Recommended values	Low risk	High risk
TC (mg/dl)	< 200	200-239	≥ 240
LDL (mg/dl)	< 100	100 –129	≥ 130
HDL (mg/dl)	≥ 60	< 40 is at risk	
TG (mg/dl)	< 150	-	-
VLDL (mg/dl)	2 to 30	-	-

3. RESULTS

The demographic characteristics of the study population were demonstrated in (**Table 4**), noting the average age and corresponding range. The table also reports the findings, which indicate a mean body mass index of 28kg/m². The selection comprised an equal number of females and males, as reflected in the percentage note, it is worthy to mention that table involve description without any statistical analysis. While the glucose level did not exhibit a statistically significant difference after Myo-inositol supplementation comparing with that

before, there was a noticeable decrease as shown in (**Table 5**). Simultaneously, the lipid profile level demonstrated an improvement in varying degrees, with a discernible decrease in the atherogenic index level. Anticipated outcomes of serotonin hormone following inositol dosing are expected to reveal a noteworthy difference between the pre-supplementation and post-supplementation stages, as illustrated in (**Figure 1 & 2**). Serotonin hormone respond in women differ from that in men after Myo-inositol supplementation as shown in (**Table 6**). It is noteworthy that in a previously unexplored study, a substantial contrast was observed in the serotonin levels of females before and after supplementation, whereas no such distinction was evident in males. The correlation of serotonin hormone with fasting blood glucose and lipid profile was displayed in (**Table 7**), in investigating the impact of serotonin on blood glucose levels, lipid profiles, and the atherogenic index, a Pearson correlation analysis was employed. Atherogenic index showed a statistically significant correlation with the levels of serotonin hormone, the more serotonin hormone, the less atherogenic index. While other parameters did not reach a statistically significant threshold, a negative association was observed with blood glucose and the lipid profile, except for HDL-Cholesterol. These findings serve as positive indicators for enhancing health quality.

Table 4. Presents average age with standard deviation, along with gender and BMI data, without any statistical analysis, (N = 22).

Variable		Value
Age (years)	Mean ± SD	33.2 ± 12.8
	Range	18-60
Gender	Female n (%)	11 (50.0%)
	Male n (%)	11 (50.0%)
BMI (kg/m^2)	Mean ± SD	28.4 ± 2.4

SD: standard deviation

Table 5. Assessing the Impact of Inositol Supplementation on Serotonin, Fasting Blood Glucose and Lipid Profile Levels, Before and After Insights.

Characteristic		Before (mean ± SD)	After (mean ± SD)	P. value
Serotonin (ng/ml)		1.47 ± 0.27	1.60 ± 0.35	0.021
Fasting blood glucose (mg/dL)		95.3 ± 18.0	90.0 ± 15.4	0.1
Lipid profile	TotalCholesterol (mg/dL)	167.1 ± 42.9	130.8 ± 30.8	<0.001
	Triglyceride (mg/dL)	119.0 ± 57.2	80.9 ± 36.4	<0.001
	LDL (mg/dL)	119.7 ± 39.2	91.21 ± 36.1	0.002
	VLDL (mg/dL)	36.6 ± 5.3	31.7 ± 6.2	0.012
	HDL (mg/dL)	34.9 ± 6.5	36.2 ± 8.6	0.45
Atherogenic index		0.50 ± 0.24	0.32 ± 0.20	<0.001
• Low risk		0 (0.0%)	3 (10.7%)	0.036
• Intermediate risk		7 (25.0%)	11 (39.3%)	
• High risk		21 (75.0%)	14 (50.0%)	

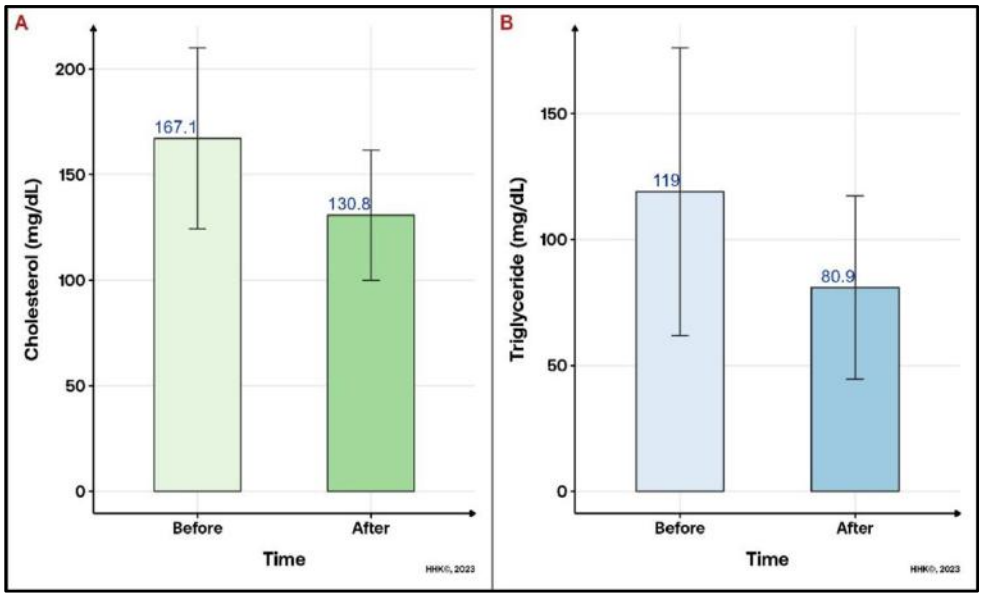

Figure 1. Bar Chart Displaying Serum Cholesterol (A) and Triglyceride (B) Levels Pre and Post Inositol Administration

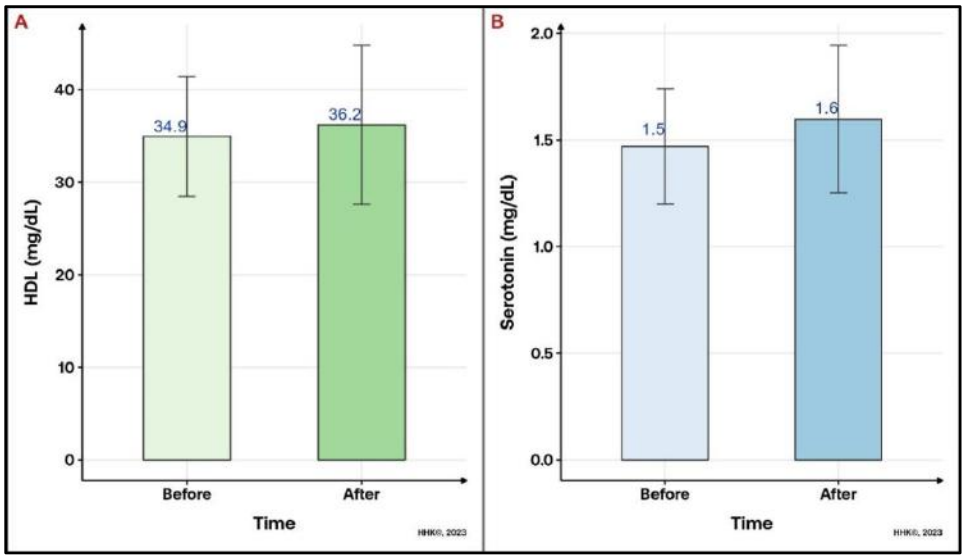

Figure 2. Bar Chart Displaying Serum HDL (A) and Serotonin (B) Levels Pre and Post Inositol Administration

Table 6. Exploring Gender Based Differences in Serotonin Hormone Levels and Its Impact on Mental Well-being in Men and Women.

Gender	Serotonin (ng/ml) mean ± SD		P. value
	Before	After	
Males (N=11)	1.50 ± 0.29	1.53 ± 0.29	0.51
Females (N=11)	1.44 ± 0.25	1.66 ± 0.39	0.023

Table 7. Exploring Correlation of Serotonin Hormone with Fasting Blood Glucose and Lipid Profile.

Parameter		R	P. value
Fasting blood glucose (mg/dL)		-0.25	0.19
Lipid profile	Cholesterol (mg/dL)	-0.17	0.37
	Triglyceride (mg/dL)	-0.27	0.16
	LDL (mg/dL)	-0.17	0.21
	VLDL (mg/dL)	-0.11	0.35
	HDL (mg/dL)	0.21	0.27
Atherogenic index		-0.37	0.048

R: Correlation coefficient

4. DISCUSSION

The study found that there is an improvement (even if it does not reach a reliable level, and the reason for this may be and is strongly attributed to the number approved in the study) of blood glucose, which may improve insulin resistance and its consequences, and the reason for this is as suggested by many studies. Myo-inositol inhibits duodenal glucose absorption and reduces blood glucoses rises via a competitive affinity for the same transporter system, however, Myo-inositol improves muscle glucose uptake. Glucose also impairs cellular uptake of Myo-inositol (54). The administration of inositol allows it to act as a direct messenger of the insulin signaling and improves glucose tissue uptake. This mechanism is extrapolated to its functions in diabetes treatment, metabolic syndrome, and weight loss (55). Due to the well-known and documented correlation between the sugar level and the fat level, also notice a decrease in the levels of both cholesterol (total cholesterol, LDL and VLDL) and triglycerides, and simple increase in HDL. Research postulated that Inositol supplementation may result in reduction in triglycerides, total- and LDL-cholesterol levels, but did not affect HDL-cholesterol levels among patients with metabolic diseases (56). Some research suggests that may see an improvement in blood pressure, as well as triglyceride, cholesterol and blood sugar levels (57). One of research didn't linked its effect to glucose but suggest that Myo-inositol or phytic acid (PA), a natural compound found in fiber (seeds and cereal grains), may play a significant role in reducing serum cholesterol by decreasing the zinc: copper ratio. A high ratio is associated with hypercholesterolemia (58). Some studies suggest taking an inositol supplement might help balance important hormones in brain, including serotonin and dopamine (49). Some studies suggest taking an inositol supplement might help balance important hormones in brain, including serotonin and dopamine (49). Myo-inositol imbalance is observed in psychiatric diseases and its use shows efficacy for treatment of depression, anxiety, and compulsive disorders (50). As phosphoinositide, inositol plays a role in phospholipase transduction, which is the signal transduction pathway of many neurotransmitter receptors (51). A study conducted by Einat et al. (52) investigated the effect of inositol on an experimental model of depression applied to laboratory rats. In particular, the study evaluated the effects of the administration of inositol alone and in association with inhibitors of both the serotonergic and noradrenergic systems, to

investigate which neurotransmitter pathway was involved in determining the clinical effect of inositol. As a result, the effects of inositol were blocked by inhibitors of the serotonergic system only (through the 5-HT2A/5-HT2C receptors), although the study could not exclude other pathways in the effects of inositol, such as the involvement of the hypothalamic-pituitary-adrenal (HPA) axis (52). Another possible suggestion shows that inositol may help regulate cortisol levels by influencing the hypothalamic-pituitary-adrenal (HPA) axis, which is responsible for the production and release of cortisol. By modulating this axis, inositol may help reduce cortisol levels and alleviate the symptoms associated with chronic stress (53). The study found, as shown in table (7), a difference between the response of women and men to Myo-inositol, which resulted in a significant difference for women but not men in the level serotonin. This response may be related to the averaging over the different brain areas, the rate of serotonin synthesis and sex related hormones.

5. CONCLUSIONS

In conclusion, the supplementation of myo-inositol has demonstrated promising effects on various health indicators.

1. The correction in athrogenic index implies a positive impact on cardiovascular health.
2. Notably, the increase in serotonin levels points towards a potential influence on mood regulation and overall well-being.

These findings collectively support the notion that myo-inositol supplementation may contribute to metabolic and mental health improvements.

Ethical Approval:

All ethical issues were approved by the author. Data collection and patients' enrollment were in accordance with Declaration of Helsinki of World Medical Association, 2013 for the ethical principles of researches involving human. Signed informed consent was obtained from each participant and data were kept confidentially.

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Citation:

Jabber T.A, Majeed M.J Estimate the Importance of Impacts that occur in Blood Glucose, Lipid Profile and Serotonin Hormone Level After Inositol Supplementation. AJMS 2024; 10 (4): 33-45