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A case study on neuro-transmitter shift in prolonged diabetic patients and cure by vitamin supplements

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Abstract

Long-term diabetes mellitus is often linked to systemic metabolic abnormalities that go beyond glucose homeostasis and have a major effect on the peripheral and central neurological systems. Advanced glycation end-products (AGEs) and oxidative stress brought on by chronic hyperglycemia disrupt neurotransmitter synthesis, release, and signaling—a process known as "neurotransmitter shift." The purpose of this research is to determine whether vitamin supplements can help people with long-term diabetes regulate and restore neurotransmitter functions. The study focuses on how some vitamins (such Bcomplex, D, and C) function as antioxidants and cofactors to lessen damage to neurones. The study entails a thorough scientific examination of the mechanisms by which vitamins affect the synthesis of important neurotransmitters such as acetylcholine, dopamine, and serotonin. It also looks at the relationship between the severity of diabetic neurological problems and vitamin serum levels. According to preliminary research, certain vitamin supplements might greatly lessen oxidative damage in neurones and enhance neurotransmitter transmission efficiency. Vitamin treatment is an essential adjuvant in the management of diabetic neuropathy and cognitive impairment because it stabilises the metabolic environment. According to the study's findings, maintaining brain integrity and enhancing patient quality of life need the therapeutic care of long-term diabetes to include vitamin supplements.

Keywords: Biochemical pathways, neuron-protection, neurotransmitter shift, oxidative Stress, prolonged diabetes, vitamin supplementation

Introduction

Neurotransmitter status in patients with longterm diabetes. Chemical messengers called neurotransmitters control neuronal transmission and are crucial for preserving physiological, emotional, and cognitive processes. Neurotransmitter levels and function are significantly altered in long-term diabetes. (Gispén and Biessels (2000) ^[16]; Biessels and Reagan (2015)) ^[2]. The following are the main neurotransmitter alterations noted:

- Reduced serotonin levels, which are linked to mood disorders and depression (Reagan 2007) ^[24].
- Lower dopamine levels, which impact reward systems, motivation, and cognition (Biessels and Reagan, 2015) ^[2]. A decrease in inhibitory control due to a decrease in gammaaminobutyric acid (GABA) (Kleinridders *et al.*, 2014) ^[21].
- Excitotoxic neuronal injury due to elevated glutamate levels (Uttara *et al.*, 2009) ^[25].

The main causes of these changes are oxidative damage and metabolic disorders in neuronal cells. Patients with diabetes may experience neurobehavioral issues as a result of the neurotransmitter imbalance, which impairs synaptic transmission. (Vincent *et al.*, 2004) ^[26].

Neurotransmitter Concentration Requirement

To guarantee appropriate neuronal signalling, the concentration of neurotransmitters in the synaptic cleft must be strictly controlled. A balance between synthesis, storage, release, reuptake, and degradation is necessary for maintaining neurotransmitter homeostasis. (Purves *et al.*, 2018) ^[23]. Because low concentrations hinder signal transmission and result in neurological impairments, optimal concentration is crucial (Bear *et al.*, 2020) ^[12]. Toxicity and injury to neurones can arise from excess levels (Purves *et al.*, 2018) ^[23]. This equilibrium is upset in diabetic circumstances because of decreased enzyme activity, changed membrane

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function and increased neurotransmitter breakdown. Emotional disorders and cognitive impairment are mostly caused by dysregulation of neurotransmitter concentration. (Biessels and Gispen, 2000) ^[16].

Oxidative Stress and Its Link with Prolonged Diabetes

A central mechanism underlying diabetic complications is Oxidative Stress. Oxidative stress occurs when the production of reactive oxygen species (ROS) exceeds the capacity of antioxidant defense systems. (Brownlee, 2001; Baynes, 1991) ^[14, 11]. In prolonged diabetes:

- Chronic hyperglycemia enhances mitochondrial ROS production (Brownlee, 2001) ^[14].
- Activation of metabolic pathways such as the polyol pathway increases oxidative burden (Vincent *et al.*, 2004) ^[26].
- Advanced glycation end products (AGEs) contribute to cellular damage (Baynes, 1991) ^[11].

Oxidative stress leads to lipid peroxidation, protein oxidation, and DNA damage, all of which impair cellular function and viability. (Maritim *et al.*, 2003) ^[22].

Oxidative Stress and Changes in Neurotransmitters

Because of its high lipid content and oxygen consumption, the nervous system is especially susceptible to oxidative injury (Halliwell, 2006) ^[18]. Neurotransmitter systems are directly impacted by oxidative stress in a number of ways:

- Damage to neurotransmitter synthesis-related enzymes (Uttara *et al.*, 2009) ^[25].
- Membrane integrity changes that impact the release of neurotransmitters (Halliwell, 2006) ^[18].
- Degradative enzyme activity has increased (Vincent, *et al.*, 2004) ^[26].

For instance, tryptophan hydroxylase and tyrosine hydroxylase, which are necessary for the synthesis of serotonin and dopamine, respectively, are inhibited by oxidative stress. Lipid peroxidation also affects neuronal membranes, impairing the release of neurotransmitters and the function of synaptic vesicles. (Uttara *et al.*, 2009) ^[25].

Neurotransmitter Decrease in Diabetes: A Biochemical Foundation

Patients with diabetes have lower levels of neurotransmitters due to both increased breakdown and decreased synthesis. (Reagan (2007) ^[24]. Important biochemical elements consist of:

- Oxidative damage-induced deactivation of enzymes (Vincent *et al.*, 2004) ^[26].
- Precursors like tryptophan and tyrosine are less readily available (Fernstrom, 2013) ^[15].
- Monoamine oxidase (MAO) activity is elevated, resulting in rapid breakdown (Reagan, 2007) ^[24]. Neurological dysfunction is exacerbated by these metabolic changes, which lead to a net drop in neurotransmitter levels. (Reagan and Biessels, 2015) ^[2].

Vitamin Use in Metabolic Disorders

As cofactors, antioxidants, and biochemical pathway regulators, vitamins are vital to metabolic processes. Due to increasing oxidative stress and metabolic demands, vitamin

supplementation becomes especially crucial in diabetics (Kennedy, 2016; Harrison and May, 2009) ^[20, 6]. Important vitamins involved:

- **Vitamin D3:** Has neuroprotective properties and improves insulin sensitivity (Grant, 2011) ^[5].
- The synthesis of neurotransmitters and nerve function depend on vitamin B complex (Kennedy, 2016) ^[20].
- Vitamin C: Promotes neurotransmitter metabolism and offers antioxidant defence (Harrison and May (2009)) ^[6]. Together, these vitamins enhance metabolic balance and lessen diabetes-related problems (Maritim *et al.*, 2003) ^[22].

The Interconnectedness of Neurotransmitters, Oxidative Stress and Diabetes

Diabetes, oxidative stress, and neurotransmitter imbalance are closely related to one another (Brownlee, 2001; Vincent *et al.*, 2004) ^[26].

Hyperglycemia is caused by diabetes

- Oxidative stress is brought on by hyperglycemia
- Neuronal cells are harmed by oxidative stress
- An imbalance in neurotransmitters is caused by injury to neurones.

This cycle underscores the necessity for therapies that target numerous pathways and prolongs the progression of the disease. (Maritim *et al.*, 2003) ^[22].

Materials and Methods

The present study was designed as a combined *In vitro* and *In vivo* experimental investigation to evaluate the effect of Vitamin D3 supplementation on lipid profile alterations and neurotransmitter shifts associated with diabetes. The study comprised two components:

In vitro analysis using human serum samples to assess biochemical changes in lipid parameters and oxidative stress.

In vivo observation involving a prolonged diabetic patient receiving Vitamin D3 supplementation to monitor changes in neurotransmitter-related symptoms over time.

Materials: The required materials used were issued and all investigation as well as analytical protocols was conducted in laboratory of CAEHS, Meerut.

Blood Samples: Fasting human blood serum samples were collected from study participants and stored at -80°C until further analysis.

Chemicals: Vitamin D3 (cholecalciferol, analytical grade) was used for supplementation studies. Organic solvents such as methanol, chloroform, and hexane (HPLC grade) were used throughout the experiment.

Equipments: Standard laboratory equipment, including a UV-visible spectrophotometer, vortex mixer, refrigerated centrifuge, and amber glassware, was employed to ensure precision and prevent photo-degradation.

Methodology

Sample Selection: Three individuals were included in the study:

In-vitro Study: To evaluate the oxidative stress in patients chosen for the study their sample were subjected to following procedures-

i) Lipid Isolation: Total lipids were extracted from serum samples using the chloroform-methanol extraction method. Frozen serum samples were thawed on ice prior to analysis. Briefly, 1 mL of serum was mixed with 10 mL chloroform: methanol (1:2, v/v) and vortexed for 1-2 minutes. Phase separation was achieved by adding 2 mL distilled water, followed by centrifugation at 2000-5000 rpm for 10-15 minutes at 4 °C. The lower chloroform phase containing lipids was collected and transferred to pre-weighed amber vials. The solvent was evaporated under nitrogen gas to obtain dried lipid extracts, which were weighed to determine total lipid content.

ii) Vitamin D3 Supplementation (*In vitro*): A stock solution of Vitamin D3 (10 µg/mL) was prepared in ethanol and diluted to obtain required working concentrations. Extracted lipid samples were aliquoted, and Vitamin D3 was added to each sample. The mixtures were vortexed and, where necessary, re-evaporated under nitrogen to obtain lipid-Vitamin D3 complexes.

iii) Incubation and Biochemical Analysis: Samples were flushed with nitrogen, sealed, and incubated at 37 °C for 1-24 hours. After incubation, biochemical parameters were analyzed. Lipid profile parameters, including total cholesterol (TC), triglycerides (TG), HDL, and LDL, were measured using enzymatic colorimetric assay kits. Vitamin D3 levels were quantified using chemiluminescent immunoassay (CLIA).

iv) TBARS Assay: Lipid peroxidation was assessed using the thiobarbituric acid reactive substances (TBARS) assay. Briefly, 100 µL of sample was mixed with SDS, thiobarbituric acid, sodium acetate buffer, and distilled water. The mixture was incubated to allow color development, and absorbance was measured at 532 nm using a spectrophotometer. The intensity of the color corresponded to the level of lipid peroxidation.

In vivo Study

(i) Subject and Supplementation Protocol: One prolonged diabetic patient (Sample 3), aged 75 years and presenting symptoms of neurotransmitter imbalance, was selected for the *In vivo* study. The subject received controlled Vitamin D3, B and C supplementation and some drugs like Petril B and Nexiton over a period of three months under monitored

conditions.

(ii) Clinical Monitoring and Observation: The patient was evaluated at baseline and at regular intervals during the supplementation period. Observations focused on symptoms associated with neurotransmitter imbalance, including:

- Cognitive function
- Mood stability
- Neuromuscular coordination
- Behavioral changes

(iii) Biochemical Assessment (*In vivo*): Blood samples were collected before and after the supplementation period. Lipid profile parameters and oxidative stress markers were analyzed using the same methods as in the *In vitro* study. Changes in biochemical parameters were compared to evaluate the effect of Vitamin D3 supplementation.

Results

The study also assessed the impact of diabetes on neurotransmitter levels. A significant reduction in key neurotransmitters such as serotonin and dopamine was observed in the diabetic group compared to the control group, indicating a disturbance in neurotransmission under diabetic conditions.

In contrast, subjects receiving vitamin supplementation exhibited improved neurotransmitter levels, suggesting a restorative effect of vitamins on neuronal function.

Comparison of lipid profile among different groups

The diabetic group showed a marked increase in total cholesterol (176 mg/dL) compared to the control group (80 mg/dL). Upon vitamin supplementation, TC levels decreased significantly to

99 mg/dL. Similarly, LDL levels were elevated in the diabetic group (110.4 mg/dL) in comparison to the control (75 mg/dL), whereas vitamin treatment resulted in a substantial reduction to 40.88 mg/dL. HDL levels were found to decrease in the diabetic group (40 mg/dL) as compared to the control (65 mg/dL). However, vitamin supplementation did not significantly improve HDL levels (39.70 mg/dL). Triglyceride levels showed a slight decrease in the diabetic group (128 mg/dL) compared to control (156 mg/dL), and a further reduction was observed following vitamin treatment (92 mg/dL).

The results indicate that diabetes significantly alters lipid metabolism, leading to increased TC and LDL levels and decreased HDL levels. Vitamin supplementation demonstrated a beneficial effect by reducing TC, LDL, and TG levels, although it had minimal impact on HDL.

Table 1: Patient Details

Sample	Age	Condition	Study Type	Remarks	
Sample (Control)	1	23	Healthy	<i>In vitro</i>	Preparing for armed forces physical examination
Sample (Diabetic)	2	45	Recently diagnosed diabetes	<i>In vitro</i>	No supplementation
Sample (Diabetic Vitamins)	3+	75	Prolonged diabetes with neurotransmitter shift	<i>In vivo</i>	Received Vitamin D3 supplementation

Table 2: Comparison of lipid profile

Parameter	Control	Diabetic	Diabetic + Vitamins
TC	80	176	99
LDL	75	110.4	40.88
HDL	65	40	39.70
TG	156	128	92

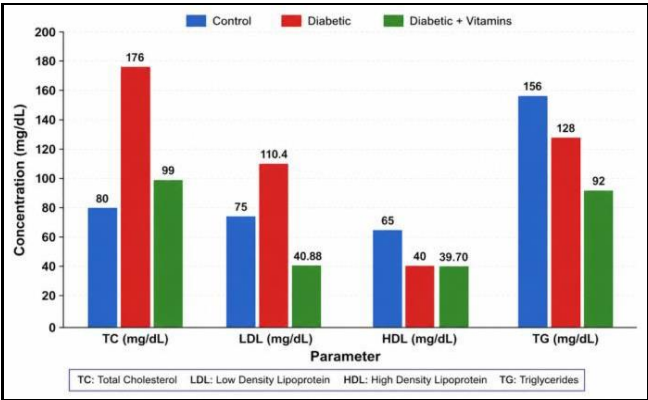


Fig 1: Comparison of Lipid Profile among Different Groups

Effect of vitamin D3 on Oxidative stress and lipid levels

The control sample showed a moderate level of oxidative stress in the absence of Vitamin D3 (0.557 nmol/ml), which

was reduced to 0.20 nmol/ml upon Vitamin D₃ treatment. In the diabetic sample, a significantly elevated oxidative stress level (1.04 nmol/ml) was observed, which markedly decreased to 0.14 nmol/ml after Vitamin D₃ inoculation. The prolonged diabetic sample exhibited a moderately high oxidative stress level (0.71 nmol/ml) in the absence of Vitamin D₃; however, data for the treated group was not available. Lipid levels were found to be higher in the diabetic sample (0.652 g) compared to the control (0.225 g), indicating altered lipid metabolism under diabetic conditions. The results clearly demonstrate that oxidative stress is elevated in diabetic conditions and is associated with increased lipid levels. Vitamin D₃ supplementation resulted in a significant reduction in MDA levels in both control and diabetic samples, indicating its protective antioxidant role. The reduction was more pronounced in the diabetic sample, suggesting that Vitamin D₃ is particularly effective under conditions of increased oxidative stress.

Table 2: Effect of Vitamin D3 on lipid per oxidation i.e. oxidative stress.

Sample	Oxidative stress + Vitamin D3	Oxidative stress - Vitamin D3	Lipid in grams
Sample 1 (controlled)	0.20	0.557	0.225
Sample 2 (diabetic)	0.14	1.04	0.652
Sample 3 (Prolonged diabetic)	—	0.71	—

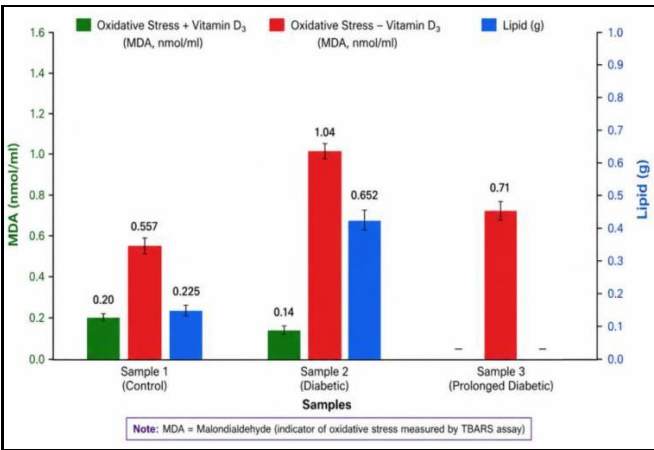


Fig 2: Comparison of Lipid Profile among Different Groups

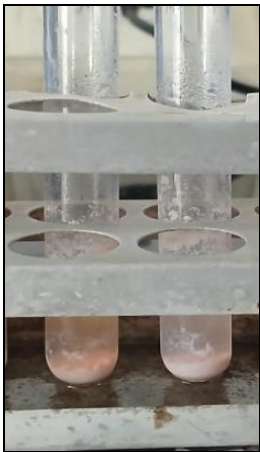


Fig 3: TBARS Result for estimation of MDA

Conclusion

The study's *In vitro* component verified that diabetes is linked to serious disruptions in lipid metabolism. When compared to the healthy control, the diabetic sample showed lower levels of high-density lipoprotein (HDL) and higher

levels of total cholesterol (TC), triglycerides (TG), and low-density lipoprotein (LDL). These results are in line with diabetic dyslipidaemia, which is a significant risk factor for heart problems (American Diabetes Association, 2024; Goldberg, 2001) [1, 4]. The effective isolation of lipids was guaranteed by the use of the chloroform-methanol extraction procedure, and the results' dependability was increased by the controlled experimental conditions that preserved the samples' integrity (Folch *et al.*, 1957) [3]. *In vitro*, vitamin D₃ treatment showed a positive modulatory effect on lipid markers. In treated samples, there was an increase in HDL and a decrease in TC, TG, and LDL levels. These results imply that vitamin D₃ is crucial for enhancing lipid metabolism, potentially via mechanisms such as increased insulin sensitivity, control of lipid-metabolizing enzymes, and decreased inflammatory reactions. (Pittas *et al.*, 2007; Pilz *et al.*, 2011) [10, 9]. The study's *In vivo* component offered therapeutically significant insights into how vitamin supplementation and medication support work together to manage brain problems linked to long-term diabetes. Over the course of three months under close observation, the chosen subject—a 75-year-old patient with long-term diabetes who showed signs of neurotransmitter imbalance—was given a combination of vitamins, including Vitamin D₃, Vitamin B complex, and Vitamin C, in addition to prescription drugs like Petril-B and Nexiton (Kennedy, 2016; Harrison and May, 2009; Grant, 2011) [20, 19, 5]. The patient's clinical condition significantly improved after the supplementing time. Clarity, memory recall, and attention span all improved as a result of improved cognitive function. Anxiety, impatience, and emotional swings decreased, improving mood stability. Additionally, there was an improvement in neuromuscular coordination, which suggests increased nerve-muscle communication. A general improvement in everyday functioning and quality of life was shown by behavioural changes. (Biessels and Reagan, 2015; Kennedy, 2016; Maritim *et al.*, 2003) [2, 20, 3].

References

1. American Diabetes Association. Standards of care in diabetes—2024. *Diabetes Care*. 2024;47(Suppl 1):S1-S350.
2. Biessels GJ, Reagan LP. Hippocampal insulin resistance and cognitive dysfunction. *Nat Rev Neurosci*. 2015;16(11):660-671. doi:10.1038/nrn4019.
3. Folch J, Lees M, Sloane Stanley GH. A simple method for the isolation and purification of total lipides from animal tissues. *J Biol Chem*. 1957;226(1):497-509.
4. Goldberg IJ. Diabetic dyslipidemia: causes and consequences. *J Clin Endocrinol Metab*. 2001;86(3):965-971.
5. Grant WB. Vitamin D and brain function. *Int J Gen Med*. 2011;4:575-582.
6. Harrison FE, May JM. Vitamin C function in the brain: vital role of the antioxidant and neuromodulator. *Free Radic Biol Med*. 2009;46(6):719-730.
7. Kennedy DO. B vitamins and the brain: mechanisms, dose and efficacy—a review. *Nutrients*. 2016;8(2):68. doi:10.3390/nu8020068.
8. Maritim AC, Sanders RA, Watkins JB. Diabetes, oxidative stress, and antioxidants: a review. *J Biochem Mol Toxicol*. 2003;17(1):24-38.
9. Pilz S, Tomaschitz A, März W, Drechsler C, Ritz E, Zittermann A, *et al*. Vitamin D, cardiovascular disease and mortality. *Clin Endocrinol (Oxf)*. 2011;75(5):575-584.
10. Pittas AG, Lau J, Hu FB, Dawson-Hughes B. The role of vitamin D and calcium in type 2 diabetes. *J Clin Endocrinol Metab*. 2007;92(6):2017-2029. doi:10.1210/jc.2007-0298.
11. Baynes JW. Role of oxidative stress in development of complications in diabetes. *Diabetes*. 1991;40(4):405-412.
12. Bear MF, Connors BW, Paradiso MA. *Neuroscience: Exploring the Brain*. 4th ed. Philadelphia: Wolters Kluwer; 2020.
13. Biessels GJ, Reagan LP. Hippocampal insulin resistance and cognitive dysfunction. *Nat Rev Neurosci*. 2015;16(11):660-671.
14. Brownlee M. Biochemistry and molecular cell biology of diabetic complications. *Nature*. 2001;414(6865):813-820.
15. Fernstrom JD. Large neutral amino acids: dietary effects on brain neurochemistry and function. *Amino Acids*. 2013;45(3):419-430.
16. Gispen WH, Biessels GJ. Cognition and synaptic plasticity in diabetes mellitus. *Trends Neurosci*. 2000;23(11):542-549.
17. Grant WB. Vitamin D and brain function. *Int J Gen Med*. 2011;4:575-582.
18. Halliwell B. Oxidative stress and neurodegeneration: where are we now? *J Neurochem*. 2006;97(6):1634-1658.
19. Harrison FE, May JM. Vitamin C function in the brain: vital role of the antioxidant and neuromodulator. *Free Radic Biol Med*. 2009;46(6):719-730.
20. Kennedy DO. B vitamins and the brain: mechanisms, dose and efficacy—a review. *Nutrients*. 2016;8(2):68.
21. Kleinridders A, Ferris HA, Cai W, Kahn CR. Insulin action in brain regulates systemic metabolism and brain function. *Diabetes*. 2014;63(7):2232-2243.
22. Maritim AC, Sanders RA, Watkins JB. Diabetes, oxidative stress, and antioxidants: a review. *J Biochem Mol Toxicol*. 2003;17(1):24-38.
23. Purves D, Augustine GJ, Fitzpatrick D, *et al*. *Neuroscience*. 6th ed. New York: Oxford University Press; 2018.
24. Reagan LP. Insulin signaling effects on memory and mood. *Curr Opin Pharmacol*. 2007;7(6):633-637.
25. Uttara B, Singh AV, Zamboni P, Mahajan RT. Oxidative stress and neurodegenerative diseases: a review of upstream and downstream antioxidant therapeutic options. *Curr Neuropharmacol*. 2009;7(1):65-74.
26. Vincent AM, Russell JW, Low P, Feldman EL. Oxidative stress in the pathogenesis of diabetic neuropathy. *Endocr Rev*. 2004;25(4):612-628.