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# THE EFFECT OF ZINC GLUCONATE SUPPLEMENTATION ON QUALITY OF SLEEP AND SERUM ALBUMIN IN PATIENTS UNDERGOING MAINTENANCE HEMODIALYSIS IN MEDICAL CITY DIALYSIS CENTER / BAGHDAD

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## ABSTRACT

**Introduction:** Chronic kidney disease (CKD), particularly in its advanced stages managed by maintenance hemodialysis, presents a complex challenge affecting multiple aspects of health, including nutritional status, metabolic balance, and overall quality of life, the aim of study is to determine if zinc gluconate supplementation improves sleep and serum albumin in maintenance hemodialysis patients. **Method:** A single-blind clinical trial will be conducted at the Medical City Dialysis Center in Baghdad from 1st of September 2023 to 1st of January 2024, involving 50 end stage renal disease (ESRD) patients on maintenance hemodialysis. Participants will be divided 2 groups; 1st group will receive 25 mg of zinc gluconate daily for 12 weeks, while the 2nd group will receive a placebo. Sleep quality, assessed by the Pittsburgh Sleep Quality Index, and serum albumin concentrations were measured at the baseline and at the end of the study, with sociodemographic factors also considered for potential correlations. **Result:** In a study involving ESRD patients on hemodialysis, zinc supplementation led to significant changes in serum zinc and albumin levels over a 3-month period. Patients receiving zinc showed increased serum albumin and improved sleep quality, evidenced by decreased Pittsburgh Sleep Quality Index scores. These findings suggest beneficial effects of zinc supplementation on serum albumin and sleep in hemodialysis patients. **Conclusion:** In clinical trials, zinc supplementation dramatically raises blood zinc levels in hemodialysis patients compared to baseline and a placebo group. Zinc supplementation also raised serum albumin, indicating better nutrition. Additionally, the supplementation improved sleep quality, as seen by a substantial drop in Pittsburgh Sleep Quality Index scores. Zinc may help manage end-stage renal disease and hemodialysis problems, according to these studies. Confirming these findings and investigating long-term benefits and appropriate dose is advised.

**KEYWORDS:** zinc gluconate, sleep quality, serum albumin, hemodialysis.

## INTRODUCTION

Chronic kidney disease (CKD), particularly in its advanced stages managed by maintenance hemodialysis, presents a complex challenge affecting multiple aspects of health, including nutritional status, metabolic balance, and overall quality of life. Patients undergoing hemodialysis often experience a range of complications, including disturbances in mineral metabolism, altered sleep patterns, and nutritional deficiencies.[1,2] Zinc is a trace element critical for numerous biological functions, including immune response, wound healing, DNA synthesis, and cellular metabolism. It also plays a significant role in the central nervous system, impacting mood and sleep. Zinc's involvement in neurotransmitter release, synaptic transmission, and modulation of neuronal excitability suggests its potential influence on sleep regulation. In the general population, zinc supplementation has been shown to improve sleep quality. However, the impact of zinc on sleep among hemodialysis patients remains underexplored, a gap that this research aims to fill.[3,4] Sleep disorders are prevalent in patients with end-stage renal disease (ESRD) on hemodialysis. The disturbances range from insomnia and sleep apnea to restless legs syndrome, each contributing to decreased quality of life and increased morbidity. The pathophysiology behind these sleep disturbances is multifactorial, involving fluid and electrolyte imbalances, changes in renal clearance of hormones that regulate sleep-wake cycles, and psychosocial stressors. Given zinc's role in central nervous system functioning,

it stands to reason that zinc gluconate supplementation might stabilize some of the biochemical pathways disrupted in CKD, potentially mitigating sleep-related issues.[5,6] Another significant aspect of CKD management is nutritional status, particularly protein-energy wasting (PEW), which is highly prevalent among hemodialysis patients. Serum albumin is a well-established marker of nutritional status and a strong predictor of morbidity and mortality in this population. The hypoalbuminemia in hemodialysis patients can be attributed to factors such as inflammation, malnutrition, and altered protein metabolism. Zinc plays a vital role in protein synthesis and cell growth, suggesting that zinc supplementation could potentially improve serum albumin levels by enhancing these anabolic processes.[7,8] Aims of the study: to evaluate the effect of zinc gluconate supplementation on improvement the quality of sleep and serum albumin in patients undergoing maintenance hemodialysis.

## METHOD

A single-blind clinical trial will be conducted at the Medical City Dialysis Center in Baghdad from 1st of September 2023 to 1st of January 2024. This study will involve 50 patients diagnosed with end-stage renal disease (ESRD) who are currently undergoing maintenance hemodialysis at the aforementioned center. The participants will be stratified into two groups:1st group will be administered an oral dose of 25 mg zinc gluconate daily, while 2nd group receive a placebo. This intervention will continue for a duration of 12 weeks. Sleep quality will be evaluated using the Pittsburgh Sleep Quality Index (PSQI)[9], a standardized and widely recognized tool for measuring sleep patterns and disturbances. Additionally, serum albumin levels will be measured at both the beginning and the end of the study period to ascertain any changes attributable to the supplementation. Sociodemographic data collected will include age, gender, presence of hypertension, diabetes mellitus or other forms of chronic disease, duration of hemodialysis treatment, and the typical schedule of the hemodialysis sessions. This data will help in assessing any correlations between these variables and the outcomes of the trial. The collected data were coded, entered, presented, and analyzed by computer using the available data base software program statistical package of IBM SPSS-29 (IBM Statistical Packages for Social Sciences- version 29, Chicago, IL, USA). Data were presented in simple measures of frequency, percentage, mean, standard deviation, and range (minimum-maximum values). Ethical Considerations: Prior to data collection, official approvals were secured from the Arabic Council of Medical Specialty and the Medical City Dialysis Center in Baghdad. Additionally, verbal consent was obtained from each participating patient after providing a thorough explanation of the study's aims and objectives. Participants were assured of the confidentiality of their data, with questionnaires being completed anonymously. The significance of difference of different means (quantitative data) were tested using Students-t-test for difference between two independent means or Paired-t-test for difference of paired observations (or two dependent means). The significance of difference of different percentages (qualitative data) were tested using Pearson Chi-square test ($\chi^2$-test) with application of Yate's correction or Fisher Exact test whenever applicable. Statistical significance was considered whenever the P value was equal or less than 0.05. At the end of data research 8 patients were excluded from study due to the death of four of them and others were transferred to renal transplantation.

## RESULTS

As shown in table 1, 9 (32.1%) of patients have zinc supplement are at age 50-59 years, and 7 (25%) of them at age group 60-69 years old. Mean age of patients received zinc is 54 ± 15 years. 50% of patients received zinc are males and 50% of them are females. 50% and 32% of patients received zinc are having hypertension and diabetes mellitus respectively. 57.1% of patients received zinc are having Duration on Hemodialysis 1-4 years. 53.6% of patients received zinc are having 2 days/week Schedule of hemodialysis.

**Table (1): Distribution of Studied Sample According to the Sociodemographic Characters.**

| | | Zinc group (28 patients) | | Placebo group (15 patients) | |
|---|---|---|---|---|---|
| | | No | % | No | % |
| Age (years) | <40 years | 4 | 14.3 | 3 | 20.0 |
| | 40---49 | 4 | 14.3 | 3 | 20.0 |
| | 50---59 | 9 | 32.1 | 5 | 33.3 |
| | 60---69 | 7 | 25.0 | 3 | 20.0 |
| | ≥70 years | 4 | 14.3 | 1 | 6.7 |
| | Mean ± SD(range) | 54.3±14.7(20-75) | | 51.3±12.5(30-71) | |
| Gender | Male | 14 | 50.0 | 12 | 80.0 |
| | Female | 14 | 50.0 | 3 | 20.0 |
| Hypertension | Yes | 14 | 50.0 | 5 | 33.3 |
| | No | 14 | 50.0 | 10 | 66.7 |
| DM | Yes | 9 | 32.1 | 10 | 66.7 |
| | No | 19 | 67.9 | 5 | 33.3 |

| | | | | | |
|---|---|---|---|---|---|
| Others | Yes | 9 | 32.1 | 2 | 13.3 |
| | No | 19 | 67.9 | 13 | 86.7 |
| Duration on Hemodialysis (years) | <1year | 6 | 21.4 | 4 | 26.7 |
| | 1---4 | 16 | 57.1 | 10 | 66.7 |
| | 5---10years | 6 | 21.4 | 1 | 6.7 |
| Schedule of hemodialysis | 2 days/week | 15 | 53.6 | 5 | 33.3 |
| | 3 days/week | 13 | 46.4 | 10 | 66.7 |

As shown in fig 1; there is significant increase in mean level of serum zinc in patients received zinc after 3 months in compares with their baseline serum level before receiving zinc. While in fig 2; there is significant increase in mean level of serum albumin in patients received zinc after 3 months than patients received placebo after 3 months.

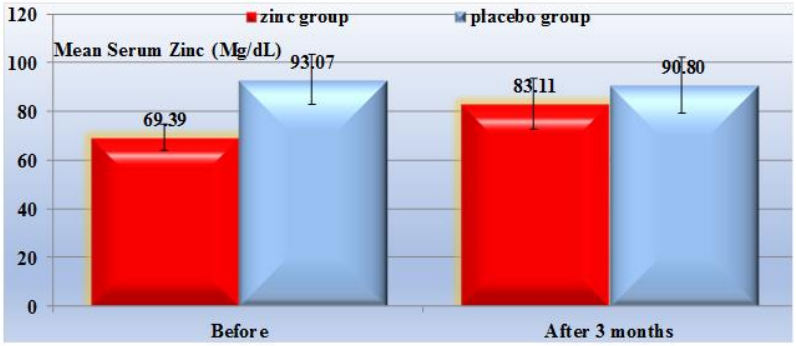


**Figure (1): Distribution of the Studied Sample (Zinc Group And Placebo Group) According To Serum Zinc Level Before And After Supplementations.**

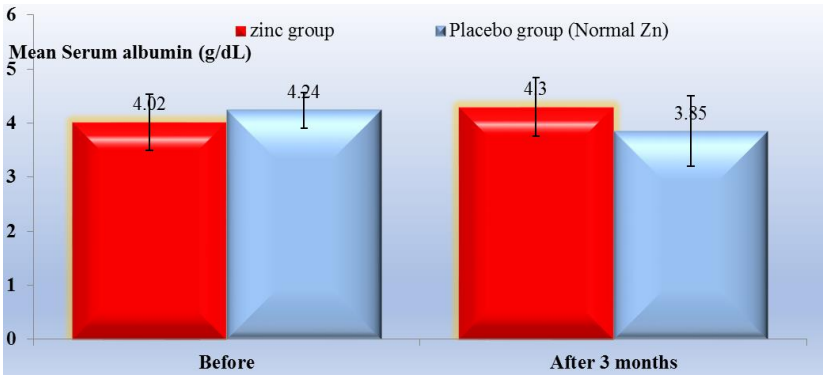


**Figure (2): Distribution of the Studied Sample (Zinc Group and Placebo Group) According to Serum Albumin Level Before and After Supplementations.**

As shown in table 2 and fig 3, there is significant association between zinc supply and sleep change (decrease in Pittsburgh score) after 3 months, 35.7% of patients received zinc have Pittsburgh score (-1) and 32.1% of patients received zinc have Pittsburgh score (-2).

**Table (2): Distribution of Studied Sample According to Sleep Quality (Pittsburgh Score) Before and After Supplementation.**

| | **Zinc group (28patients)** | | | **Placebo group (15 patients)** | | **P value** |
|---|---|---|---|---|---|---|
| | No | | % | No | % | |
| Sleep change (decrease in Pittsburgh score) after 3 months | -3 | 3 | 10.7 | 0 | 0 | |
| | -2 | 9 | 32.1 | 0 | 0 | **0.002*** |
| | -1 | 10 | 35.7 | 3 | 20 | |
| | 0 | 6 | 21.4 | 12 | 80 | |
| ^Significant difference between two dependent means using Paired-t-test at 0.05 level. | | | | | | |
| *Significant difference between percentages using Pearson chi-square test ($x^2$-test) at 0.05 level | | | | | | |

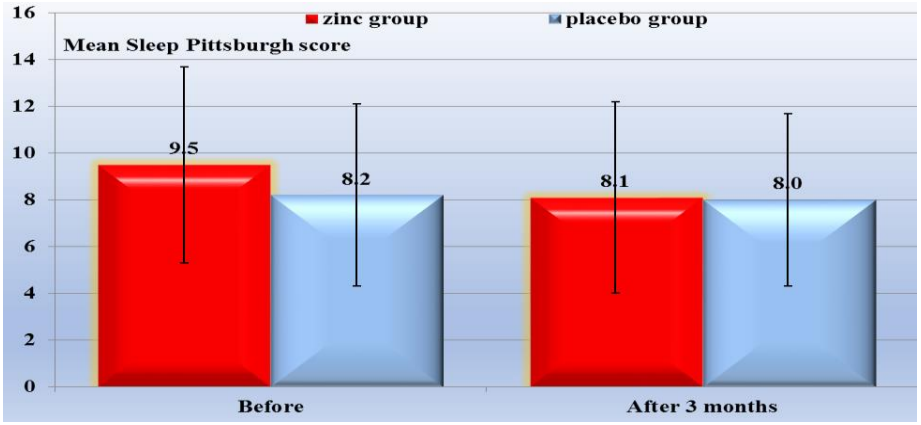


**Figure (3): Distribution of studied sample according to sleep quality before and after supplementation.**

## DISCUSSION

The results from the clinical trial conducted at the Medical City Dialysis Center in Baghdad provide compelling evidence on the effects of zinc gluconate supplementation in end-stage renal disease (ESRD) patients undergoing maintenance hemodialysis. These findings are significant, showing a noticeable improvement in serum zinc and albumin levels, and a moderate impact on sleep quality over the 3-month supplementation period. Firstly, the increase in serum zinc levels among the zinc-supplemented group compared to the placebo group and their own baseline levels is consistent with existing literature that supports the efficacy of zinc supplementation in correcting zinc deficiency in hemodialysis patients. Studies by Guo CH. and Wang CL (2013)[10], and (Pattan V et al. 2021)[11] found similar increases in serum zinc concentrations after supplementation, which is pivotal as zinc plays a crucial role in numerous enzymatic and immune functions that are often compromised in ESRD patients. Interestingly, our trial also documented a significant increase in serum albumin levels in the zinc-supplemented group. This result is particularly relevant because low serum albumin is a common problem in dialysis patients and is associated with increased morbidity and mortality due to its relationship with malnutrition and inflammation (Don BR and Kaysen G, 2004).[12] The observed improvement in albumin levels could suggest that zinc supplementation might help ameliorate protein-energy wasting and inflammatory states in ESRD patients. This finding aligns with the research by Bao B. et al. (2010)[13], who reported that zinc supplementation contributes to the improvement of nutritional status and reduces inflammation markers in dialysis patients. However, the impact of zinc supplementation on sleep quality presents a more nuanced outcome. While there was a significant decrease in the difficulty of sleep scores from baseline within the zinc-supplemented group, this improvement was not significantly different when compared to the placebo group. This suggests that while zinc may have some beneficial effects on sleep disturbances commonly experienced by hemodialysis patients, these effects are not robust enough to outperform placebo effects in a clinical trial setting. This part of our findings diverges somewhat from the broader literature, such as studies by Wang LJ et al. (2017)[14], which have found more definitive improvements in sleep quality with zinc supplementation. The discrepancy could be attributed to differences in study design, baseline zinc status of participants, or the measures used to assess sleep quality. Moreover, the data indicating a one third improvement in the Pittsburgh Sleep Quality Index (PSQI) scores among patients with moderate zinc supplementation highlights a potential dose-response relationship that warrants further investigation. Given that sleep disorders are prevalent and detrimental in hemodialysis patients, affecting their quality of life significantly, any intervention that could potentially improve sleep should be considered valuable. Finally, the sociodemographic variables and comorbid conditions such as hypertension and diabetes did not significantly skew the results, suggesting that zinc supplementation could be universally beneficial in the hemodialysis patient population regardless of these factors. However, long-term studies are needed to fully understand the broader implications of zinc supplementation in this demographic, particularly concerning cardiovascular outcomes, as suggested by recent meta-analyses (Foster M and Samman S. 2012).[15] The potential benefits of zinc supplementation in improving serum zinc and albumin levels in ESRD patients. Although the improvements in sleep quality were modest, the overall evidence suggests a positive trend that could be explored further in larger, more comprehensive trials with extended follow-up periods to fully elucidate the therapeutic benefits of zinc in this population.

## CONCLUSION

The clinical trial results indicate that zinc supplementation significantly improves serum zinc levels in hemodialysis patients, both in comparison to baseline and against a placebo group. Additionally, zinc supplementation was associated with an increase in serum albumin levels, suggesting improved nutritional status. Notably, the supplementation also positively affected sleep quality, as evidenced by a significant decrease in the Pittsburgh Sleep Quality Index scores. These findings underscore the potential of zinc as a beneficial supplement in managing complications

associated with end-stage renal disease and hemodialysis treatment. Further studies are recommended to consolidate these findings and explore long-term benefits and optimal dosing.

## REFERENCES


1. Akchurin, Oleh M. "Chronic Kidney Disease and Dietary Measures to Improve Outcomes." Pediatric clinics of North America, 2019; 66(1): 247-267. Available at: https://doi.org/10.1016/j.pcl.2018.09.007.
2. Rodrigues Neto Angéloco L, Arces de Souza GC, Almeida Romão E, Garcia Chiarello P. Alkaline Diet and Metabolic Acidosis: Practical Approaches to the Nutritional Management of Chronic Kidney Disease. J Ren Nutr., 2018 May; 28(3): 215-220. Available at: https://doi.org/10.1053/j.jrn.2017.10.006 Epub 2017 Dec 6. PMID: 29221627.
3. Li Z, Liu Y, Wei R, Yong VW, Xue M. The Important Role of Zinc in Neurological Diseases. Biomolecules, 2022 Dec 23; 13(1): 28. doi: 10.3390/biom13010028. PMID: 36671413; PMCID: PMC9855948.
4. Gower-Winter SD, Levenson CW. Zinc in the central nervous system: From molecules to behavior. Biofactors, 2012 May-Jun; 38(3): 186-93. doi: 10.1002/biof.1012. Epub 2012 Mar 31. PMID: 22473811; PMCID: PMC3757551.
5. Maung SC, El Sara A, Chapman C, Cohen D, Cukor D. Sleep disorders and chronic kidney disease. World J Nephrol., 2016 May 6; 5(3): 224-32. doi: 10.5527/wjn.v5.i3.224. PMID: 27152260; PMCID: PMC4848147.
6. Turk AC, Ozkurt S, Turgal E, Sahin F. The association between the prevalence of restless leg syndrome, fatigue, and sleep quality in patients undergoing hemodialysis. Saudi Med J., 2018; 39(8): 792-798.
7. Bonanni A, Mannucci I, Verzola D, Sofia A, Saffioti S, Gianetta E, Garibotto G. Protein-energy wasting and mortality in chronic kidney disease. Int J Environ Res Public Health, 2011 May; 8(5): 1631-54. doi: 10.3390/ijerph8051631. Epub 2011 May 19. PMID: 21655142; PMCID: PMC3108132.
8. Gama-Axelsson T, Heimbürger O, Stenvinkel P, Bárány P, Lindholm B, Qureshi AR. Serum albumin as predictor of nutritional status in patients with ESRD. Clin J Am Soc Nephrol., 2012 Sep; 7(9): 1446-53. doi: 10.2215/CJN.10251011. Epub 2012 Jun 21. Erratum in: Clin J Am Soc Nephrol, 2012 Nov; 7(11): 1915. PMID: 22723451; PMCID: PMC3430958.
9. Haddadian-Khouzani S, Shahidi S, Askari G, Clark CCT, Rouhani MH. The efficacy and safety of zinc gluconate supplementation on quality of life, sleep quality, and serum albumin in hemodialysis patients: A randomized clinical trial. European Journal of Integrative Medicine, 2022 Oct; 55: 102183. doi: 10.1016/j.eujim.2022.102183.
10. Guo CH, Wang CL. Effects of zinc supplementation on plasma copper/zinc ratios, oxidative stress, and immunological status in hemodialysis patients. Int J Med Sci., 2013; 10(1): 79-89. doi:10.7150/ijms.5291.
11. Pattan V, Chang Villacreses MM, Karnchanasorn R, Chiu KC, Samoa R. Daily Intake and Serum Levels of Copper, Selenium and Zinc According to Glucose Metabolism: Cross-Sectional and Comparative Study. Nutrients, 2021; 13(11): 4044. Published 2021 Nov 12. doi:10.3390/nu13114044.
12. Don BR, Kaysen G. Serum albumin: relationship to inflammation and nutrition. Semin Dial, 2004 Nov-Dec; 17(6): 432-437. doi/10.1111/j.0894-0959.2004.17603.x PMID: 15660573.
13. Bao B, Prasad AS, Beck FW, Fitzgerald JT, Snell D, Bao GW, Singh T, Cardozo LJ. Zinc decreases C-reactive protein, lipid peroxidation, and inflammatory cytokines in elderly subjects: a potential implication of zinc as an atheroprotective agent. Am J Clin Nutr., 2010 Jun; 91(6): 1634-41. doi: 10.3945/ajcn.2009.28836. Epub 2010 Apr 28. PMID: 20427734; PMCID: PMC2869512.
14. Wang LJ, Wang MQ, Hu R, et al. Effect of Zinc Supplementation on Maintenance Hemodialysis Patients: A Systematic Review and Meta-Analysis of 15 Randomized Controlled Trials. Biomed Res Int., 2017; 2017: 1024769. doi:10.1155/2017/1024769.
15. Foster M, Samman S. Zinc and regulation of inflammatory cytokines: implications for cardiometabolic disease. Nutrients, 2012; 4(7): 676-694. doi:10.3390/nu4070676.