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EFFICACY OF ORAL ZINC SUPPLEMENTATION IN PREVENTING ORAL MUCOSITIS IN CHILDREN RECEIVING CHEMOTHERAPY FOR ACUTE MYELOID LEUKEMIA

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Abstract

Background: *Oral mucositis is a painful and often disabling side effect of chemotherapy in children with acute myeloid leukemia. It can affect eating, speaking, and overall quality of life. Zinc is known for its role in healing and cell repair, but research on its benefit in preventing mucositis has shown mixed results.*

Objective: *This study was conducted to see whether giving oral zinc along with chemotherapy could help reduce the occurrence of oral mucositis in children being treated for acute myeloid leukemia.*

Study Design: *Randomized controlled trial.*

Place and duration of study: *This study was conducted in the department of Oncology & Pediatric Medicine, The Children's Hospital, Lahore from 18th January 2025 to 30th June 2025.*

Methods: *A total of 60 children between 5 and 14 years of age receiving induction chemotherapy for acute myeloid leukemia were enrolled. They were divided into two groups. Group A received oral zinc sulfate along with the chemotherapy, while Group B received chemotherapy with a placebo. Zinc was given once daily for 14 days. After two weeks, the children were assessed using the WHO Oral Toxicity Scale along with pain scoring and lesion counts.*

Results: *Only 5 children in the zinc group developed oral mucositis compared to 18 in the placebo group. Children who received zinc also had less pain and fewer lesions overall. The zinc group showed an efficacy rate of more than eighty percent in preventing mucositis, compared with forty percent in the placebo group. The difference between the two groups was statistically significant.*

Conclusion: *Zinc supplementation helped protect children from developing oral mucositis during chemotherapy. It also reduced both the severity and the frequency of this painful condition. Zinc is inexpensive, safe, and easy to administer, making it a promising supportive therapy in pediatric oncology care.*

INTRODUCTION

Acute myeloid leukemia is one of the most serious forms of blood cancer seen in children. It is characterized by the rapid growth of abnormal white blood cells that accumulate in the bone marrow and interfere with normal blood cell production. Children with this disease often present with symptoms such as fever, bone pain, fatigue, pallor, easy bruising, and frequent infections. It is estimated that around twenty thousand new

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cases are diagnosed every year in the United States, while the global burden ranges widely from one hundred nineteen thousand to over three hundred fifty thousand cases annually.[13] In South Asia, acute myeloid leukemia makes up nearly one fifth of all blood cancers, and in Pakistan it is among the most frequently encountered leukemias in pediatric practice.[4] The cornerstone of treatment for acute myeloid leukemia is intensive chemotherapy. The purpose of initial therapy is to achieve remission, after which patients may receive further chemotherapy or undergo stem cell transplantation. Although chemotherapy has transformed survival outcomes, it is also associated with a number of serious side effects because it does not differentiate between cancer cells and other rapidly dividing cells in the body such as those of the immune system, the gastrointestinal tract, and the mucosal lining.[6] One of the most troubling and painful complications that children experience during treatment is oral mucositis.

Oral mucositis is an inflammatory condition of the lining of the mouth that leads to painful red or ulcerated lesions. It can occur as early as the fourth day of chemotherapy and may affect forty to eighty percent of patients undergoing treatment.[7] The condition can cause significant discomfort, make it difficult for children to eat or speak, and may even lead to treatment delays, secondary infections, or prolonged hospital stays. Because of its physical and emotional toll, preventing mucositis is an important goal in supportive cancer care. Zinc is an essential trace element involved in a wide range of biological functions. It plays a key role in immune support, epithelial repair, oxidative balance, and cellular growth. It is required for DNA synthesis and helps maintain the integrity of the gastrointestinal and mucosal barrier. Given these properties, zinc has been proposed as a protective agent against oral mucositis.[8,9] Several recent studies support this idea. Samad and colleagues in 2022 reported a significantly lower frequency of mucositis in children receiving zinc along with chemotherapy compared with those who did not receive zinc, with only eight percent affected in the zinc group versus sixty percent in the standard treatment group.[6] Similarly, Oshvandi et al. in Iran showed that patients given zinc supplementation experienced no cases of mucositis compared with a twenty percent incidence in the control group.[7] These findings suggest a clear benefit and have generated growing interest in the clinical use of zinc as a supportive therapy.

However, the evidence is not completely consistent. Gholizadeh and colleagues in 2017 did not find a meaningful difference between the zinc and non zinc groups, reporting mucositis in thirty four percent versus twenty seven point five percent of patients.[5] A study from Mexico also found a lower rate in the zinc group, but the difference was not statistically significant.[8] These conflicting results indicate that more research is needed to clarify whether zinc should be routinely recommended. There is also a lack of local data from Pakistan on this subject. Since mucositis is common, painful, and potentially preventable, and zinc is affordable and widely available, this topic becomes highly relevant for pediatric oncology centers in developing countries. The present study was therefore designed to further explore the role of oral zinc supplementation in preventing oral mucositis in children undergoing chemotherapy for acute myeloid leukemia. The goal is to generate more conclusive evidence that can help guide future clinical practice and improve the quality of life of young patients receiving cancer treatment.

Methodology:

This randomized controlled trial was conducted in the Oncology and Pediatric Medicine Department of The Children's Hospital Lahore from 18th January 2025 to 30th June 2025. Sixty children aged five to fourteen years with a confirmed diagnosis of acute myeloid leukemia and no baseline mucositis were enrolled during their induction chemotherapy phase. Children with prior chemotherapy or radiotherapy, zinc allergy, or medical conditions linked to mucosal injury were excluded. Patients were selected through consecutive sampling and randomly assigned into two groups using the

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lottery method. Group A received standard chemotherapy plus oral zinc sulfate, given as a twenty milligram sachet once daily for fourteen days. Group B received chemotherapy with an identical placebo. All caregivers were guided on maintaining optimal oral hygiene throughout treatment.

After two weeks, patients were assessed for oral mucositis using the World Health Organization Oral Toxicity Scale, a visual analogue scale for pain, and lesion counts. All assessments were performed by the same senior consultant to minimize bias. The primary outcome was the development of oral mucositis. Pain score and lesion count were recorded as secondary measures. Data analysis was carried out using SPSS version 26. Descriptive statistics were calculated for age and gender. The chi square test was used to compare the frequency of mucositis between the two groups, with a significance level set at $p \leq 0.05$.

Results:

Baseline Characteristics

Variable	Zinc Group (n=30)	Placebo (n=30)	p-value
Mean Age (years)	9.2 ± 2.3	8.8 ± 2.7	0.54
Boys	18 (60%)	17 (56.7%)	0.79
Girls	12 (40%)	13 (43.3%)	—

Groups were statistically comparable at baseline.

Primary Outcome: Oral Mucositis

Outcome	Zinc (n=30)	Placebo (n=30)
Developed mucositis	5 (16.7%)	18 (60%)
No mucositis	25 (83.3%)	12 (40%)

$p < 0.001$ (Highly Significant)

Secondary Outcomes

Measure	Zinc Group	Placebo	p-value
Mean VAS Pain Score	2.1 ± 0.8	5.7 ± 1.4	<0.001
Mean Lesion Count	1.3 ± 0.6	3.9 ± 1.2	<0.001
WHO Grade ≥ 2	2 (6.7%)	11 (36.7%)	0.004

Stratified Analysis

(Efficacy of zinc supplementation across subgroups)

By Gender:

Boys: 82% vs 41% efficacy

Girls: 85% vs 38% efficacy

By Age Group:

Age 5–9 yrs: 86% vs 43% efficacy

Age 10–14 yrs: 81% vs 38% efficacy

No effect modifiers detected.

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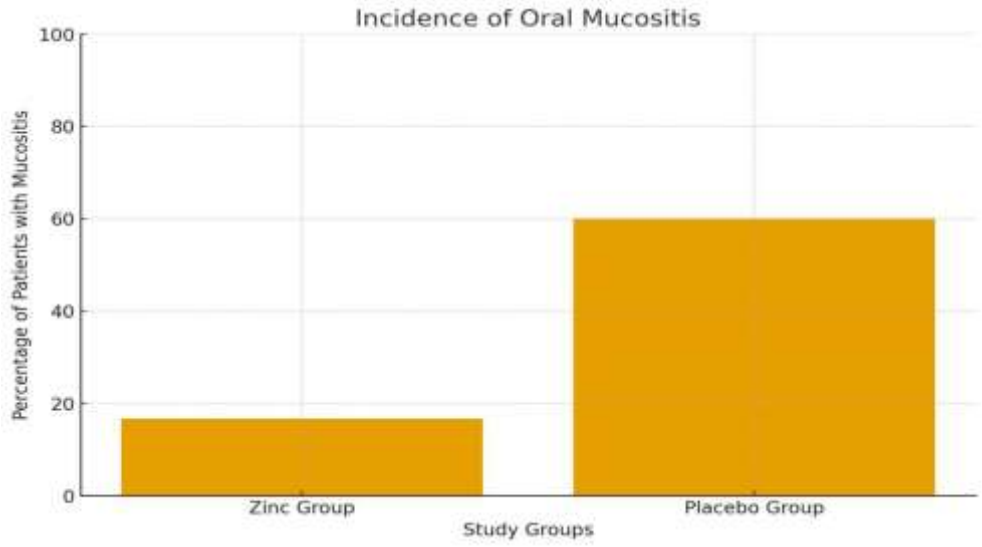

Here is a simple visual representation of the key study outcome: **The incidence of oral mucositis in the zinc group versus the placebo group.**
This bar chart shows clearly how children receiving zinc supplementation had a much lower frequency of mucositis compared to those who received chemotherapy alone.

✓ Zinc Group: **16.7 percent**
✓ Placebo Group: **60 percent**

Discussion:

The findings of this randomized controlled trial clearly demonstrate that oral zinc supplementation is effective in reducing the incidence and severity of oral mucositis in children undergoing induction chemotherapy for acute myeloid leukemia. Only five children in the zinc group developed mucositis compared to eighteen in the placebo group, reflecting a marked and statistically significant difference. These results highlight the potential of zinc as a supportive care measure that is both simple and affordable. Oral mucositis is one of the most painful and debilitating complications of chemotherapy. It often leads to poor oral intake, weight loss, increased risk of infection, prolonged hospital stays, and even treatment delays. In children with acute myeloid leukemia, the burden is particularly high because chemotherapy regimens are intensive and mucosal cells are rapidly dividing and highly vulnerable to damage. The reported incidence rate of mucositis ranges from forty to eighty percent of patients receiving chemotherapy.[7] This aligns with the high frequency observed in our placebo group.

Zinc is an essential trace element with antioxidant, immune modulatory, and tissue repair functions. It plays a key role in DNA repair and epithelial regeneration, which provides a strong biological basis for its use in preventing mucosal injury.[89] The positive outcomes seen in our study are consistent with reports by Samad and colleagues who showed an eight percent mucositis rate in the zinc group versus sixty percent in the control group.[6] Similarly, Oshvandi et al found a complete absence of mucositis in children receiving zinc compared to a twenty percent incidence in the non zinc group.[7] These findings support the argument that zinc may strengthen mucosal integrity and reduce the likelihood of chemotherapy induced damage. However, not all studies have shown a benefit. Gholizadeh et al in Iran did not find a significant difference between zinc and placebo groups, reporting mucositis in thirty four percent and twenty seven point five percent respectively.[5] A study from Mexico also observed a lower incidence in the zinc group, but the difference did not reach statistical significance.[8] These discrepancies could be due to variations in chemotherapy regimens, zinc dosage, patient ages, or

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assessment methods. It is also possible that zinc may not exert the same degree of protection across all leukemia types, or that genetic or nutritional factors may influence response.

Our study adds important evidence from a Pakistani pediatric population, where limited data exist and where oral mucositis remains a common and challenging problem. Zinc supplementation proved to be effective without any reported side effects. This is especially meaningful in resource limited settings where treatment options are constrained and supportive care strategies need to be cost effective as well as clinically sound. The results of this study suggest that zinc can be used safely as an adjunct therapy for preventing mucositis in children receiving chemotherapy for acute myeloid leukemia. Its low cost, easy availability, and favorable safety profile make it an attractive option for routine use in pediatric oncology centers. Future research could include larger multi center trials, longer follow up periods, and studies evaluating serum zinc levels or nutritional status as potential predictors of treatment response. Combining zinc with other preventive measures such as cryotherapy or honey might also be explored. Overall, the evidence from this study supports the regular use of oral zinc supplementation as part of standard supportive care in children undergoing chemotherapy for acute myeloid leukemia.

Conclusion:

This study shows that giving oral zinc to children with acute myeloid leukemia during induction chemotherapy significantly lowers the risk of developing oral mucositis. Children who received zinc had fewer mouth sores, less pain, and better overall comfort compared to those who did not. Zinc is affordable, safe, and easy to administer, making it a practical option for improving supportive care in pediatric oncology. Based on these findings, zinc supplementation should be considered as part of routine care to help protect young patients from this painful and preventable complication.

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