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# Efficacy of Intravenous Magnesium Sulphate in Children Admitted with Severe Acute Bronchiolitis

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## ABSTRACT

**Background:** Acute bronchiolitis ranks among the top causes of respiratory distress in children, and current options for treatment are limited. Magnesium sulfate has been proposed as a possible treatment based on bronchodilator as well as anti-inflammatory effects. Yet, in children with severe acute bronchiolitis, the efficacy of the drug is still in question, especially when compared with a placebo. **Objective:** To determine the efficacy of intravenous magnesium sulphate compared to placebo in children admitted with severe acute bronchiolitis. **Study Design:** Randomized controlled trial. **Duration and Place of Study:** This study was conducted from August 2023 to February 2024 at the Department of Pediatric Medicine, Ibn-e-Siena Hospital, Multan. **Methodology:** A total of 98 children aged 2 to 24 months with severe acute bronchiolitis were enrolled. Children were randomly assigned to either receive a single intravenous dose of magnesium sulfate (75 mg/kg, maximum 2 grams) or a placebo (0.9% saline). The primary outcome was the change in Wang clinical severity score after 24 hours, with secondary outcomes including hospital stay duration and response rate. **Results:** In this study, Group A (magnesium sulfate) showed significantly lower Wang scores at 24 hours (3.88 ± 0.88) compared to Group B (placebo) (4.69 ± 1.04), with a treatment response rate of 83.7% in Group A compared to 44.9% in Group B ($p < 0.001$). Age, gender, symptom duration, and initial severity were all significant factors influencing the treatment's efficacy. **Conclusion:** Intravenous magnesium sulfate significantly improves clinical outcomes and shortens hospital stay in children with severe acute bronchiolitis.

## INTRODUCTION

Bronchiolitis is a respiratory illness in infants and toddlers caused predominantly by the respiratory syncytial virus.[1] It includes inflammation and congestion of the lower airways in the lungs, with associated cough, wheezing, shortness of breath, and respiratory distress.[2] Bronchiolitis would normally happen in children younger than two years, with the highest incidence occurring among infants aged 3-6 months.[3] Bronchiolitis may be mild or severe, with some severe enough for the child to be admitted into the hospital due to respiratory failure.[4] Severe acute bronchiolitis includes labored breathing, hypoxia, and dehydration, and immediate medical intervention by a doctor should be undertaken.[5] Treatment for severe acute bronchiolitis includes supportive care since no antiviral treatment has been proven for the vast majority.[6] Hospital admission largely includes supplemental oxygen, intravenous fluids, and breathing support in severe cases.[7] Some children are treated with medications such as nebulized saline or bronchodilators, though the benefit of these interventions is uncertain.[7] Monitoring for and preventing secondary infections, including pneumonia, is also included in care. Most children who have an episode of bronchiolitis recover with supportive care alone, but some will require intensive care, particularly children who have underlying illnesses such as prematurity or congenital heart disease.[8]

Magnesium sulphate has been a possible adjuvant therapy in severe bronchiolitis, especially in children with severe wheezing and bronchospasm.[9] Intravenous delivery of magnesium sulphate is reported to have a beneficial bronchodilator effect, possibly augmenting airflow and diminishing the work of breathing.[10] Its use in the context of bronchiolitis as a help in severe unresponsive respiratory failure unrelieved by conventional maneuvers, including exogenous inhaled bronchodilators, has been explored.[10] While the clinical evidence for efficacy is currently inconsistent, some studies report that magnesium sulphate may be an advantage in reducing the need for mechanical ventilation as well as augmenting improvement in oxygenation in severely impaired children with acute bronchiolitis.[11] For this reason, the sulphate figures in the

management of severely ill children who are unresponsive to first line management.

Ara A et al. conducted a study involving 108 patients, ranging from 2 months to 2 years of age, diagnosed with acute bronchiolitis. Their results revealed a statistically significant difference in treatment efficacy, with Magnesium Sulfate achieving a success rate of 88.9% compared to 68.5% in the control group ($p = 0.01$).[12] Similarly, in a study by Sik N et al., 74 patients were treated with IV MgSO4 and 33 patients received a placebo. The study demonstrated a significant reduction in respiratory rate and mRDAI score at the 2nd, 4th, 8th, and 12th hours in the Magnesium Sulfate group compared to the placebo. The Magnesium Sulfate treatment also showed a higher S/F ratio at the 4th hour. Patients treated with the placebo required higher rates of intervention, including an earlier initiation of high-flow nasal cannula oxygen therapy and a longer hospital stay compared to those treated with Magnesium Sulfate.[13]

Severe acute bronchiolitis continues to be a major cause of hospitalization of infants and young children, with no proven effective treatments other than supportive care. However, no definitive therapy has decreased disease severity or shortened stay that has occurred persistently. However, recent studies indicate that intravenous magnesium sulfate's bronchodilatory and anti-inflammatory properties make this medication a potential powerful tool in the clinical treatment of severe cases. Despite that, progression of science with evidence is challenged by lack of resolution, which stress needs more research to establish if it is credible and perhaps a part of standard treatment strategies.

## METHODOLOGY

This randomized controlled trial was conducted from August 2023 to February 2024 at the Department of Pediatric Medicine, Ibn-e-Siena Hospital, Multan. The study aimed to assess the efficacy of intravenous magnesium sulfate compared to a placebo in children admitted with severe acute bronchiolitis. A total of 98 children, aged 2 to 24 months, were enrolled, meeting the inclusion criteria of presenting with severe bronchiolitis, a Wang clinical severity score greater than 8, and symptoms lasting no more than three days. The sample size was determined using the WHO sample size calculator with a 95% confidence level and 80% power, based on an anticipated treatment efficacy of 88.9% in the magnesium sulfate group and 68.5% in the placebo group.

Patients were selected using a non-probability consecutive sampling technique. Exclusion criteria included children with congenital heart disease, chronic respiratory conditions, known magnesium sulfate hypersensitivity, and a personal or family history of atopy or early-onset asthma. After obtaining informed consent from parents, baseline characteristics, such as age, gender, and symptom duration, were recorded. A Wang clinical severity score was assessed by a postgraduate trainee, and all patients received standard treatment consisting of oxygen therapy, nebulized hypertonic saline, and intravenous rehydration if necessary.

Participants were randomly assigned to either the magnesium sulfate or placebo group via sealed opaque envelopes. Group A received a single intravenous dose of magnesium sulfate (75 mg/kg, maximum 2 grams), while Group B was given an equal volume of 0.9% saline. The efficacy of treatment was determined based on the Wang score at 24 hours, as assessed by a consultant pediatrician who was blinded to treatment allocation. Treatment efficacy was defined as a Wang score of less than 5 at 24 hours. Discharge readiness was determined by the absence of supplemental oxygen requirements, adequate feeding, and minimal or absent wheezing, crackles, and chest retractions, with an oxygen saturation of at least 94% and a Wang score below 4.

Data analysis was performed using SPSS 23.0, with continuous variables presented as mean ± standard deviation and categorical variables as frequencies and percentages. A chi-square test was used to compare the efficacy of treatment between the two groups, with a significance level set at $p \leq 0.05$. Stratification by age, gender, duration of illness, and pre-treatment severity score was also conducted to examine their effects on treatment efficacy, and post-stratification analysis was performed using chi-square tests

## RESULTS

As shown in Table 1, the mean age for Group A was 10.77 ± 5.23 months, and for Group B, it was 11.10 ± 4.98 months. Both groups had similar symptom durations (1.96 ± 0.76 days for both groups) and Wang scores at admission (9.92 ± 0.78 for Group A and 10.00 ± 0.81 for Group B). However, Wang scores at 24 hours were significantly different, with Group A showing a lower score (3.88 ± 0.88) compared to Group B (4.69 ± 1.04). Hospital stays were slightly shorter for Group A (2.78 ± 0.68 days) compared to Group B (3.14 ± 0.64 days). Gender distribution was also varied, with 61.2% males in Group A and 73.5% males in Group B.

**Table 1**

*Demographics of the Patients (n=98)*

| Demographics | | Group A n=49 Mean ± SD | Group B n=49 Mean ± SD |
|---|---|---|---|
| Age (months) | | 10.775±5.23 | 11.102±4.98 |
| Duration of Symptoms (days) | | 1.959±0.76 | 1.959±0.76 |
| Wang score at admission | | 9.918±0.78 | 10.000±0.81 |
| Wang score at 24 hours | | 3.877±0.88 | 4.693±1.04 |
| Hospital stay (days) | | 2.775±0.68 | 3.142±0.64 |
| Gender | Male n(%) | 30 (61.2%) | 36 (73.5%) |
| | Female n(%) | 19 (38.8%) | 13 (26.5%) |

Table 2 compares the efficacy between the two groups, revealing that 83.7% of children in Group A showed a positive response, while only 44.9% in Group B did, with a statistically significant p-value of <0.001.

**Table 2**

*Comparison of Efficacy in Both Groups.*

| Efficacy | n=49 Group A | n=49 Group B | P Value |
|---|---|---|---|
| Yes | 41 (83.7%) | 22 (44.9%) | |
| No | 8 (16.3%) | 27 (55.1%) | <0.001 |
| Total | 49 (100%) | 49 (100%) | |

Table 3 presents stratified efficacy based on demographic variables. Age stratification revealed that in children aged 1-12 months, Group A had 87.9% efficacy compared to 62.5% in Group B, and for those over 12 months, 75% in Group A responded positively, whereas only 11.8% in Group B did. Gender-specific results showed that 80% of male children in Group A responded positively, compared to 55.6% in Group B, while 89.5% of females in Group A responded positively, significantly higher than the 15.4% in Group B. Duration of symptoms also influenced efficacy, with 88.9% efficacy in Group A for those with 1-2 days of symptoms, compared to 58.3% in Group B, whereas in children with symptoms lasting more than 2 days, only 69.2% in Group A showed efficacy, compared to just 7.7% in Group B. Lastly, the Wang score at admission played a role in efficacy, with 91.7% efficacy for Group A in those with a score of ≤10, compared to 54.5% in Group B, while for those with a score of >10, efficacy dropped to 61.5% in Group A and 25% in Group B as shown in Graph-I.

**Table 3**

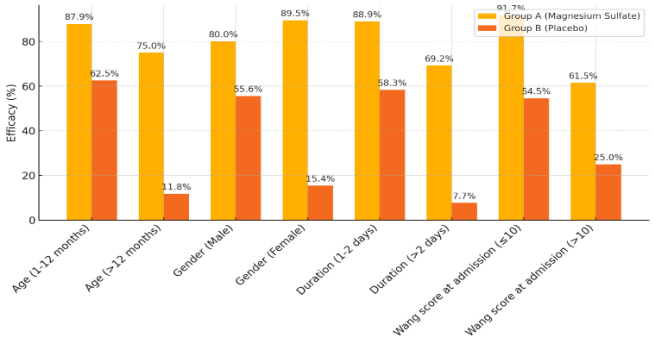
*Stratification of Efficacy Based on Demographic Variables Across Groups*

| Demographics variables | | Group | Efficacy Yes (n, %) | Efficacy No (n, %) | P-value |
|---|---|---|---|---|---|
| Age (months) | 1-12 | A | 29(87.9%) | 4(12.1%) | 0.023 * |
| | | B | 20(62.5%) | 12(37.5%) | |
| | >12 | A | 12(75%) | 4(25%) | 0.000 * |
| | | B | 2(11.8%) | 15(88.2%) | |
| Gender | Male | A | 24(80%) | 6(20%) | 0.036 |
| | | B | 20(55.6%) | 16(44.4%) | |
| | Female | A | 17(89.5%) | 2(10.5%) | 0.000 |
| | | B | 2(15.4%) | 11(84.6%) | |
| Duration of Symptoms (days) | 1-2 | A | 32(88.9%) | 4(11.1%) | 0.007 * |
| | | B | 21(58.3%) | 15(41.7%) | |
| | >2 | A | 9(69.2%) | 4(30.8%) | 0.004 * |
| | | B | 1(7.7%) | 12(92.3%) | |
| Wang score at admission | ≤10 | A | 33(91.7%) | 3(8.3%) | 0.001 * |
| | | B | 18(54.5%) | 15(45.5%) | |
| | >10 | A | 8(61.5%) | 5(38.5%) | 0.067 * |
| | | B | 4(25%) | 12(75%) | |

*Fischer Exact Test

**Graph 1**

*Association of Efficacy with Demographic Variables in Both Groups*




## DISCUSSION

The results show significantly higher efficacy in the magnesium sulfate treatment group, as evidenced by the lower Wang scores at 24 hours and the substantial difference in positive outcomes (83.7% in the magnesium sulfate group vs. 44.9% in the placebo group). These findings align with previous studies that highlight the anti-inflammatory and bronchodilator effects of magnesium sulfate, which help reduce airway obstruction and improve respiratory function in bronchiolitis.

In stratified analyses, children aged 1-12 months demonstrated the highest efficacy with magnesium sulfate (87.9%), suggesting that younger children may benefit more from the treatment. Magnesium sulfate's bronchodilatory properties could be particularly effective in this age group, where respiratory distress is often more severe. Gender-specific results indicated a notably higher response in females (89.5%) compared to males (80%) in the magnesium sulfate group, possibly pointing to gender-based differences in drug metabolism or immune response.

Duration of symptoms also influenced treatment outcomes. For children with symptoms lasting 1-2 days, 88.9% in the magnesium sulfate group showed a positive response, suggesting that early intervention may prevent disease progression. However, for those with symptoms lasting more than two days, the efficacy of magnesium sulfate was less pronounced (69.2%), emphasizing the importance of early treatment. Finally, children with a lower Wang score at admission (≤10) responded better to magnesium sulfate, which indicates that early intervention in less severe cases might lead to more favorable outcomes.

Our study results closely align with the findings from previous research investigating the use of magnesium sulfate in the treatment of acute bronchiolitis. The objective of our study was to evaluate the efficacy of intravenous magnesium sulfate (Group A) compared to placebo (Group B) in children admitted with severe acute bronchiolitis. The results demonstrated significantly higher efficacy in Group A, with 83.7% of children in the magnesium sulfate group showing a

positive response, compared to only 44.9% in the placebo group. This agrees with the findings of previous studies showing that magnesium sulfate produced bronchodilatory and antiinflammatory effects and may improve respiratory function in bronchiolitis. Similar, Janakwade et al. [14] also reported significant improvements in clinical severity scores and oxygen saturation levels of the infants treated with nebulized magnesium sulfate.

In addition, the same results were seen across other studies, and Guruprasad et al. [15] reported that 88.3% of children in the treatment group demonstrated significant clinical improvement after administration of nebulized magnesium sulfate. Our results are consistent with those obtained here, in that magnesium sulfate effectively reduces clinical severity and improves patient outcome, especially in subjects with moderately to severely affected bronchiolitis.

In our stratified analyses, we found the highest efficacy in Group A (87.9%) in children aged 1-12 months, suggesting that younger children may be more responsive to magnesium sulfate. This result is in line with results from other studies which also found higher efficacy in younger children. For example, in the study by Griffiths B. [16] younger children less than 12 months old in contrast to older children treated with intravenous magnesium sulfate showed significantly better outcomes which supports the idea that magnesium sulfate may be more beneficial in the younger infant often experiencing more severe respiratory distress.

Moreover, our study demonstrated, gender related differences in treatment efficacy, with females responding more (86%) than males (80%). Previous research of Janakwade et al. [14] also found that there are gender differences in response to treatment that are similar to the findings of this study. However, the actual mechanisms of these differences are not clear, though it is thought that it may be due to differences in how the drug is metabolized or how the immune system works between the genders. Therefore, the biological factors behind this observation need further investigation.

However, in our study, the duration of symptoms was a significant factor to determine the efficacy of treatment. Furthermore, Group A which treated children with symptoms for 1 – 2 days had shown a higher response rate (88.9%) indicating the possibility that early administration of magnesium sulfate might prevent progression of bronchiolitis. However, the efficacy was lower (69.2%) in children with symptoms lasting more than 2 days, demonstrating the need for early intervention. This is consistent with these studies by Kan et al. [17] and Kose et al. [18], which demonstrate the ability of early magnesium administration to improve outcomes, particularly in those with more acute symptoms. In both studies, children who received magnesium sulfate early in the course of their disease had improved oxygen saturation and clinical severity scores.

Our last finding was that children with a lower Wang score (Wang score≤10) at admission responded better to magnesium sulfate. Taken together, this implies that early intervention in milder cases may result in better outcomes, as also indicated by the Cochrane review by Chandelia et al. [19] who stated that magnesium sulfate treatment resulted in amelioration of the clinical severity scores in children, though it was of low certainty. The review also calls for larger trials to confirm or refute the efficacy of magnesium sulfate in acute bronchiolitis.

Overall, our findings are indeed consistent with previous work and support the use of magnesium sulfate both intravenously and nebulized as a treatment for acute bronchiolitis. Magnesium sulfate, however, needs further research with larger multi-center trials to confirm these results and the long term benefits and safety of this agent in treating bronchiolitis.

However, our study has some limitations with regards to promising results. First, being a single center study limits the generalizability of results to whole population. Additionally, the sample size was small, which might decrease the contingency of statistical power and precision of the results. It did not study long-term outcomes like the risk of recurrent wheezing or other respiratory problems — these are things that would be good to assess to determine how effective magnesium sulfate is overall.

## CONCLUSION

In conclusion, we have shown that intravenous magnesium sulfate gives good results and improves clinical severity and oxygen saturation compared to placebo in children with severe acute bronchiolitis. The results support the use of it, especially in younger children, shorter symptom duration, to improve recovery and shorten hospital stay. This contradicts existing literature and establishes magnesium sulfate as a potential therapeutic for bronchiolitis. But additional research will be needed to verify its long-term benefits and safety to all people.

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**Author's Contribution:** The authors have each played a pivotal role in the creation of this manuscript, as outlined below:

**Dr. Tahira Yasin** spearheaded the conceptualization of the study, the drafting of the article, and the collection of hospital data.

**Dr. Asif Javed** was instrumental in the development of the article, as well as in the conceptualization of the study and the analysis and interpretation of the data.

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