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# COMPARATIVE EFFICACY AND SAFETY OF NEBULIZED VERSUS INTRAMUSCULAR GLYCOPYRROLATE FOR FLEXIBLE BRONCHOSCOPY PREPARATION: A RANDOMIZED CONTROLLED TRIAL

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**Abstract:**
**Background**: Flexible bronchoscopy is widely used for pulmonary diagnostics, but preprocedural preparation is critical to manage secretions and enhance procedural success. Glycopyrrolate, administered either via nebulization or intramuscular injection, is effective for secretion control, though their comparative efficacy remains underexplored.
**Aim and Objectives:** This study aimed to compare the efficacy and safety of nebulized and intramuscular glycopyrrolate as preprocedural medications for flexible bronchoscopy, focusing on secretion management, procedural comfort, and safety profiles.
**Materials and Methods:** A randomized, double-blind controlled trial was conducted with 101 patients. Participants were assigned to receive either nebulized or intramuscular glycopyrrolate. Primary outcomes included secretion management and procedural comfort. Secondary outcomes evaluated adverse effects and patient satisfaction. Data were analyzed using GraphPad Prism version 9, with $p < 0.05$ considered statistically significant.
**Results**: Nebulized glycopyrrolate demonstrated superior secretion clearance ($91.74 \pm 18.23$ mL vs. $86.64 \pm 16.93$ mL, $p < 0.01$) and reduced saline discrepancies ($42.01 \pm 9.11$ mL vs. $46.26 \pm 8.87$ mL, $p < 0.01$). Both groups showed comparable patient satisfaction, with no significant difference in procedural comfort.
Conclusion: Nebulized glycopyrrolate offers superior secretion management and enhanced safety while maintaining comparable procedural comfort to intramuscular administration. These findings support its routine use in bronchoscopy preparation.

**Keywords**: Flexible bronchoscopy, glycopyrrolate, nebulization, secretion management, preprocedural preparation.

## INTRODUCTION

Flexible bronchoscopy has revolutionized pulmonary diagnostics and interventions by allowing direct visualization of the airway and access to lung tissues for biopsy or lavage. This minimally invasive technique is widely employed for conditions like lung cancer, chronic infections, and foreign body aspiration (1). However, optimizing the preprocedural preparation is critical to ensuring patient comfort and procedural success, particularly in managing airway secretions and minimizing risks like laryngospasm and bronchospasm (2, 3).
Anticholinergic agents, such as glycopyrrolate, are commonly used to reduce secretions and improve bronchoscopic visibility. Glycopyrrolate, a synthetic quaternary ammonium compound, is favoured for its efficacy in controlling secretions with minimal central nervous system side effects, as it does not cross the blood-brain barrier (4, 5). Traditionally, intramuscular glycopyrrolate has been the mainstay in preprocedural preparation. However, its systemic administration can lead to adverse effects such as tachycardia and dry mouth (6, 7). These

limitations have driven interest in nebulized glycopyrrolate, which delivers the medication directly to the airways, thereby enhancing local action and reducing systemic exposure (8, 9).

Nebulized glycopyrrolate has been shown to significantly reduce secretion volume, improving the ease of bronchoscopy and reducing the need for suctioning during the procedure (9, 10). Additionally, its shorter onset of action and fewer systemic side effects have made it a preferred option in many clinical settings (11-13). However, the comparative efficacy of nebulized versus intramuscular glycopyrrolate remains underexplored, particularly in randomized controlled settings.

This study aims to address this gap by conducting a double-blinded randomized controlled trial comparing nebulized and intramuscular glycopyrrolate as preprocedural medications for flexible bronchoscopy. By evaluating key outcomes such as secretion management, patient and operator satisfaction, and incidence of adverse effects, this research seeks to provide critical insights for clinicians and optimize preprocedural strategies. Such findings have the potential to refine clinical protocols, improve patient outcomes, and contribute to the growing evidence base supporting the use of nebulized glycopyrrolate in respiratory medicine.

## MATERIALS AND METHODS:

### Study Design

This study was a randomized, double-blind controlled trial comparing the efficacy of nebulized glycopyrrolate and intramuscular glycopyrrolate as preprocedural medications for patients undergoing flexible bronchoscopy. The study aimed to evaluate secretion management, procedural comfort for patients and operators, and safety profiles of the two routes of administration Population The study was conducted at the Department of Respiratory Medicine, Saveetha Medical College and Hospital, over a period of seven months (January 1, 2024, to July 30, 2024). A total of 101 patients, aged 18 to 80 years, were enrolled based on inclusion and exclusion criteria.

### Ethical clearance

The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Ethics Committee of Saveetha Medical College and Hospital. Written informed consent was obtained from all participants before enrolment.

### Inclusion and Exclusion Criteria

Patients were eligible if they required bronchoscopy for conditions such as suspected lung cancer, persistent cough, or haemoptysis, suspected foreign body aspiration, airway stenosis, pneumonia, or for procedures like lung biopsy and airway clearance. Exclusion criteria included age below 18, inability to provide consent, pregnancy, unstable cardiopulmonary status, severe coagulopathy, recent myocardial infarction or stroke, severe respiratory distress, and uncooperative behaviour.

### Randomization and Blinding

Participants were randomized into nebulized or intramuscular glycopyrrolate groups using a computer-generated table. Double blinding was ensured by concealing group assignments from patients and staff with identically labelled medications.

### Intervention

The nebulized group received glycopyrrolate via nebulizer, while the intramuscular group received standard dose injections. Both groups were monitored for adverse reactions post-administration.

### Outcome Measures

Primary outcomes were procedure-related discomfort, bronchoscopy duration, and operator-reported ease. Secondary outcomes included adverse effects, patient satisfaction, recovery time, and post-procedural complications.

### Data Collection

Pre-procedural assessments, including medical histones, were documented. During the procedure, standardized forms were used to record outcomes and adverse events. Follow-up visits were scheduled to evaluate long-term outcomes and recovery.

### Statistical Analysis

Data were analysed using GraphPad Prism version 9. Continuous variables were reported as mean ± standard deviation and compared using independent t-tests. Categorical variables were analysed with chi-square or Fisher's exact tests. A p-value of $<0.05$ was considered statistically significant.

## RESULTS:

This study evaluated the efficacy and safety of nebulized glycopyrrolate compared to intramuscular glycopyrrolate as preprocedural medication for patients undergoing flexible bronchoscopy. Data were collected from 101 patients, with 51 receiving nebulized glycopyrrolate and 50 receiving intramuscular glycopyrrolate.

### Baseline Characteristics

The baseline characteristics of the study population are summarized in Table 1. The age distribution was comparable between the groups, with most patients aged above 50 years (54.9% in the nebulized group and 46.0% in the intramuscular group). The gender distribution was also similar, with 62.7% of males in the nebulized group and 62.0% in the intramuscular group. Common comorbidities included diabetes (27.45% nebulized, 28.0% intramuscular) and no comorbidities (29.4% nebulized, 24.0% intramuscular). Other conditions, such as asthma, pulmonary tuberculosis (PTB), and renal disease, were evenly distributed across the two groups, ensuring balanced comparability.

**Comparison of Procedural Parameters**

Five procedural parameters were analysed and compared: saline instilled, mucous extractor secretions, suction jar secretions, total secretions output, and the difference between saline instilled and secretions output. The results are illustrated in Figure 1. The mean volume of saline instilled was found to be comparable between the nebulized glycopyrrolate group (85.17 ± 20.43 mL) and the intramuscular glycopyrrolate group (88.74 ± 21.62 mL), with a statistically significant difference observed ($p < 0.01$). This indicates that while both groups required similar volumes of saline, the slight variations in instillation were meaningful. The mean volume of secretions collected via mucous extractor was slightly lower in the nebulized group (41.92 ± 11.76 mL) compared to the intramuscular group (44.24 ± 12.58 mL). Despite this small difference, the comparison yielded statistical significance ($p < 0.01$), suggesting that nebulized glycopyrrolate may be marginally more effective in minimizing secretion output at this stage. For secretions collected in the suction jar, the nebulized group showed a slightly higher mean volume (50.00 ± 15.21 mL) compared to the intramuscular group (44.60 ± 14.37 mL). However, this difference did not reach statistical significance, indicating that both methods performed similarly in this regard. The total secretions output, calculated as the sum of mucous extractor and suction jar secretions, was significantly higher in the nebulized group (91.74 ± 18.23 mL) compared to the intramuscular group (86.64 ± 16.93 mL, $p < 0.01$). This result highlights a notable difference in the overall efficiency of secretion clearance between the two groups. Lastly, the saline-secretions difference, calculated as the volume of saline instilled minus the total secretions output, was significantly lower in the nebulized group (42.01 ± 9.11 mL) compared to the intramuscular group (46.26 ± 8.87 mL, $p < 0.01$). This suggests that the nebulized group demonstrated more efficient utilization of the instilled saline, resulting in a reduced discrepancy between instilled and retrieved volumes.

**Operators and Patients' Views**

The procedural ease and comfort were assessed from both the operators' and patients' perspectives (Table 2). The mean scores for operators' views were nearly identical between the groups (13.13 ± 2.42 for nebulized vs. 13.06 ± 2.55 for intramuscular, $p = 0.877$). Similarly, the patients' views showed minimal differences, with mean scores of 11.00 ± 1.00 in the nebulized group and 11.36 ± 1.42 in the intramuscular group ($p = 0.80$), indicating comparable patient comfort across both treatments.

## DISCUSSION:

Bronchoscopy is a critical tool in respiratory diagnostics, with advancements in preparation techniques enhancing procedural success. This study compared nebulized glycopyrrolate and intramuscular glycopyrrolate as preprocedural medications, focusing on secretion management, procedural ease, and patient comfort. The double-blinded, randomized design ensured robustness, allowing valid comparisons, and highlighting significant findings. The study revealed that nebulized glycopyrrolate demonstrated superior efficacy in secretion clearance, as indicated by a significantly higher total secretions output (91.74 ± 18.23 mL vs. 86.64 ± 16.93 mL, $p < 0.01$) and lower saline-secretions difference (42.01 ± 9.11 mL vs. 46.26 ± 8.87 mL, $p < 0.01$). These results underline the localized action of nebulized glycopyrrolate in targeting airway secretions effectively. While the suction jar secretions were similar between groups, the overall secretion management in the nebulized group emphasizes its clinical advantages. These findings align with Walker et al. (1987), who reported enhanced secretion management with inhaled glycopyrrolate in asthma patients, suggesting its potential application across respiratory procedures (14).

Patient and operator satisfaction were comparable across both groups, highlighting the versatility of these approaches. Operators' scores showed no significant differences ($p = 0.877$), aligning with findings by Karewicz et al. (2022), who identified procedural ease and comfort as key factors influencing satisfaction (15). Patients' comfort was also similar between groups ($p = 0.80$), demonstrating that both routes meet patient-centric outcomes. Despite these similarities, the ease of administration and localized effects of nebulization offer an edge, particularly in resource-limited settings.

In terms of systemic safety, nebulized glycopyrrolate minimizes systemic exposure, reducing potential side effects like tachycardia and dry mouth, which are more common with intramuscular administration. This supports findings by Malik et al. (2009), who highlighted fewer systemic anticholinergic effects with inhaled preparations (12). The lack of significant adverse events in both groups emphasizes the safety of these approaches, although longer-term studies could provide further insights.

This study highlights several key findings that reinforce the value of nebulized glycopyrrolate in clinical practice. Firstly, nebulized glycopyrrolate demonstrated superior efficacy in secretion management, significantly enhancing secretion clearance and optimizing saline utilization during bronchoscopy. These findings support its potential to improve procedural efficiency and visibility, making it a preferred choice for secretion control.

Both nebulized and intramuscular glycopyrrolate were found to be equally effective in terms of patient and operator satisfaction. This comparability offers clinicians the flexibility to choose between the two routes based on individual patient needs, resource availability, or institutional protocols. Such adaptability underscores the utility of both approaches in diverse clinical settings.

Additionally, the safety profile of nebulized glycopyrrolate, marked by fewer systemic side effects, positions it as an especially valuable option for patients with comorbid conditions. By minimizing systemic exposure and associated risks, nebulized glycopyrrolate offers an enhanced safety margin, making it a safer and more tolerable alternative for preprocedural preparation.

A limitation of this study is the relatively small sample size, which may restrict generalizability. Additionally, the focus on short-term outcomes limits the evaluation of potential long-term effects or complications. Future research should aim to validate these findings across larger, more diverse populations while exploring cost-effectiveness and patient-reported outcomes to guide clinical decision-making.

## CONCLUSION:

This study highlights the benefits of nebulized glycopyrrolate for flexible bronchoscopy, offering improved secretion clearance and fewer systemic side effects. Comparable satisfaction levels across administration routes provide flexibility for clinicians to tailor treatments to patient needs. These findings support its integration into routine practice, enhancing safety and procedural outcomes.

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**Authors contribution:**

Rajamani Kasi collected and interpretated the data. Rajamani Kasi and Gangadharan Vadivelu drafted the manuscript. Prasanth Gururaj critically reviewed and revised the manuscript. All authors contributed equally and agreed to be accountable for all aspects of the work.

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**Tables and Figures:**

**Table 1:** Demographic and Baseline Clinical Characteristics of Study Participants

| Variable | **Nebulized Glycopyrrolate** (n=51) | **Intramuscular Glycopyrrolate** (n=50) | **Total** (n=101) |
|---|---|---|---|
| **Up to 40 years** | 9 (17.65%) | 13 (26.0%) | 22 (21.8%) |
| **41-50 years** | 14 (27.5%) | 14 (28.0%) | 28 (27.7%) |
| **Above 50 years** | 28 (54.9%) | 23 (46.0%) | 51 (50.5%) |
| **Male** | 32 (62.7%) | 31 (62.0%) | 63 (62.4%) |
| **Female** | 19 (37.3%) | 19 (38.0%) | 38 (37.6%) |
| **Asthma** | 2 (3.92%) | 3 (6.0%) | 5 (4.95%) |
| **Cor Pulmonale** | 1 (1.96%) | 1 (2.0%) | 2 (1.98%) |
| **Diabetes** | 14 (27.45%) | 14 (28.0%) | 28 (27.72%) |
| **EPTB** | 1 (1.96%) | 1 (2.0%) | 2 (1.98%) |
| **Hypertension** | 0 (0%) | 1 (2.0%) | 1 (0.99%) |
| **PTB** | 2 (3.92%) | 3 (6.0%) | 5 (4.95%) |
| **Renal Disease** | 2 (3.92%) | 2 (3.92%) | 4 (3.96%) |
| **No Comorbidities** | 15 (29.4%) | 12 (24.0%) | 27 (26.7%) |

**Table 2:** Comparison of nebulized glycopyrrolate and intra Muscular glycopyrrolate regarding operators and Patients view

| | **Group** | **Mean** | **SD** | **t-value** |
|---|---|---|---|---|
| **Operators View** | Nebulized Glycopyrrolate | 13.13 | 2.42 | 0.156 |
| | Intra muscular Glycopyrrolate | 13.06 | 2.55 | (p=0.877) |
| **Patient View** | Nebulized Glycopyrrolate | 11.00 | 1.00 | 1.804 |
| | Intra muscular Glycopyrrolate | 11.36 | 1.42 | (p=0.80) |

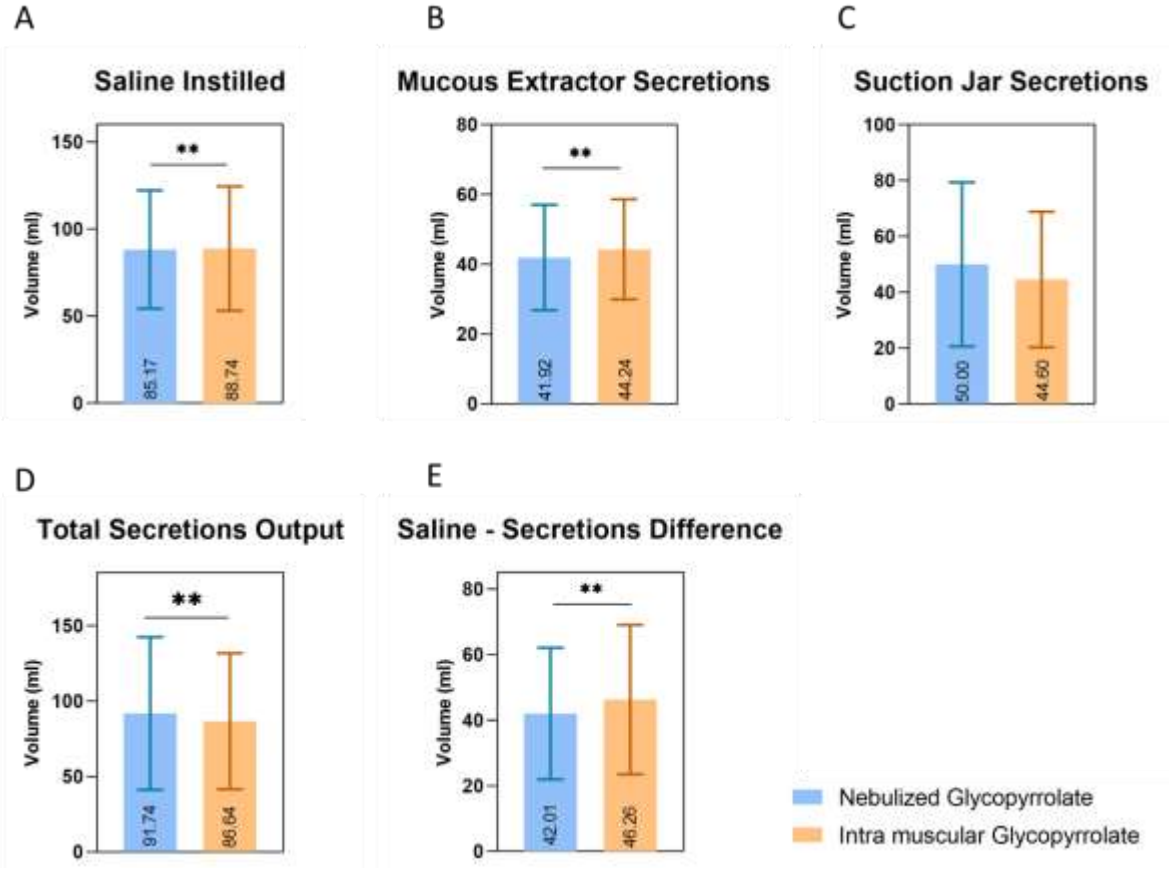


**Figure 1:** Comparison of Nebulized Glycopyrrolate and Intramuscular Glycopyrrolate across five parameters: (A) Saline Instilled, (B) Mucous Extractor Secretions, (C) Suction Jar Secretions, (D) Total Secretions Output, and (E) Saline-Secretions Difference. Data are presented as mean ± standard deviation. Statistical analysis was performed using an independent samples t-test. A p-value of <0.05 was considered statistically significant.