Health related cross-sectional drug utilization surveillance study on Home Nebulization in Bronchial asthma (HRAA study): Post-hoc analyses

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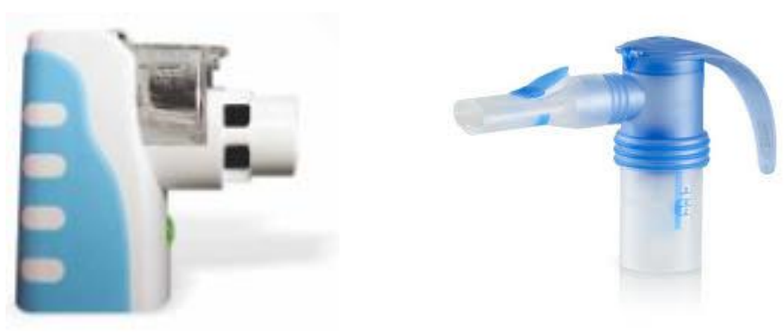
Introduction

Severe asthma remains a clinical enigma with waxing and waning course characterized by poorly controlled symptoms and frequent exacerbations. The aggravating factors include non-adherence, poor inhaler technique, comorbidities, and patient characteristics leading to under treatment or difficult-to-control asthma with Home nebulization with ICS/LABA making a critical impact on successful treatment outcomes. In such cases, add-on therapy with nebulized anticholinergics &/or oral xanthines offers complimentary bronchodilatory or anti-inflammatory actions for the underlying definable or undefined treatable traits of acute asthma.

In this line. Vibrating mesh nebulizers are the new generation inhaler devices that are compact, portable, noiseless offering optimal convenience or compliance for patients in Home or Ambulatory settings in such cases. More importantly they generate a gentle, soft mist aerosol with a droplet size distribution and acceptable respirable fraction suitable for central and peripheral lung deposition while offering short nebulization time for better patient compliance and adherence rate .



ERS (2001) recommends the use of Nebulization strategy in obstructive airway disease patients with severe airflow limitation (acute exacerbation), frequent users of rescue medications and patients unable to use or coordinate or carry spacers along with pMDIs. The delivery of long-acting antimuscarinic agents including Ipratropium and Glycopyrronium remains an interesting prospect especially for High risk COPD, ACO and/or Severe asthma

Unmet need

Clinical algorithmic approach for Severe asthma or evolving small airway disease becomes a challenge especially in light of the limitations associated with investigative approach with Sr. eosinophils and FeNO in Indian subcontinent.

To further assess clinical perceptions, and best practices for Symptomatic management with Home Nebulization for High risk Severe asthma, a retrospective, observational, case control analyses was planned

Methods and Materials

A Drug utilization, observational, case control study was conducted for Consecutive cases of Severe asthma (n=60) accrued in 2:1 ratio at two centres during Sept ’18 utilizing Home nebulizers while delivering anticholinergics with or without ICS/LABA & oral xanthines

The study was conducted according to ICH GCP principles and Declaration of Helsinki with local Ethics committee approval and Clinical Trial Registry of India registration.

Statistical consideration for primary and post-hoc analyses were carried out by QuickCalcs GraphPad Prism ver. 7 software with $p<0.05$ considered statistically significant

Results

Sixty consecutive home nebulization cases receiving anticholinergics were assessed for analyses, of which Fifty-three receiving LAMAs as nebulization therapy with ICS/LABA and oral xanthines for High risk Severe asthma cases were analysed. Baseline demographics included Male/Female (29/23); mean Age 60.3y; Wt 64kg; Uncontrolled symptoms (30.2%), Exacerbation history (69.8%)); FEV1 (43%), Reversibility (13%), Sr. eosinophil (4%); FeNO (12.1 ppb); prior pMDI use (30.2%); Formoterol/Budesonide (53,100%), Glycopyrronium (40,75.5%)), Xanthines (34,64.1%).

At 8 wks, Severe asthma cases (FEV1, 38%) receiving ‘add-on’ Nebulized Glycopyrronium to Formoterol/Budesonide & oral xanthines showed significant improvement in FEV1 (27.7%, $p<0.0001$), versus baseline. **The intergroup difference of 16.5% or 320 ml improvement in FEV1 with Nebulized Glycopyrronium addition that was statistically significant ($p<0.03$)**

Post-hoc analyses showed comparative improvement in FEV1 (27.7% vs 26.2%, $p<0.03$), PEFR (↑68% vs ↑61.6%;p=NS) and GINA scores (↓67.5% vs ↓67.1% p=NS) at 8 wks for group receiving add-on Nebulized Glycopyrronium/ICS/LABA & oral xanthines with (n=14) or without (n=8) history of exacerbations respectively.

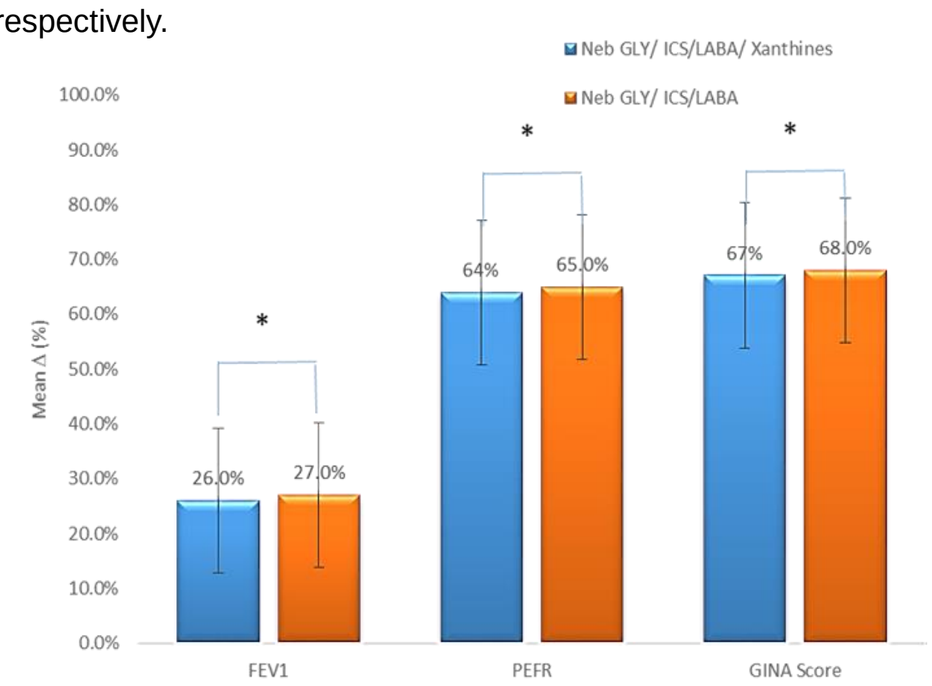


Fig : Mean change in FEV1, PEFR & GINA assessment score at 8wks for Add-on therapy with Nebulized Glycopyrronium +/- Xanthines (*p=NS)

Similarly there was improvement in FEV1 (26% vs 27%; p=NS), PEFR (64% vs 65%; p=NS) and GINA scores (67.1% vs 68%;p=NS) at 8 wks for group receiving add-on Nebulized Glycopyrronium with (n=25) or without (n=15) xanthines respectively None of the patients had any SAEs or TEAEs including tachycardia or UTI that required any treatment withdrawal or discontinuation

Conclusion

Home Nebulization with Add-on Glycopyrronium to nebulized ICS/LABA is a clinically effective *alternative* for Severe Asthma

What’s New

- **Clinical utilization of Home Nebulization with Glycopyrronium is useful Add-on for patients with frequent Rescue medication use**
- **Clinical evidence to *rationalize* the role of LAMAs or Glycopyrronium for Severe (FeNO negative) asthma cases**

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