North Carolina Thoracic Society
ATS Chapter

"Advancing Lung Health in North Carolina"

North Carolina Thoracic Society Newsletter

Spring 2023

Message from the President – Praveen Mannam, MD (Cone Health)

Greetings from the North Carolina Thoracic Society (NCTS), a state chapter of the American Thoracic society (ATS). It my honor to serve as the President this year. We are dedicated to building relationships and fostering networking and collaborations between the different practices in our state and have special interest in engaging academic and community practices, as both play a vital role in delivering patient care. As someone who has trained and worked in both academic and community practice settings, I am keenly aware of the unique contributions each kind of practice brings to patient care and to advancement of lung health. As a group we are not just focused on highlighting cutting edge topics but also discuss issues facing community practices and local issues. To that end we are committed to engaging with our community practices by holding our meetings throughout the state and alternating the leadership every year between academic and community providers.

To summarize the events of the past year, our Annual NCTS Education Conference was held in March 2022 at beautiful Asheville when Joe Govert, Duke University was awarded the NCTS Outstanding Clinician Award. We also hosted the NCTS Digital Health Conference in Sept 2022 at Duke with topics on the emerging concept of using digital technology and monitoring for resp care. Both conferences were well attended, and we had great discussions and interactions.

Looking forward, NCTS is collaborating with the NC Respiratory Care Board in adding an emerging advanced practice respiratory therapist role to the professional licensing process known as the Advanced Respiratory Care Practitioner (ARCP). We will have more information and updates about this change later this year.

Starting in 2024 ATS will assist state chapters with their memberships with an option to add local membership when they renew their ATS membership and will require each chapter to have a minimum 30 of members who are full ATS members. The state chapters who have less members may merge with other chapters. I believe these changes will support us and help increase our membership to enable growth from strength to strength.

Our annual conference planned for April 29th at Wilmington, NC with a focus on airway disease. We are looking forward to meeting you in person but have a virtual option as well. I hear that the beaches on the NC coast are superb that time of the year. We also hope to have a specialty conference later this year on a topic to be decided.

Finally, I would like you to help me extend a warm welcome to our new executive leadership member; Ross Hoffman from Asheville Pulmonary and Critical Care who has joined as Secretary/Treasurer.

Sincerely, Praveen Mannam, MD
Division Chief, LeBauer Pulmonary and Critical Care, Cone Health & President NCTS 2022-23

NCTS Events and Announcements

2023 North Carolina Society Annual Education Conference, Saturday April 29, 2023, Embassy Suites Riverfront Wilmington, NC. Topics include COPD update, Pulmonary hypertension update, asthma disparities, bronchoscopic lung volume reduction surgery for emphysema. In addition speakers will discuss disease remission in asthma with biologics, and in CF with CFTR modulators. Pulmonary fellows from each of the training programs will present. We also have activities Friday and Saturday evenings. Wilmington is awesome mid-Spring. Learners are free, register at the this Eventbrite link. https://www.eventbrite.com/e/the-north-carolina-thoracic-societys-2023-annual-educational-conference-tickets-477613674357

2022 Digital Health Conference, Durham, NC(Sept 24) NCTS held a daylong conference, led by Mashael Al-Hegelan, MD (President, NCTS, Duke University), on many topics about using digital technology for the care of patients with respiratory diseases. The program was live and offered internationally, and was the most comprehensive such program conducted on this topic thus far. Our keynote, Garrett Greene, PhD (Royal College of Surgeons, Dublin) provided details on a sophisticated model employing digital inhalers to optimize ICS in severe asthma, also presented a few weeks earlier at ERS. Other topics included clinical application of digital inhalers, cybersecurity in digital health, wearables, digital health in pediatrics, remote monitoring with oscillometry, digital OSA monitoring, and remote pulmonary rehabilitation.

Carlos Nunez, MD (Chief Medical Officer ResMed) provided insights into how artificial intelligence can be used to monitor and improve adherence with ambulatory treatment of OSA.

Rakesh Alva, MD (Cone Pulmonary) shared an innovative smartphone-based remote pulmonary rehab program. While effective, he pointed out that some of his rural patients only had “flip’ phones and the associated challenges.

Bach Tran– Pre-dental Student, UNC Chapel Hill

Impact of Asthma on Dental Health

Asthma is a chronic condition marked by the inflammation and narrowing of the airway that can impact breathing rates and depth. A common treatment for this condition is inhalation therapy, which involves the use of inhaled corticosteroids and/or beta-2 agonists. Although effective, these medications can negatively impact patients' oral health, especially those undergoing prolonged treatment at higher dosages.

Xerostomia (or dry mouth) is a common adverse effect found in patients who rely on prolonged use of beta 2-agonists. In fact, studies have shown a correlation between the use of beta 2-agonists and a significant reduction patients' salivary production and secretion (ranging from 26-36%). Given the antibacterial property of saliva, a reduction in salivary rate is associated with an increase in the concentration of Streptococcus mutans – a bacteria strain which contributes to tooth decay. Increased food retention in the teeth is a common condition resulted from diminishing salivary production, which may contribute to plague formation in the gum and ultimately gingivitis.

In addition, inhalers have also been shown to decrease salivary pH significantly (below the critical value of 5.5). There are multiple reports of increased soft drinks consumption, especially children, among inhalers users to counter dry mouth. Over-consumption of carbonated beverages combined with lower salivary pH will create an acidic environment in the oral cavity, giving rise to an uncontrollable growth of aciduric bacteria. Higher prevalence of these bacteria along with maladaptive dietary habits in response to dry mouth can further increase the risk of dental caries development.

Reference: Godara N, Godara R, Khullar M. Impact of inhalation therapy on oral health. Lung India. 2011;28(4):272-275. http://libproxy.lib.unc.edu/login?url=https://www.proquest.com/scholarly-journals/impact-inhalation-therapy-on-oral-health/docview/900730875/se-2. DOI: https://doi.org/10.4103/0970-2113.85689.

Editor's Note: I became familiar with this ADR ~ 10 yrs ago, and the patient type I have seen horrible dentition occur most often has been in severe young female asthmatics (caries, cracked teeth). These were typically patients with good oral health habits under care of a dentist regularly and long-term. Oral health with inhalers is not just about ICS. If dental health is an issue, I recommend an alcohol-based mouthwash after inhaler use as most inhaled drugs are not very water soluble, and to use spacers for MDI users to minimize oral deposition. A smaller aerosol particle size lowers oral deposition (eg Spiriva Respimat® vs Handihaler® – incidence of dry mouth 50% lower with wet aerosol) Studies are needed to further characterize this ADR (eg drug A vs B, Nebs vs DPI vs MDI vs MDI + spacer, +/- OCS).

Ross Hoffman, MD (Asheville Pulmonary and Critical Care; Secretary-Treasurer, NCTS)

Yes We Can - Narcan

On February 15, 2023, an advisory panel to the US Food and Drug Administration voted to recommend that the agency approve a nasal spray version of naloxone to be sold over the counter.

The recommendation addressed several problems. The first was urgency. According to the CDC, of the 107,622 drug overdose deaths in the US in 2021, nearly 75% involved opioids. Naloxone prescriptions have risen dramatically, from approximately 400,000 in 2017 to about 1.5 million in 2021. Then there was the rise of fentanyl, which went from being used to enhance the high of injectable drugs to appearing in all sorts of places. Reports of deaths from blackmarket Xanax, Ativan, Adderall, and other pills laced with fentanyl, often procured from dealers operating on social media, have become common.

The key issue was access. Narcan is available without a prescription in all 50 US states, but it still has to be stored behind the counter – and to be bought from the pharmacist. Predictably, the FDA will pass the measure. So the next big question will be: How will we support the public health campaign to help ensure that Narcan becomes accessible to everyone who needs it, when they need it? In this case, "we" means far more than just pharmacists and medical types. It means parents, youth, shop clerks, concert venue operators, mall security, park rangers, and residents in every college dormitory, to start a list. Where should the Narcan be located in your parking garage? Next to the AED?

The issue of access won't end with an OTC approval. Stigma will remain. What can each of us do to help destigmatize the drug? So that teenagers can buy it off the shelf in their local pharmacy without having to talk to a grown-up (unless they want to). So that hotel staff will put it in the vending machine, maybe between the Tylenol and the Benadryl – and hopefully at the modest cost of pressing a button.

There will be those who seek to demean the campaign, arguing that easy access to the reversal agent will only encourage irresponsible people to overdose. We've heard that line of reasoning before. The FDA is expected to make a decision by March 29 – which means by the time we gather in Wilmington, Narcan will probably be OTC.

Drugs Therapies for the COPD/CHF Phenotype

Roy A. Pleasants, PharmD (Executive Director, NCTS, aka "Roy The Inhaler Guy" 😉)

Among COPD patients, CAD and CHF are leading causes of death(Divo). There are several pertinent pharmacotherapy issues I would like to highlight that can affect outcomes in the COPD/CHF phenotype.

1) β-blockers are under-prescribed in COPD patients with CHF and/or CAD, in part because of concerns of worsened respiratory status. There are a number of studies showing cardioselective β-blockers decrease CV mortality in COPD patients with comorbid heart disease, and are unlikely to worsen lung function. (atenolol, bisoprolol, metoprolol).Pleasants
2) Bronchodilators can improve cardiac function by decreasing hyperinflation (primarily studied with LAMAs)
3) I believe we need to pay much closer attention to the safety of inhaled medications in patients with advanced CHF, and this should affect monitoring and inhaled drug therapy

selection. First, COPD patients with HFrEF (NYHA III and IV) have been excluded from nearly all Phase II, II and IV clinical trials of inhaled medications. The SUMMIT study reported on ICS/LABA safety in COPD patients with CV diseases that included patients with NYHA I-III, but did not distinguish outcomes in this subgroup, particularly relevant is NYHA III. Overall, in the primary study analysis, there was no benefit on all-cause mortality of this therapy. Safety or efficacy of long-acting inhaled medications in HFrEF (NYHA III/IV) has not been adequately studied. Second, we also know that the β2:β1 ratio changes in the myocardium in advanced heart failure, where β2-receptors become more upregulated, β1-receptors are down-regulated. Cardiac muscarinic receptors are not significantly altered in CHF.[Pleasants]

Here's why I am concerned about greater risks of ADRs of inhaled medicines in COPD patients with HFrEF.

All inhaled long-acting bronchodilators and ICS are heavily metabolized by the liver, and they are considered high-extraction ratio drugs. This means they are heavily dependent on liver blood flow for metabolism and clearance from the body, which of course the liver tends to be congested in NYHA III/IV HFrEF because of decreased CO. They are not inclined to be solely affected by liver enzyme activity without decreases in liver blood flow.

This impaired clearance with HFrEF is most likely to occur with inhaled medications that have minimal or no renal elimination of unchanged parent drug(some LABAs). Typically, if a drug has both significant hepatic and renal clearance, the kidneys kick in when the liver doesn't metabolize drug efficiently. For drugs with low hepatic first pass metabolism (eg prednisone, albuterol), clearance from the body is unlikely to be affected by decreased liver blood flow associated with HFrEF. The low first-pass effect drugs are more affected by intrinsic liver enzyme activity, and are inclined to be affected by other drugs that impair enzyme activity (eg itraconazole – prednisone DDI).

Here are my thoughts on how to approach this clinically:

(Inhaled Antimuscarinics) All LAMAs (and SAMAs) have significant renal clearance, so decreased hepatic first-pass metabolism from CHF is unlikely to affect blood levels to a significant extent. They may prove to be the safest long-acting bronchodilators in this patient type.[Milne] I do not advise using full doses of SAMA with LAMAs.

(ICS) For all <u>inhaled</u> corticosteroid molecules, drug clearance is likely impaired in NYHA III/IV with HFrEF. So what does this mean – I recommend to avoid high-dose ICS as FP 500, FF 200 or MOM 200 in COPD/CHF patients. Luckily, for COPD in the USA, recommended doses of combination ICS products are low-medium (fluticasone furoate 100 mcg, BUD 160 mcg and fluticasone propionate 250 mcg). FP/SALM 500 is recc'd in many countries for COPD (Ugghh!). Consider cortisol, excess fatigue, K+, BMD as biomarkers here. High maintenance doses of ICS gain little in COPD, but might in asthma.

(Inhaled β2-agonists) Inhaled LABAs are high-first pass effect drugs and have slight-moderate (FOR, OLO, SAL) or no renal clearance (VIL) of unchanged parent drug when it reaches the systemic circulation from the lungs or orally absorbed. In the presence of HFrEF, the active parent drug with no renal clearance of systemically absorbed drug would likely stick around longer, possibly associated with increased CV effects. The half-life of the LABA

may also play a role in increased CV ADRs in HFrEF (VIL>OLO~FOR~SALM). Consider K+, HR, xs tremors, QTc as biomarkers with any of the agents. In the acute care setting, albuterol may be the preferred B2-agonist over LABAs in a decompensated CHF patient or other serious cardiac disease.

These pharmacokinetic principles are strong,(Mangoni) but we have no real good data with inhaled meds. In this situation, I advise careful prescribing and monitoring of inhaled LABAs and ICS in HFrEF, especially in the inpatient setting with a decompensated HFrEF/COPD patient, and/or if tachyarrhythmias are present. Outpatient, low to medium dose ICS's should be the preferred dose in this phenotype, and if a monotherapy bronchodilator is indicated, a LAMA is likely safest. I personally think FOR or OLO would be the preferred LABA. With initial prescribing of a LABA in COPD patients with cardiac disease– Drs Milne and Sin recommend close monitoring for 2-3 weeks. PS – we can never solve a problem without first identifying it. (RAP - COI in last 3 yrs, research AZ, BI, Grifols, Teva)

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