Advanced Pharmacology for Nurse Practitioners- Clinical Correlation
Assignment: Acute Asthma - "I Can't Catch My Breath!!!"
Sherri Rowell RN, MSN, C
Shreveport, LA
Feb. 8, 2000

Asthma Statistics

- Fatal disease for > 5000 people/year
- Expensive - United States with an estimated cost of $5.8 billion dollars in 1994.
- Common - 15 million physician visits, over 445,000 hospitalizations, 1.2 million emergency department visits, and 10 million missed days per year.
- Continues to increase in prevalence in the United States, affecting 14 to 15 million people despite our advances in treatment.
- Underdiagnosis and inadequate therapy are recognized as major contributors to asthma morbidity and mortality.

Asthma Pathophysiology

- Historically has been characterized as a disorder of smooth muscle spasm and bronchoconstriction.
- Now known to be characterized by airway infiltration by inflammatory cells, secretion of proinfalmmatory molecules and airway fibrosis and remodeling.

Pathophysiology process: A sensitized person inhales an antigen that initiates an acute allergic response. This takes place within just a few minutes and is termed early phase response. Result is mediator production and bronchoconstriction. Mediators secreted include the interleukons and granulocyte-marcrophage colony stimulating factor. Leukotrience pathway that stimulated in response to injury or inflammation through the breakdown of arachidonic acid. Leukotrienes have been associated with many of the pathogenic mechansims or actions and we now have some agents that work by blocking these pathways

2 - 6 hours later, a second bronchoconstrictor response called the late phase response brings infiltration of the airways by eosinophils, mononuclear cells and lymphocytes which are crucial to cellular recruitment of inflammatory mediators including cytokiness and chemokines. This response represents cellular infiltration and the clinical characteristics of bronchial hyperreactivity. One crucial factor that is critical to the formation of these adhesions molecules and cytokine formation is a DNA-binding protein that results in the liberation of a transcription factor called Necrosis Factor B that allows adhesion molecules to adhere to inflammatory cells. It is interesting to note that glucocorticoids inhibit this factor and prevent the adherence to inflammatory cells.

Realize that as we learn more about the pathophysiology, we are finding new treatments at the molecular level to fight it.

Patient Presentation

Chief Complaint - "I am having trouble catching my breath"

HPI - Jocelyn Carter is a 56 year old woman who presents to the ED with a 3-day history of increasing SOB, wheezing, non-productive cough and flu-like symptoms (nausea, vomiting, headache). She has had to increase the use of her inhalers over the last three days because of increasing SOB (approximately 5 to 6 times a day). She does not monitor her peak flows at home; she just knows when her symptoms become

severe. She claims medication compliance but has been out of prednisone for 5 days; her last dose of Theo-Dur was earlier in the day.

PMH

Asthma with H/O intubation	HTN
H/0 of drug abuse	H/O stomach upset (cimetidine started one week ago)

SH - Positive ETOH and tobacco use

Meds

Theo-Dur 500mg (P0) QD	Albuterol MDI 2 puffs BID
Albuterol via nebulizer PRN	Procardia XL 90mg (PO) QD
Cimetidine 400mg (P0) BID	Prednisome 10mg (P0) QD
All -None	

ROS

No URI symptoms other than cough and wheezing

PE

Gen -The patient is a WDWN woman in obvious respiratory distress

VS - BP 140/90, P120, RR 30, T36.7C; Wt65 kg

Chest -Diffuse expiratory wheezes bilaterally

Neuro - Alert and oriented x 2, but confused

Labs

Glucose 108 mg/dL	Sodium 145 mEq/L
Potassium 3.5 mEq/L	Chloride 109 mEq/L
C02 content 27 mEq/L	BUN 17 mg/dL
Serum creatinine 1.0 mg/dL	
Hemoglobin 14.6 g/dL	Hematocrit 44%
Platelets 227,000/mm	

WBC 6000/mm3

- 66% PMNS
- 2%, bands
- 28% lymphocytes
- 4% monocytes

Theophylline 25 mcg/mL (previous level 10 mcg/mL)
Peak flow 175 L/min (baseline 450 L/min)

ABG -PaO2 60, PaCO2 35, pH 7.45
ECG - Sinus tach with occasional PVCs
CXR - Mild atelectasis - hyperinflated lungs with air trapping

Questions:

1.a. What information indicates the severity of this patient's asthma?

Significant Information from history & PE
3-day increasing SOB, wheezing, non-productive cough
Respiratory distress, P 120, RR 30
Diffuse expiratory wheezes bilaterally
Alert and oriented x 2, but confused
Asthma with H/O intubation
Increased use of her inhalers
Does not monitor her peak flows

Chart here

Caution - According to the National Heart, Lung and Blood Institute's National Asthma Education and Prevention Program, 1997 "Symptoms are not reliable indicators of the severity of asthma, especially since patients can become accustomed to chronic airflow impairment without realizing that it signals their asthma is worsening." "Objective measures of lung function (are needed) to assess the severity of asthma and to monitor the course of therapy"

The Significant Objective Information for our patient include:

Peak flow 175 L/min (baseline 450 L/min)
Hyperinflated lungs with air trapping
Theophylline 25 mcg/mL (previous level 10 mcg/mL)

Based on the above findings Jocelyn Carter is classified as experiencing an Asthma exacerbation of moderate severity.

b. Which of the patient's problems could have been caused by drug therapy?

- *She claims medication compliance but has been out of prednisone for 5 days* - Prednisone is used to suppress inflammation. Glucocorticoid steroids appear to speed the resolution of airflow obstruction and reduce the rate of relapse. The lack of compliance (for whatever reason) probably contributed to the exacerbation.

- *H/O stomach upset (cimetidine 400 mg BID started 1 week ago)* - Perhaps stomach upset is secondary to the gastritis associated with oral prednisone. Perhaps cimetidine 400 mg BID started 1 week ago and the choice not to refill her prednisone are related to this as well.

- *Theophylline 25 mcg/mL (previous level 10 mcg/mL)* - Introduction of cimetidine may have led to this theophylline level. We know cimetidine has many drug interactions with other drugs due to the fact that it inhibits the hepatic cytocrome P-450 system. This resulted in an accomulation of theophylline in her system.

- *Flu- like symptoms* -Inhibition of theophylline metabolism was probably the culprit for her flu like symptoms of nausea, vomiting, headache and possibly some of the cardiac effects . Theophylline has a narrow therapeutic range/dosage must be carefully controlled. Drug levels of around 20 are associated

with the accumulation of cAMP and results in excess secretion of catecholamines causing GI, CNS and cardiovascular effects. Another question I might want to know is how the exacerbation affected her smoking. If it slowed down her cigarette consumption, this too might have increased her level.

- *Increased use of her inhaler* -One might be tempted to categorize this increased use of her inhalers as an overdose action where too much of the medication is being administered. Actually, this should be viewed as a cry for help. Overuse of a beta agonist is an indication that the asthma is not being adequately controlled.

2. What are the goals of treatment for this asthma exacerbation?

Goals of treatment include cure of disease, reduction of symptoms, arresting or slowing progression of disease, minimizing adverse effects of treatment, providing cost-effective treatment, and maintaining quality of life. While all of these goals are not possible in the treatment of asthma, most of these can be met. For example, asthma is a chronic condition that cannot be cured, however with proper treatment, adverse effects can be minimized and a quality of life can be maintained.

The treatment goals from the 1997 National Heart, Lung and Blood Institute's National Asthma Education and Prevention Program guidelines go hand in hand with the goals from our book, but are more specific for our disease condition. They include :

- **Correction of significant hypoxemia** by administering supplemental oxygen. In rare instances,alveolar hypoventilation requires mechanically assisted ventilation.

- **Rapid reversal of airflow obstruction**. This is best achieved by repetitive or continuous administration of an inhaled beta 2 -agonist AND early in the course of treatment, administration of systemic corticosteroids to patients with moderate-to-severe exacerbations or to patients who fail to respond promptly and completely to an inhaled beta 2 -agonist

- **Reduction of the likelihood of recurrence of severe airflow obstruction** by intensifying therapy.

- **Close monitoring by serial measurements of lung function** to quantify the severity of airflow obstruction and its response to treatment.

3. What pharmacologic alternatives are available to treat this acute exacerbation of asthma?

Here we will identify the kinds of treatments that might be beneficial in meet our goals. This includes all feasible pharmacologic alternatives including non-drug therapy.

Home remedites - There are numerous treatments and remedies that have been tried during an acute asthma attack such as drinking large volumes of liquids or breathing warm, moist air (e.g., the mist from a hot shower) but none of these has been shown to be helpful.

Over-the-counter bronchodilators - may provide transient bronchodilation, but their use should not be permitted to delay seeking medical care.

OTC anti-histamines and cold remedies - haven't been shown to be helpful either

Alterative/complementary medicine - There have been multiple trials on the use of acupuncture in asthma however the trials lacked quality and that the effectiveness of acupuncture in treating asthma has not been clearly established.

New treatments - Recently other medications such as intravenous administration of magnesium sulfate and substituting a mixture of helium and oxygen for oxygen-enriched air have been used in acute episodes to help prevent the need for intubation. Although limited observations suggest that these therapies may be effective, possibly among certain subgroups there is not enough data to support routine use of these interventions.

Standard treatment - Medication classified as either quick relief meds (short- acting) or long-term control meds. These are the typical meds used to treat chronic asthma, and the short acting ones are also used in the treatment of exacerbations. Current investigation is underway comparing bioavailability and effectiveness of alternative delivery including nebulization vs inhalers, IV vs PO, time of day administration, nasal vs inhaler, etc. Established routes will be discussed below in the specific pharmacotherapeutic plan.

4. Outline a specific pharmacotherapeutic plan for the initial management of this patient's asthma in the Emergency Department.

- **Oxygen at 2 L / NC**

  Supplemental oxygen for patients with significant hypoxemia and to patients with FEV 1 or PEF <50 percent of predicted. Administer by nasal cannulae or mask, whichever is best tolerated to maintain an SaO 2 >90 percent

- **Inhaled short-acting beta 2 –agonists** - Three treatments (2.5 - 5 mg) of albuterol spaced every 20 to 30 minutes x 1 hour by nebulizer, then 2.5-10 mg every 1-4 hours as needed

  The repetitive or continuous administration of inhaled short-acting beta 2 -agonists is the most effective means of reversing airflow obstruction. The onset of action for inhaled beta 2 -agonist is less than 5 minutes and repetitive administration produces incremental bronchodilation. Studies show that equivalent bronchodilation can be achieved by either high doses (6 to 12 puffs) of a beta 2 -agonist by MDI with a spacer/holding chamber under the supervision of trained personnel or by nebulizer therapy. However, nebulized therapy is more effective in patients who are unable to coordinate inhalation of medication from an MDI because of their age, agitation, or severity of the exacerbation. So because of our patient’s confusion and severity, we will give her treatments via nebulizer.

- **Systemic corticosteroids** - Prednisone 50 mg PO TID x 48 hours

  Current research suggests oral administration of prednisone has been shown to have effects equivalent to those of intravenous methylprednisolone provided gastrointestinal transit time or absorption is not impaired. Controversy exist about dose regimens. No advantage has been found for higher dose corticosteroids in severe asthma exacerbations. One option for oral prednisone is to give 120-180 mg/day in 3 or 4 divided doses for 48 hours, then 60-80 mg/day until PEF reaches 70% of predicted or personal best. Other dose regimens recommend therapy following a hospitalization or emergency department visit to last from 3 to 10 days. If patients are then started on inhaled corticosteroids, studies indicate there is no

need to taper the systemic corticosteroid dose, however most people still taper the dose. If systemic corticosteroid therapy is to be given once daily, one study indicates that it may be more clinically effective to give the dose in the afternoon at 3:00 pm with no increase in adrenal suppresion.

Anticholinergics - Ipatropium bromide 0.5 mg every 30 minute by nebulizer For 3 doses Then every 2 - 4 hours as needed

May be beneficial in the ER treatment of our patient by competitive inhibition of muscarinic cholinergic receptor to block bronchocontriction, but only after initial treatment with beta agonists. Some studies suggest adding high doses of ipratropium bromide (0.5 mg in adults) has been shown to cause additional bronchodilation, particularly in those with severe airflow obstruction. This may provide some additive effects, but with a slower onset. Should not be continued after exacerbation unless patient has underlying COPD.

- **No Theophylline/aminophylline**

  In the emergency department: Theophylline/aminophylline is not recommended because it appears to provide no additional benefit to optimal inhaled beta 2 -agonist therapy and may increase adverse effects. In patients currently taking a theophylline-containing preparation, determine serum theophylline concentration to rule out theophylline toxicity, which in our case was done.

Clinical Course - Ms. Carter initially had an incomplete response to the treatment plan you recommended, as indicated by persistent mild wheezing and a PEFR >40% but <70% of baseline. With continued treatment, she improved further, as assessed by the presence of only slight wheezing and a PEFR >70%. The decision was made to discharge the patient home.

b. What pharmacologic interventions would you recommend for the Patient upon discharge?

- Continue treatment with Albuterol 90 mcg/puff MDI 2 – 4 puffs q 3-4 hr prn - The regularly scheduled daily use of short-acting beta 2 -agonists is no longer generally recommended. She will also need a long-acting beta 2 agonists, but this can wait until follow-up apointment
- Continue Prednisone 60 mg PO TID x 48 hours, then 60 mg/ day at 3 pm x 5 days
- D/C Theo-Dur
- Continue Procardia XL 90 mg po QD
- D/C Cimetidine
- Begin famotidine 20 mg po BID
- Begin triamcinolone acetonide MDI 100 mcg/puff 4 puffs BID

- **Other discharge interventions** - A visit to the emergency department is often an indication of inadequate long-term management of asthma or inadequate plans for handling exacerbations. The following need to be completed prior to discharge.

  Obtain medical follow-up - In the case of our patient, I would schedule an appointment with a provider prior to discharge, and since our patient is at high risk patient - a referral to an asthma specialist for consultation should be considered. This has been reported to reduce the rate of subsequent emergency department visits. It's evident she needs better chronic control of her asthma. Followup needs to occur within 3 to 5 days.

Review written discharge medications and provide patient education on avoidance of asthma triggers (like smoking perhaps) and correct use of an inhaler. Instruct the patient in a simple action plan for increasing medications or returning for care should asthma worsen. See the example in the packet I faxed.

Issue a peak flow meter and provide education on how to measure and record daily PEF rates.

5. What will you monitor to assess the efficacy and side effects of therapy?

Assessment parameters are needed to evaluate achievement of our therapeutic outcomes, prevention of adverse effects. They should be well defined and measurable. So for our patient we would measure the following:

- *Signs and sympto*ms *of asthma*
- *Quality of life/functional status*
- *History of asthma exacerbation* - There are numerous tools to monitor S&S, document hx and monitor quality of life issues
- *Pulmonary function* - Peak expiratory through peak flow monitoring provides a simple, quantitative, and reproducible measure of the existence and severity of airflow obstruction. This is a wonderful tool for ongoing monitoring, not diagnosis. Peak flow monitoring can be used for short-term monitoring, managing exacerbations, and daily long-term monitoring.
- *Pharmacotherapy* - The following factors should be monitored: patient adherence to the regimen, inhaler technique, level of usage of as-needed inhaled short-acting beta 2 -agonist, frequency of oral corticosteroid "burst" therapy, changes in dosage of inhaled anti-inflammatory or other long-term-control medications, and side effects of medications. For example - we all know the adverse effects of oral corticosteriods to monitor, but how about inhaled? In this case our choice of route will help us prevent the serious adverse effects of systemic steroids. In high doses systemic effects may occur, although studies are not conclusive, and clinical significance of these effects has not been established (e.g., adrenal suppression, osteoporosis, growth suppression, and skin thinning and easy bruising). Local Adverse Effects - Oral candidiasis (thrush) is one of the most common adverse effects of inhaled corticosteroids, however with lower dosages and good technique, rate is about 5 percent although it is more frequent in adults than in children. Use of calcium supplements (1,000 to 1,500 mgper day) and vitamin D (400 units a day) for doses that exceed 1,000 mcg of inhaled corticosteroid a day may help prevent these adverse effects. Some studies suggest caution in administering inhaled corticosteroids immediately after an exacerbation secondary to the potential for worsening PERF by causing increased airway hyperreactivity. Monitor for this effect.

6. What information should be given to the patient about her new corticosteroid inhaler and use of her peak flow meter?

Monitoring Peak Expiratory Flow Rate (PEFR) is to a patient with asthma what monitoring blood sugars is to a patient with diabetes and blood pressure readings are to a patient with hypertension. She needs to be instructed how to perform this and then provide adequate return demonstration. She needs to keep a log of her PEFR and have this reviewed by her physician at the office visit. PEFR should be measured on waking in the morning (before taking a bronchodilator) and again in the afternoon. PEFR below 50 % of personal best value indicates severe asthma and warrants immediate intervention by the physician. She needs to know how her PEFR fit into her personalized action plan.

As far as the her new corticosteroid inhaler, I would tell her they reduce need for oral corticosteroid and that early intervention with inhaled corticosteroids can improve asthma control and normalize lung function and may prevent irreversible airway injury. However they do have adverse effects - many which can be prevented by using a spacer. To reduce the potential for adverse effects she needs to use a spacers/holding chambers. She also needs to rinse and spit following inhalation and to use the lowest possible dose of inhaled corticosteroid to maintain control. (No if a little will do you good, a lot will do you better). Because she is postmenopausal woman, I would advise calcium supplements (1,000 to 1,500 mgper day) and vitamin D (400 units a day) for doses that exceed 1,000 mcg of inhaled corticosteroid a day. I would also tell it takes at least 4 weeks to reach maximum improvement, although she should start to feel results in 1-2 weeks.

One thing I wouldn't tell her (and this was news to me) is t0 use her inhaled beta 2-agonist prior to her inhaled corticosteroids. There is no evidence to support this practice which I've done for years!!

Also because of her history of noncompliance I would also tell her that before she quits any of her medicines she needs to call her provider and talk about her problems. Many of the issues can be fixed through minor adjustments in therapy.

References

Byrd, R., Fields, C, Ossrio, M. & Roy, T. (1999). Theophylline Toxicity Revisited. Federal Practitioner 16 (12) 35 – 39.

Curtis J. Hudson L. (1994). Emergent assessment and management of acute respiratory failure in COPD. Clin Chest Med. 138(4): 1006-1033.

Krishnaswamy, G., Mukkamala,, L, & Smith, J. (1998). Asthma: New Guidelines and New Strategies. Veterans Health System Journal 3(4), 20 – 32.

Krishnaswamy, G., Kelley, J. & Smith, J. (1999). Therapeutic Implications of Airway Remodeline in Asthma. Veterans Health System Journal 4(6), 44 – 52.

Krishnaswamy, G., Kelley, J., Yerra, L. & Smith, J. (1999). Molecular Therapies for Asthma. Federal Practitioner 16 (1), 16 – 26.

National Asthma Education and Prevention Program (NAEPP). (1997). Expert panel report 2: Guidelines for the diagnosis and management of asthma. National Heart, Lung and Blood Institute. National Institutes for Health Publication No. 97-4051.

O'Hollaren, M. (1999). Asthma: Current Management Techniques. Federal Practitioner 16 (7), 12 – 21..

Spiegler, P. & Ilowite, J. (1998). Antileukotriene Agents in Asthma. Federal Practitioner 15 (9) 20 – 31.

Wells, B., Dipiro, J., Schwinghammer, T., Hamilton, C. (1998). Pharmacotherapy Handbook (2 nd ed). (pp 940-952) Connecticut: Appleton &Lange.