Family Physician Airways Group of Canada

Airways Update

October 2013

In this issue:

4 Monitoring your Patient with Asthma

12 Bronchodilator Efficacy of Tiotropium-formoterol via Single Pressurized Meter Dose

14 Pneumonia and Pneumonia Related Mortality in Patients with COPD Treated with Fixed Combinations of Inhaled Corticosteroid and Long Acting β2 Agonist

Chairperson's Report

Autumn comes and a time for post summer reflection. Did I spend time with my family and loved ones, or did I again work harder than I planned? What initiatives do you have for your office this year? I consider this as I implement a new EMR system (last company went bankrupt) and have to unlearn and relearn many skills relating to my chart. However a new season brings the potential for new initiatives. How do I monitor my patients with airway diseases. What works in a primary care office? What can I do better?

We are very proud of the tools section of the website, giving you some practical ready tools that you could consider implementing to your EMRs; from flow sheets to action plans to predictive models. How do you assess an asthmatic review control tools (see last newsletter for a comprehensive review)? How do you assess a COPD patient? Ask about exacerbations and use the CAT tool. Which patients with AECOPD need to go to the hospital; use the BAP65 tool. Which of your patients need a sleep study; use the STOP-BANG tool.

We continue being the Lung Health Portal for MDBriefcase , where you can review top rate educational programs and earn Mainpro M1 credits doing so! Your pharmacy colleagues can also view these and other programs for credit. We have also begun housing the programs which have expired on our website for your review. These will not, however, be eligible for Mainpro M1, although they are for Mainpro M2.

We have continued to provide Mainpro C programs at various national and provincial assemblies and at Primary Care Today, a large Toronto based conference in May each year. Please let us know if we can be of assistance in your setting up a spirometry program locally in your area; we can potentially come to you! We have been involved in creating accredited educational programs for a few of our pharmaceutical companies. It was a wonderful process where FPAGC members along with selected specialists, which was completely hands off by pharma, worked together to provide a meaningful program for our primary care colleagues.

We continue to advocate for optimal primary care respiratory care by being involved in provincial and national government initiatives. Let me know if you want more information on these, or have some local concerns.

In conjunction with the special interest focused practice section of the CFPC, a full respiratory medicine program has been created for the Family Medicine Forum at the CFPC in Vancouver from November 7-9, 2013.Our program centres on four themes: Cough, Asthma, COPD, and respiratory infections. Rob Hauptman and I will also be providing a Mainpro C Spirometry program if any of you feel the need to brush up on those skills....

I wanted to remind you of our forum; your questions and comments will be responded to. Please join up and get involved!

As always, I would like to thank our national executive and secretariat for their contributions to respiratory care in Canada.
Enjoy the fall season,
Alan Kaplan MD CCFP(EM) FCFP
Chair, FPAGC

Does Oseltamivir work?

Ebell MH, Call M, Shinholser J. Effectiveness of oseltamivir in adults: a meta-analysis of published and unpublished clinical trials. Fam Pract 2013;30(2):125-133.

This meta-analysis looked at published and unpublished trials on Oseltamivir, or Tamiflu, on efficacy of decreasing duration of influenza symptoms or complications. They looked at the results of studies including more than 4200 patients. The bottom line? There was a decrease in duration of symptoms of about 25 hours in those treated. There was no difference in the rate of hospitalization, but overall the rate of hospitalization was only about 1%. However, among patients with laboratory-confirmed influenza, patients treated with oseltamivir had a slightly lower rate of pneumonia (0.5%) than placebo-treated patients (1.6%; number needed to treat = 111; 95% CI, 59 - 1000).

Editors Note: This highlights the continued controversy of the value of antivirals in influenza. I cannot help but put my personal bias in this. I have suffered from influenza an amazing four times (yes, despite flu shots!) and can tell you the difference between EARLY treatment vs. no treatment was not small. With treatment, I was up and around in less than 24 hours. Without it, it was 2-3 weeks of morbidity.

I think the keys are three:
1) Prevent influenza by flu shots and hand hygiene
2) Early initiation of Tamiflu means that treatment is required within 48 hours. So your patients have to know how to access you for treatment quickly during influenza season.
3) High- risk patients are at risk of more than just morbidity; so #2 is especially important for your vulnerable population.

Effects of montelukast on the healing of ischemic colon anastomoses.

Celik A, Ergun E, Koksal N, Celik AS, Altinli E, Uzun MA, Eroglu E, Kemik A. Am J Surg. 2013 Jun 25. [Epub ahead of print]

Aim and Methods:
The aim of this study was to examine whether treatment with montelukast, a selective leukotriene antagonist, would affect anastomotic healing in a reperfused colon rat model with remote ischemia/reperfusion injury. Rats (n = 12 per group) were intraperitoneally administered normal saline or 10 mg/kg montelukast sodium 60 minutes before and for 5 days after surgery. Ischemia was induced for 45 minutes through superior mesenteric artery occlusion. A left colon anastomosis was made. Blood and perianastomotic tissue samples were obtained on postoperative day 5.

Results:
Mean anastomotic bursting pressures of the control and montelukast groups were 159.17 ± 29.99 and 216.67 ± 26.40, respectively ($P < .001$). Compared with saline, montelukast treatment increased the mean tissue hydroxyproline level (2.46 ± .30 vs 3.61 ± .33 μmol/L) and decreased tissue caspase-3 activity (36.06 ± 5.72 vs 21.78 ± 3.87) and malondialdehyde levels (3.43 ± .34 vs 2.29 ± .34 nmol/g) ($P < .001$ for all). Other plasma markers of injury also showed differences.

Conclusion:
Montelukast prevented ischemia/reperfusion-induced damage in a rat model of colonic anastomotic wound healing.

Editorial:
Nothing we do in medicine is completely safe. We think of Singulair as a drug which is efficacious in some, and having no downsides. Perhaps it should be stopped in someone undergoing colonic surgery? Something to consider....

Early diagnosis of COPD, actually examine your patient!

Oshaug K, Halvorsen PA, Melbye H. Should chest examination be reinstated in the early diagnosis of chronic obstructive pulmonary disease? International Journal of Chronic Obstructive Pulmonary Disease July 2013 Volume 2013:8 Pages 369 - 377 DOI: http://dx.doi.org/10.2147/COPD.S47992

Chest signs have been associated with bronchial obstruction, but are not listed among cues that should prompt spirometry in the early diagnosis of chronic obstructive pulmonary disease (COPD) in established guidelines. **This study** aimed to explore how chest findings add to respiratory symptoms and a history of smoking in the diagnosis of COPD. They used a cross-sectional study, patients aged 40 years or older, previously diagnosed with either asthma or COPD in primary care, answered questionnaires and underwent physical chest examination and spirometry.

Results: 39.7% of the 375 included patients who had forced expiratory volume in 1 second/forced vital capacity <0.7, diagnosing COPD. Hyperresonance to percussion was the strongest predictor of COPD, with a sensitivity of 20.8, a specificity of 97.8, and likelihood ratio of 9.5. In multivariate logistic regression, where pack-years, shortness of breath, and chest findings were among the explanatory variables, three physical chest findings were **independent** predictors of COPD. Hyperresonance to percussion yielded the highest odds ratio (OR = 6.7), followed by diminished breath sounds (OR = 5.0), and finally wheezes (OR = 2.3). **They concluded that** chest signs may add to respiratory symptoms and a history of smoking in the diagnosis of COPD, and that chest signs should be reinstated as cues to early diagnosis of COPD in patients 40 years or older.

Monitoring your Patient with Asthma

(originally printed in Medical Post earlier this year)

Author: Alan Kaplan

Asthma is a chronic inflammatory disease of the airways, common in both adults and children. The most recent epidemiologic data suggests that asthma afflicts 300 million people worldwide and the global burden is projected to increase by another 100 million by 2025.Asthma therefore needs to be treated as a chronic illness, rather than an episodic illness, which is often how patients regard it and as such, requires continual assessment of the disease, both its physiologic effects as well as resultant effects on quality of life. It is clear that good asthma control equates to improved outcomes. How do you assess control? This article will review the different ways an asthmatic can be assessed in your office.

All patients who present to the office can be questioned regarding their current symptoms. The Canadian landscape changed in this regard with the advent of the 30 second asthma test . With this test, the symptoms of asthma control became better recognized in Canada, and they have been basically unchanged since. (Figure one). Other questionnaires have been developed since, with variations in the time of assessment, use of lung function and other quality of life issues, and they can also be used in primary care; though often they are used in research (Table one). The IPCRG developed a tool to look at these tools to help pick a preference, with no clear winner (Figure 2).

When a patient comes in to the office, a history is first taken. This can be how they are feeling at the moment, but should also include their symptoms over the past week and past month, including their day and night symptoms, use of rescue medications, missed life opportunities, and any exacerbations. The use of patient diaries can be of a lot of value in assisting accurate memory, but does require a fair bit of time investment. Physical examination is fairly insensitive and much less reliable than spirometry for assessing the degree of airflow obstruction, which highlights the need of lung function testing in addition to history and physical examination. That being said, normal airflow does not rule out asthma, but does indicate better control.

We should take a history from both patient and caregiver, even in younger children, in order to also understand the child's perception of the impact of the illness. Interestingly, a history obtained from older children correlates well with physiologic measures and diary records. The frequency of symptoms and exacerbations can be assessed more precisely by reviewing the patient's symptom or PEF diary; however diaries are often not done accurately, especially in children . More recently, electronic devices such as PIKO and COPD6 automatically record the actual time records made and create an electronic record which may improve the accuracy of PEF and other diaries. Personal electronic spirometers are also coming to the market, which are more expensive, but include a likely better measurement of lung function as well as an electronic diary. A little used measurement of asthma control includes PEF variability, which correlates with airway hyperreactivity, and can be ascertained from properly done PEF monitoring.

As a physician, we must take the visit further and include some objective assessment of airflow. Spirometry (for measurement of FEV_1 and FEV_1/forced vital capacity) is more reliable than PEF when carried out according to

recommended standards. PEF can frequently result in underestimation of airway obstruction when compared to FEV_1 but is more easily available. A physician treating asthma should have access to a spirometer or have a PEF meter for office use, and testing should be done before and 10-15 minutes after an inhaled β_2-agonist. Doing pre and post testing also allows observation and review of inhaler technique. Spirometers do need to be calibrated and maintained according to published standards, albeit some of the newer smaller electronic metres are more stable. Airflow reduction will usually reflect poorly controlled asthma, however in some patients it may represent the best function possible due to airway remodelling in chronic asthma. There is not great evidence for the use of peak flow monitoring of asthmatics, and spirometry in the office is clearly superior.
There are a number of barriers to the use of Spirometry in primary care. These include access, funding, knowledge, and timing of the test. An organized approach can deal with these barriers, however. See Box One for a review of potential solutions to these barriers.

Perhaps because of this, unfortunately nearly half of patients with physician-diagnosed asthma have **never** undergone spirometry and many more have never received the more specific testing required to distinguish asthma from other obstructive lung diseases. Without such testing, clinical diagnosis of asthma, even by asthma specialists, is incorrect in about one third of patients as asthma symptoms are similar to symptoms of many other respiratory conditions. Since the vast majority of asthma patients are diagnosed and managed by their family doctor, the responsibility to ensure the diagnosis is accurate inevitably falls mainly to primary care physicians. Clearly, the first step in monitoring a patient with asthma is ensuring an adequate diagnosis.

Part of monitoring of asthma can, and should, be done by the patient. As such, there may be a role for PFR monitoring as there is some evidence that it is superior to just symptom monitoring in some patients. This amount of work by your patients to do self monitoring with PEF will not be for all of your asthma patients, but can be especially useful for those that have issues with perception of their asthma, for those with communication issues, or for some children.

As you monitor the patient for loss of control, you must have an approach to the uncontrolled asthma patient. Review adherence (you may have to check with the pharmacy!), device technique, co morbid illness (rhinitis, GERD, obesity), and trigger exposure (remember smoking!) in these patients. Have a look at the asthma management flow sheets in the tools section at *www.fpagc.com* for tools to assist the office based management of asthmatic patients.

Optimizing control results in improvement in a stepwise manner in our patients. Symptoms improve first, spirometry normalizes next, then measures of bronchial hyperreactivity; but these are really fairly surrogate measurements for the physiology of the disease- asthma inflammation. Inflammation may take longer to settle down and has been difficult to measure outside of specialized laboratories. Canada, led by the late Dr. Freddie Hargreave has taken the lead in a sputum analysis (differential cell count, measurement of eosinophil cationic protein) which has been shown to accurately assess airway inflammation and to manage and monitor asthma. Managing an asthmatic based on sputums has clearly been shown to reduce exacerbations in patients with moderate to severe disease.

Sputums are not universally available, and patients may not be able to produce a sample

limiting its utility. More recently, a more portable measurement of inflammation with the use of exhaled Nitric Oxide has received attention to help diagnose and monitor patients with asthma, and has been shown to be quite acceptable to do in primary care. It has also been shown when added to symptom-based management to lead to more optimal pharmacotherapy guidance, in adjusting the dosage of anti-inflammatory agents, and positive long-term disease outcome. This can be measured by small handheld units that are commercially available in the USA and Europe, though they have not yet been approved in Canada. There is developing evidence on how to use eNO in practice with guidelines in the USA while in Canada it is rarely used as the most recent Canadian Asthma guidelines has said: "We do not suggest the routine use of FeNO, either in addition to or instead of standard measures of asthma control, to adjust anti-inflammatory therapy in children or adults with asthma" despite the evidence that eNO measurement decided treatment is more sensitive to the efficacy of ICS in patients than FEV1.

Newer ideas in patient monitoring include electronic internet based monitoring. There is evidence that show when physicians and patients used an interactive Internet-based asthma monitoring tool, better asthma control was achieved. In one study, treatment and monitoring with the Internet-based management tool lead to significantly better improvement in the Internet group than in the routine office based management in both family physicians and specialists regarding asthma symptoms (Internet vs. specialist: odds ratio of 2.64, $P = .002$; Internet vs. GP: odds ratio of 3.26; $P < .001$), quality of life (Internet vs. specialist: odds ratio of 2.21, $P = .03$; Internet vs. GP: odds ratio of 2.10, $P = .04$), lung function (Internet vs. specialist: odds ratio of 3.26, $P = .002$; Internet vs. GP: odds ratio of 4.86, $P < .001$), and airway responsiveness (Internet vs. GP: odds ratio of 3.06, $P = .02$). This can be carried forward to more formal interactive home monitoring systems. It is clear that there are some real barriers in the home monitoring of patients, which include the reliance on patient performance of tests, documentation, physician response time, and the lack of timely clinical decision support tools.

A patient has to understand their asthma in order to make changes. Symptoms of asthma can be viewed as worsening, and thus require a change in behavior. Further deterioration of symptoms becomes an exacerbation that requires changes recommended by the physician, or even better, to be done proactively by the patient with a written asthma action plan. Action plan utilization earlier on in the symptoms can certainly prevent severe exacerbations. Appropriate monitoring during an acute attack can also direct which patients need emergent care.

Conclusion

Asthma is a chronic disease that requires regular monitoring for control. This should be done by the patient and reinforced by the physician and health care team. Symptoms, lung function, and eventually measures of inflammation like eNO, are all office based methods to evaluate asthma control. Having a good approach to the loss of control will be important in preventing adverse outcomes in your patients with asthma.

Table One: Asthma Control symptom based measurement tools
30 second test
ACT: Asthma Control Test
ACQ: Asthma Control Questionnaire
ATAQ: Asthma Therapy Assessment Questionnaire
RCP: Royal College Physician questionnaire

(3 and 21 questions versions)
Rules of Two
St. George Respiratory Questionnaire

Box: Ways to deal with barriers to obtaining pulmonary function testing.

- Know where your pulmonary function labs are and their waiting lists
- Labs that will book an appointment for you while the patient is still in the office make it more likely that patients will go for testing
- Ask laboratories to fax the uninterpreted result to the ordering physician so that the physician can begin interpreting the test without having to wait for the official report
- A mentor system, in which primary care physicians could access an expert colleague for help with difficult spirometry interpretations, can be a useful support

Continuing education programs for personnel conducting testing can be used to reinforce proper testing technique

Stanbrook MB, Kaplan A. The error of not measuring asthma. CMAJ. 2008;179 (11):1099–102.

Figure One: Parameter of Asthma Control per CTS guidelines[xxii]/ GINA[i]

In order to be in control our patient with asthma should:

- Have daytime symptoms less than four times per week/2 or less times per week
- Have night-time symptoms on <1 night per week
- Have full physical activities
  Have mild infrequent/no exacerbations of their asthma

- Use rescue therapy with beta agonists <4/2 or less times per week
- Lung function of ≥ 90% and have peak flow variability of no more than 15%
- If sputums are available, keep the sputum eosinophils less than 3% of the cells isolated.

[Continued on page 8]

FPAGC ANNUAL GENERAL MEETING

The Family Physician Airways Group of Canada will be holding their Annual General Meeting on Thursday November 7, 2013 at 6:30pm. The meeting will be held in conjunction with the FMF in Vancouver and will be held in Salon C at the Renaissance Vancouver Hotel Harbourside, 1133 West Hastings Street. 1-604-689-9211, 1-855-823-6348

There will be a short presentation on COPD by Dr. Alan Kaplan followed by the AGM. Items included on the agenda are election of officers and the adoption of the new by-laws to comply with the Canada Not For Profit Corporations Act. A dinner will be served during the meeting.

All members are invited to attend this meeting. Please notify the national office no later than Tuesday October 29, 2013 if you plan to attend.

Contact Glyn at admin@fpagc.com to confirm your attendance.

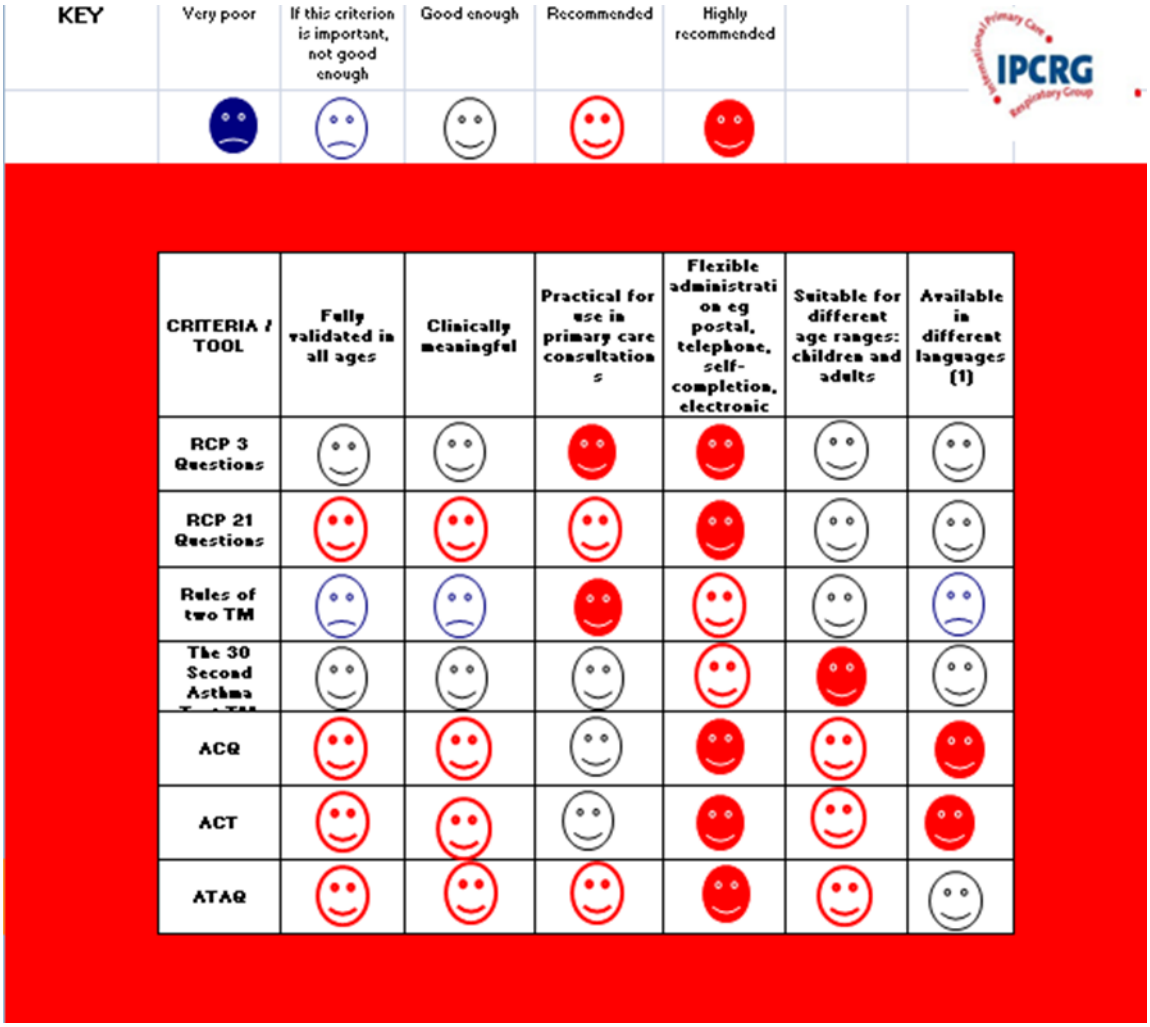


Figure 2. IPCRG ranking of Asthma control tools (www.theipcrg.org)

Masoli M, Fabian D, Holt S, Beasley R. Global burden of asthma. http://www.ginasthma.com/ReportItem.asp?l1=2&l2=2&intId=94.

FitzGerald JM, Boulet LP, McIvor RA, Zimmerman S, Chapman KR. Asthma control in Canada remains suboptimal: the Reality of Asthma Control (TRAC) study. Can Respir J. 2006 Jul-Aug;13(5):253-9.

Ahmed S, Ernst P, Tamblyn R, Colman N.Validation of The 30 Second Asthma Test™ as a measure of asthma control. Can Respir J. 2007 March; 14(2): 105–109.

Shim CS, Williams MH Jr. Relationship of wheezing to the severity of obstruction in asthma. Arch Intern Med 1983;143:890-2.

Guyatt GH, Juniper EF, Griffith LE, Feeny DH, Ferrie PJ. Children and adult perceptions of childhood asthma. Pediatrics 1997;99:165-8.

Hyland ME, Kenyson CAP, Allen R, Hwarth P. Diary keeping in asthma: comparison of written and electronic methods. BMJ 1993;306:487-9.

Klein RB, Fritz GK, Yeung A, McQuaid EL, Mansell A. Spirometric patterns in childhood asthma: peak flow compared with other indices. Pediatr Pulmonol 1995;20:372-9.

American Thoracic Society. Standardization of spirometry, 1994 update. Am J Respi Crit Care Med 1995;152:1107-36.

Brand PL, Roorda RJ. Usefulness of monitoring lung function in asthma Arch Dis Child 2003;88:1021–1025

Yawn BP, Enright PL, Lemanske RF Jr., et al. Spirometry can be done in family physicians' offices and alters clinical decisions in management of asthma and COPD. Chest 2007;132:1162-8.

Stanbrook MB, Kaplan A. The error of not measuring asthma. CMAJ. 2008;179(11):1099–102

Chapman KR, Boulet L-P, Rea RM, Franssen E. Suboptimal asthma control: prevalence, detection and consequences in general practice. Eur Respir J 2008;31:320-5

Tinkelman DG, Price DB, Nordyke RJ, Halbert RJ. Misdiagnosis of COPD and asthma in primary care patients 40 years of age and over. J Asthma 2006;43:75-80

Garcia J, Gonzalez-Santos P. Asthma self-management education program by home monitoring of peak expiratory flow. *Am. J. Respir. Crit. Care Med.* February 1, 1995 vol. 151 no. 2 353-359

Bheekie A, Syce J, Weinberg E. Peak expiratory flow rate and symptom self-monitoring of asthma initiated from community pharmacies Journal of Clinical Pharmacy and Therapeutics. Volume 26, Issue 4, pages 287–296

Haughney J, Price D, **Kaplan A**, et al. Achieving asthma control in practice: understanding the reasons for poor control. Respir Med. 2008;102:1681-93

Gibson PG, Dolovich J, Denburg JA, Girgis-Gabardo A, Hargreave FE. Sputum cell counts in airway disease: a useful sampling technique. Agents Actions Suppl 1990;30:161-72.

Jayaram L, Pizzichini MM, Cook RJ, Boulet LP, Lemière C, Pizzichini E, Cartier A, Hussack P, Goldsmith CH, Laviolette M, Parameswaran K, Hargreave FE. Determining asthma treatment by monitoring sputum cell counts: effect on exacerbations. Eur Respir J. 2006 Mar;27 (3):483-94

Stonham C, Ward S, Gruffydd-Jones K, Thomas M. Is exhaled nitric oxide monitoring possible in general practice asthma clinics: a feasibility and acceptability study. PCRJ Volume 15 Issue 3 June 2006: 185

Khalili B, Boggs PB, Shi R, Bahna SL.Discrepancy between clinical asthma control assessment tools and fractional exhaled nitric oxide. Ann Allergy Asthma Immunol. 2008 Aug;101(2):124-9.

Dweik et al. Am J Respir Crit Care Med. 2011;184(5):602-615

Lougheed D, Lemiere C, et al. Canadian Thoracic Society 2012 guideline update: Diagnosis and management of asthma in preschoolers, children and adults Can Respir J Vol 19 No 2 March/April 2012

Paro-Heitor ML, Bussamra MH, Saraiva-Romanholo BM, Martins MA, Okay TS, Rodrigues JC. Exhaled nitric oxide for monitoring childhood asthma inflammation compared to sputum analysis, serum interleukins and pulmonary function. Pediatr Pulmonol. 2008 Feb;43(2):134 -41

Rasmussen L, Phanareth K, Nolte H, Backer V. Internet-based monitoring of asthma: A long-term, randomized clinical study of 300 asthmatic subjects Journal of Allergy and Clinical Immunology. Volume 115, Issue 6, June 2005: 1137–1142

Finkelstein J, Hripcsak G, Cabrera MTelematic system for monitoring of asthma severity in patients' homes Studies in Health Technology and Informatics [1998, 52 Pt 1:272-276]

Balter, P Ernst, W Watson, …**Kaplan A**, et al. Asthma worsenings: Approaches to prevention and management from the Asthma Worsenings Working group. Can Respir J 2008;15(Suppl B):1B-19B.

Action Plans in Asthma. **Kaplan A.** The (Canadian) Family Physician, August 2002

Primary Pneumothorax Better with Pleurodesis + Drainage vs Drainage Alone

Chen JS, Chan WK, Tsai KT, et al. Simple aspiration and drainage and intrapleural minocycline pleurodesis versus simple aspiration and drainage for the initial treatment of primary spontaneous pneumothorax: an open-label, parallel-group, prospective, randomised, controlled trial. Lancet 2013;381(9874):1277-1282.

These researchers conducted this study in two hospitals in Taiwan. They included patients between the ages of 15 and 40 years who presented with a first episode of primary spontaneous pneumothorax; they excluded patients with underlying pulmonary disease, hemothorax, or tension pneumothorax. The clinicians treated all 214 patients with simple aspiration plus drainage with a small-bore pigtail catheter, and randomly assigned 106 to also be treated with minocycline pleurodesis. All patients received acetaminophen after the procedures for pain relief. If the pain was inadequately controlled by acetaminophen, the clinicians administered pethidine (meperidine) intramuscularly. Patients treated with minocycline received 30 mL of 1% lidocaine hydrochloride followed by 300 mg of minocycline through the pigtail catheter (unlike the current practice, which is to administer sclerosing agents via chest tube or during thoracostomy). The caregivers repositioned the patients every 30 minutes to facilitate adequate distribution of the minocycline. The researchers assessed the primary outcome -- pneumothorax recurrence within 1 year -- by intention to treat.

Results:

The initial treatment failed in 14 of the pleurodesis-treated patients and in 20 of the control patients, resulting in thoracoscopic surgery. At the end of one year, 31 pleurodesis-treated patients (29%) and 53 control patients (49%) had a recurrent pneumothorax (number needed to treat [NNT] = 5; 95% CI, 3 - 15). Furthermore, approximately 33% of the minocycline-treated patients underwent thoracoscopic surgery compared with approximately 40% of control patients (NNT = 7; 4 - 43). Approximately two thirds of the pleurodesis-treated patients requested additional pain relief compared with one fifth of the control patients. However, by 6 months, most patients no longer had pain.

Summary:

Patients with primary spontaneous pneumothoraces treated with minocycline pleurodesis after simple aspiration and drainage have fewer recurrences in the following year than those treated only with simple aspiration and drainage. However, they experienced more pain after the procedure.

Editorial

Even though this study was conducted in two hospitals in Taiwan only, the outcomes are consistent with the results of 4 other randomized trials of pleurodesis with tetracycline or talc. This study reaffirms that a pneumothorax is a frequently recurrent condition, and consideration to not only treating the problem, but preventing the next one, should be considered at initial clinical contact. Minocycline in Xylocaine is a simple, non-toxic poudrage that these authors used.

A Comprehensive Care Management Program to Prevent Chronic Obstructive Pulmonary Disease Hospitalizations. A RCT

Fan, Vicent et al - Annals of Internal Medicine 15 May 2012 Vol. 156 No. 10.

A randomized, controlled trial comparing comprehensive care management program (CCMP) with guideline-based usual care regarding risk for COPD hospialization with 20 Veterans Affairs hospital-based outpatient clinics, in patients identified as having been hospitalized for COPD in the past year.

Intervention: The CCMP included COPD education during 4 individual sessions and 1 group session, an action plan for identification and treatment of exacerbations, and scheduled proactive telephone calls for case management. Patients in both the intervention and usual care groups received a COPD informational booklet; their primary care providers received a copy of COPD guidelines and were advised to manage their patients according to these guidelines. Patients were randomly assigned, stratifying by site based on random, permuted blocks of variable size.

Measurements: The primary outcome was time to first COPD hospitalization. Staff blinded to study group performed telephone-based assessment of COPD exacerbations and hospitalizations, and all hospitalizations were blindly adjudicated. Secondary outcomes included non-COPD health care use, all-cause mortality, health-related quality of life, patient satisfaction, disease knowledge, and self-efficacy.

Results: Of the eligible patients, 209 were randomly assigned to the intervention group and 217 to the usual care group. Citing serious safety concerns, the data monitoring committee terminated the intervention before the trial's planned completion after 426 (44%) of the planned total of 960 patients were enrolled. Mean follow-up was 250 days. When the study was stopped, the 1-year cumulative incidence of COPD-related hospitalization was 27% in the intervention group and 24% in the usual care group (hazard ratio, 1.13 [95% CI, 0.70 to 1.80]; $P = 0.62$). There were 28 deaths from all causes in the intervention group versus 10 in the usual care group (hazard ratio, 3.00 [CI, 1.46 to 6.17]; $P = 0.003$). Cause could be assigned in 27 (71%) deaths. Deaths due to COPD accounted for the largest difference: 10 in the intervention group versus 3 in the usual care group (hazard ratio, 3.60 [CI, 0.99 to 13.08]; $P = 0.053$).

Conclusion: A CCMP in patients with severe recently hospitalized patients with COPD had not decreased COPD-related hospitalizations when the trial was stopped prematurely. The CCMP was associated with unanticipated excess mortality, results that differ markedly from similar previous trials.

Editorial: Available data could not fully explain the excess mortality in the intervention group. This finding flies in the face of prior studies on this topic. The study was limited as it was unable to assess the quality of the educational sessions provided by the case managers which was limited. In fact, I would suppose that the quality of the managers was likely not sufficient, as there was no use of certified respiratory educators like we have in Canada! Very competent and well- trained educators are necessary to assist this high- risk population. In addition, the physicians involved had limited knowledge on COPD exacerbation prevention may have been a factor as there was no mention of medication use, drug availability and coverage and socio economic status. This study will NOT change my recommendation of using a COPD Action Plan in my patients. See www.COPDActionPlan.com

Bronchodilator Efficacy of Tiotropium-formoterol via Single Pressurized Meter Dose Inhaler (pMDI) versus Tiotropium Alone in COPD.

Pulm Pharmacol Ther. 2013 Jun 8. doi: 10.1016/j.pupt.2013.05.010. [Epub ahead of print].
Salvi S, Brashier B, Gothi D, Karkhanis V, Madas S, Gogtay J, Joshi J

The aim of this study was to compare the bronchodilator effects of a single dose of 18 mcg of tiotropium versus a single dose of a combination of 18 mcg tiotropium plus 12 mcg formoterol administered via a pMDI in subjects with moderate-to-severe COPD. They were combined together in a single device by a company in India.

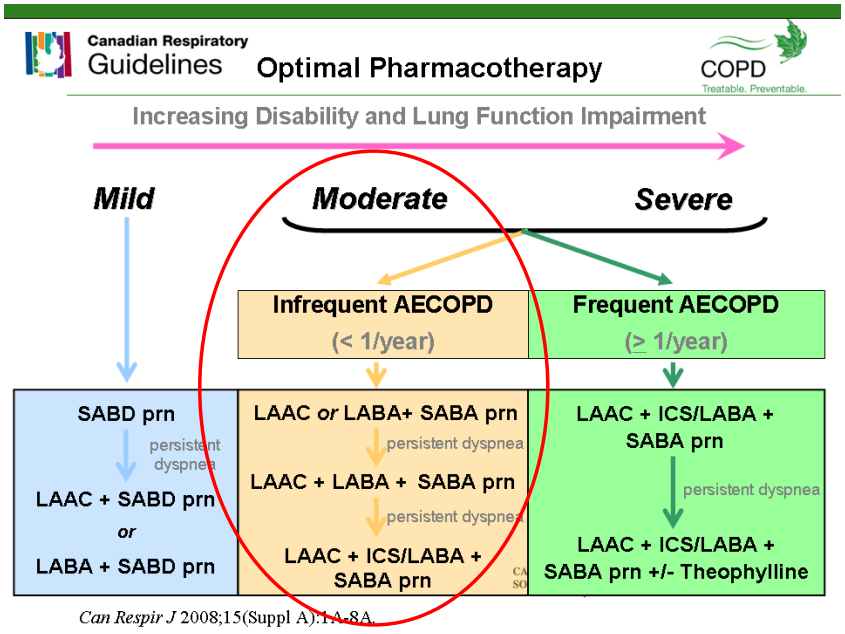
44 COPD subjects were enrolled in this randomized, double-blind, multi-centre, cross-over study. 18 mcg tiotropium and 18 mcg tiotropium plus 12 mcg formoterol were administered via pressurized metered dose inhalers on two separate days. FEV_1, FVC and Inspiratory capacity (IC) were measured before, 15, 30 min, 1, 2, 3, 4, 6, 8, 12 and 24 hrs after the study drugs were administered. Compared with tiotropium alone, a combination of tiotropium plus formoterol showed a faster onset of bronchodilator response ($p < 0.01$ for FEV1 and FVC), a greater mean maximum change in FEV1 ($p = 0.01$) and FVC ($p = 0.008$) and greater $AUC_{0\text{-}24h}$ values for FEV_1, FVC and IC. Trough FEV_1 and FVC values were also greater in the combination group.

What does this mean?

A combination of tiotropium plus formoterol administered via a single inhaler produced a superior bronchodilator response than tiotropium alone over a period of 24 h.

Editorial:

Bronchodilators form the main stay of treatment for COPD. When symptoms are not adequately controlled with one bronchodilator, addition of another bronchodilator is recommended by all guidelines. This is the middle column of our Canadian guidelines, and ICS should only be added for those with continued disability or frequent exacerbations. This Indian product, which is via a pressured metered dose inhaler, whereas both of these products are only available currently in dry powder, is unlikely to make it to Canada, but there are a number of newer long acting agents which are being combined to create similar LABA/LAAC combos coming to us soon!



Can Respir J 2008;15(Suppl A):1A-8A.

Could Propranolol be Safe in Patients with Stable Asthma?

Short PM, Williamson PA, Anderson WJ, Lipworth BJ. Randomized placebo-controlled trial to evaluate chronic dosing effects of propranolol in asthma. Am J Respir Crit Care Med 2013;187(12):1308-1314

This study randomly assigned 18 patients with stable asthma to receive propranolol or placebo and then, after a wash-out period, the alternate treatment, a randomized crossover trial. Stable asthma in this trial meant the patient had mild-to-moderate persistent asthma with a forced expiratory volume in 1 second greater than 80%. Each patient used inhaled corticosteroids during a run-in period so the authors could confirm that the patient had stable disease.

Each treatment phase consisted of a dose titration period of 2 to 4 weeks (propranolol target dose = 80 mg daily) followed by a 4-week maintenance phase. During the titration periods, the investigators added inhaled tiotropium but only used the inhaled steroids during the maintenance phase.
Results: The main outcome of interest was based on methacholine challenge testing. Overall, the methacholine challenge results were similar after each treatment interval. Additionally, the patients reported no differences in asthma quality of life or severity scales.

In this cross-over study of patients with stable asthma, adding propranolol had negligible effects on methacholine challenge testing, quality of life, or asthma severity.

Editors Note:
This is a small study, but the main advantage of a cross-over study is that each patient gets to serve as his or her own control and the sample size requirements are generally much smaller than in traditional clinical trials. That being said, **this is a very dangerous thing to do!** If an asthmatic patient needs a beta blocker, then one must assume that they do NOT need a beta agonist. Thus it could not be done on someone on LABA/ICS, or someone unstable enough to still be needing SABA. If your patient's asthma inflammation is resolved, then they should not have any bronchospasm and as such, beta blockade should not matter. I should also note that many of these patients were treated with an alternative bronchodilator, tiotropium, to ensure bronchodilation. Tiotropium use in asthma is not uncommon in severe/uncontrolled asthmatics, but not yet a frequent prescription in primary care. So be very careful with this information and it would still be prudent, if you must try a beta blocker to use a cardioselective one.

ak

Pneumonia and Pneumonia Related Mortality in Patients with COPD Treated with Fixed Combinations of Inhaled Corticosteroid and Long Acting β2 Agonist: Observational Matched Cohort Study (PATHOS).

Janson C, Larsson K, Lisspers KH, Ställberg B, Stratelis G, Goike H, Jörgensen L, Johansson G. BMJ. 2013 May 29;346:f3306. doi: 1136/bmj.f3306.

Background:

A number of studies, included Dr. Yawn's article reviewed in this newsletter, have recognized the increased risk of pneumonia in patients with COPD treated with ICS. This study investigated the occurrence of pneumonia and pneumonia related events in patients with chronic obstructive pulmonary disease (COPD) treated with two different fixed combinations of inhaled corticosteroid/long acting β2 agonist in Sweden via an observational retrospective pairwise cohort study matched (1:1) for propensity score. Investigated were primary care medical records data linked to Swedish hospital, drug, and cause of death registry data for years 1999-2009.

Patients with COPD, diagnosed by a physician who were given prescriptions of either budesonide/formoterol or fluticasone/salmeterol, were studied with the outcomes including yearly pneumonia event rates, admission to hospital related to pneumonia, and mortality.

Results:

9893 patients were eligible for matching (2738 in the fluticasone/salmeterol group; 7155 in the budesonide/formoterol group), yielding two matched cohorts of 2734 patients each. In these patients, 2115 (39%) had at least one recorded episode of pneumonia during the study period, with 2746 episodes recorded during 19,170 patient years of follow up.

Fluticasone/salmeterol compared with budesonide/formoterol, had a higher rate of pneumonia (rate ratio 1.73 (95% confidence interval 1.57 to 1.90; P<0.00) and admission to hospital 1.74 (1.56 to 1.94; P<0.001). The pneumonia event rate per 100 patient years for fluticasone/salmeterol versus budesonide/formoterol was 11.0 (10.4 to 11.8) versus 6.4 (6.0 to 6.9) and the rate of admission to hospital was 7.4 (6.9 to 8.0) versus 4.3 (3.9 to 4.6). The mean duration of admissions related to pneumonia was similar for both groups, but mortality related to pneumonia was higher in the fluticasone/salmeterol group (97 deaths) than in the budesonide/formoterol group (52 deaths) (hazard ratio 1.76, 1.22 to 2.53; P=0.003). All causes of mortality did not differ between the treatments (1.08, 0.93 to 1.14; P=0.59).

Study conclusion

There is an intra-class difference between fixed combinations of inhaled corticosteroid/long acting β2 agonist with regard to the risk of pneumonia and pneumonia related events in the treatment of patients with COPD.

Editorial:

There does seem to be a difference as to the risk of pneumonia between different steroids. There are theories, including one that suggests that the local anti-inflammatory/anti-immune activity is higher with the more potent fluticasone than budesonide. This article has some limitations. First of all, it is not a study, but a chart review with patient matching. Some will criticize it as not a double blind study, and it is not, but this is still evidence using patient matching with a large number of criteria to get matched groups to analyze. Secondly, this study was funded by Astra Zeneca which makes Symbicort.

Irregardless, if there is a safety message, perhaps we should pay attention....

ak

Inhaled Corticosteroid Use in Patients with Chronic Obstructive Pulmonary Disease and the Risk of Pneumonia: A Retrospective Claims Data Analysis.

Yawn BP, Li YF, Tian HJ, Zhang J, Arcona S, Kahler KH.
International Journal of COPD June 2013 Volume 2013:8;295 - 304

Background:

The use of inhaled corticosteroids in patients with chronic obstructive pulmonary disease (COPD) has been associated with an increased risk of pneumonia in controlled clinical trials and case-control analyses. The authors used claims databases as a research model of real-world diagnosis and treatment, to determine if the use and dose of inhaled corticosteroids (ICS) among patients with newly diagnosed COPD are associated with increased risk of pneumonia. In a retrospective cohort analysis of patients diagnosed with COPD between January 01, 2006 and September 30, 2010, drawn from databases (years 2006–2010), patients (aged ≥45 years) were followed until first pneumonia diagnosis, end of benefit enrollment, or December 31, 2010, whichever was earliest. A Cox proportional hazard model was used to assess the association of ICS use and risk of pneumonia, controlling for baseline characteristics. Daily ICS use was classified into low, medium, and high doses (1 µg–499 µg, 500 µg–999 µg, and ≥1000 µg fluticasone equivalents daily) and was modeled as a time-dependent variable.

Results:

Among 135,445 qualifying patients with a total of 243,097 person-years, there were 1020 pneumonia incidences out of 5677 person-years on ICS (crude incidence rate, 0.180 per person-year), and 27,730 pneumonia incidences out of 237,420 person-years not on ICS (crude incidence rate, 0.117 per person-year). ICS use was associated with a **dose-related increase** in risk of pneumonia, with adjusted hazard ratios (versus no use; (95% confidence interval) of 1.38 (1.27–1.49) for low-dose users, 1.69 (1.52–1.88) for medium-dose users, and 2.57 (1.98–3.33) for high-dose users ($P < 0.01$ versus no use and between doses).

Conclusion:

The use of ICS in newly diagnosed patients with COPD is potentially associated with a dose-related increase in the risk of pneumonia.

Editorial:

This excellent work by a colleague of mine from the United States shows once again that ICS in COPD is not benign, and does have an increased risk of pneumonia. It does not show, however, whether all inhaled steroids are equal. There is a body of literature that suggests that certain steroids are safer than others. For instance, the PATHOS trial, a database trial in Sweden suggested a very significant lower risk in pneumonia for Budesonide than Fluticasone.
AK

[see page 16 for figures]

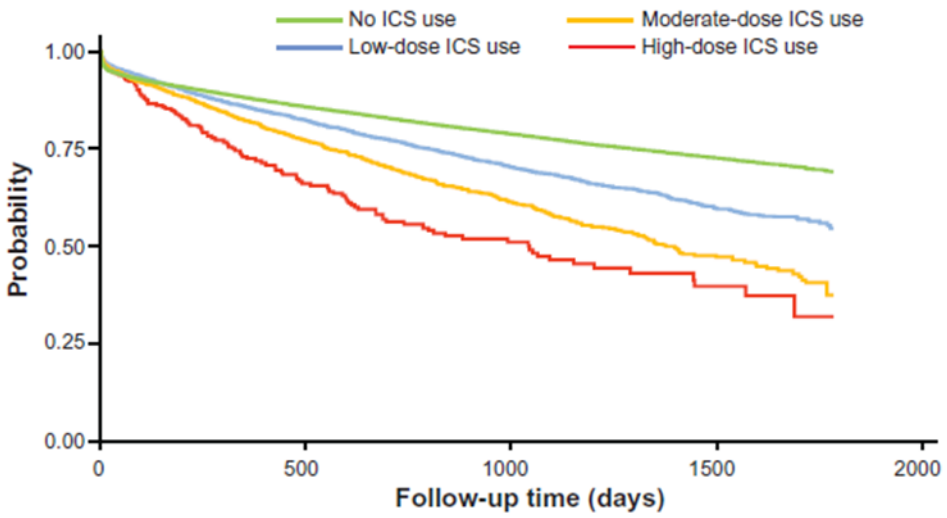


Figure 2 Kaplan–Meier pneumonia-free survival estimates during follow up period by inhaled corticosteroid dose level.
Abbreviation: ICS, inhaled corticosteroid.

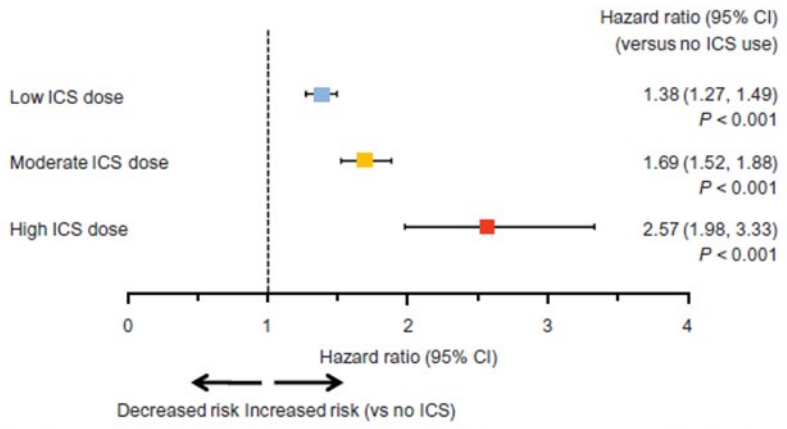


Figure 3 Adjusted hazard ratio for risk of pneumonia according to inhaled corticosteroid dose. Pairwise comparisons between the three ICS dose levels were all significantly different at $P < 0.01$. The hazard ratios were from multivariate Cox proportional hazards model, with ICS use and dose level as time-dependent variables.
Abbreviations: CI, confidence interval; ICS, inhaled corticosteroid.

Characteristics of Children with Asthma Who Achieved Remission of Asthma

Javed A, Kwang H, et al. Journal of Asthma 2013

The study was a retrospective cohort study based on 117 asthmatic children who participated in a previous study. The children were categorized into two groups: asthmatics with remission versus asthmatics without remission. Remission of asthma was defined as a lack of symptoms/signs of asthma, or asthma-related medications, or health care services for at least three consecutive years. Long-term remission was defined by no relapse of asthma after achieving remission.

Results

Of the 117 subjects, 70 (60%) were male, 91 (78%) were Caucasians, and the mean age at index date of asthma was 8.1 years. A total of 59 asthmatic children (50%) achieved remission and 28 asthmatics (24%) achieved long-term remission. Asthmatics with remission were more likely to be Caucasian (87%) compared to those without (69%) ($p = .039$) There were no differences in the frequency of visits for viral (0.3 vs. 0.4 per person-years, $p = .29$) or bacterial infections (0.7 vs. 0.5 per person-years, $p = .49$) between asthmatics with and without remission. Gender, socioeconomic status, smoking exposure, family history of asthma or atopy, breastfeeding history, peak flow meter availability, asthma action plan, and influenza vaccinations were not associated with remission.

Conclusions

Only half of asthmatic children accomplished remission of asthma ever and 24% of asthmatic children had long-term remission. Ethnicity may affect remission of asthma but microbial infections may not influence the likelihood of remission of asthma and vice versa.

Editorial:

No answer here! This US study only showed an increase in remission in some Caucasians vs other ethnicities, which you might expect to blame on socioeconomic status, but apparently not per their analysis. Bottom line, no way to predict which ones will go into remission, so treat each asthmatic individually!

Risk of Acute Kidney Injury Associated with the use of Fluoroquinolones.

Bird ST, Etminan M, Brophy JM, Hartzema AG, Delaney JA, CMAJ. 2013 Jul 9;185(10):E475-82. doi: 10.1503/cmaj.121730. Epub 2013 Jun 3.

BACKGROUND:

Case reports indicate that the use of fluoroquinolones may lead to acute kidney injury. These authors studied the association between the use of oral fluoroquinolones and acute kidney injury, and particularly examined interaction with renin-angiotensin-system blockers.

METHODS:

The authors formed a nested cohort of men aged 40-85 enrolled in the United States IMS LifeLink Health Plan Claims Database between 2001 and 2011. They defined cases as men admitted to hospital for acute kidney injury, and controls were admitted to hospital with a different presenting diagnosis. Using risk-set sampling, they matched 10 controls to each case based on hospital admission, calendar time (within 6 wk), cohort entrance (within 6 wk) and age (within 5 yr). They used conditional logistic regression to assess the rate ratio (RR) for acute kidney injury with current, recent and past use of fluoroquinolones, adjusted by potential confounding variables. The analysis was repeated with amoxicillin and azithromycin as controls.

RESULTS:

1292 cases and 12 651 matched controls were identified.. Current fluoroquinolone use had a 2.18-fold (95% confidence interval [CI] 1.74-2.73) higher adjusted RR of acute kidney injury compared with no use. There was no association between acute kidney injury and recent (adjusted RR 0.87, 95% CI 0.66-1.16) or past (RR 0.86, 95% CI 0.66-1.12) use. The absolute increase in acute kidney injury was 6.5 events per 10 000 person-years. We observed 1 additional case per 1529 patients given fluoroquinolones or per 3287 prescriptions dispensed. The dual use of fluoroquinolones and renin-angiotensin-system blockers had an RR of 4.46 (95% CI 2.84-6.99) for acute kidney injury. The use of amoxicillin or azithromycin was not associated with acute kidney injury.

INTERPRETATION:

This study found a small, but significant, increased risk of acute kidney injury among men with the use of oral fluoroquinolones, as well as a significant interaction between the concomitant use of fluoroquinolones and renin-angiotensin-system blockers.

EDITORIAL

Once again, there is nothing in medicine completely safe. Respiratory flouroquinolones are indicated for pneumonia and AECOPD. Perhaps we should think twice in prescribing these drugs to those with renal disease or those on renin-angiotensin-system blockers.

ak

The Board of Directors

CHAIR
Alan Kaplan
17 Bedford Park Avenue
Richmond Hill, ON L4C 2N9
Bus:905-883-1100
Fax: 905-884-1195
for4kids@gmail.com

VICE CHAIR
Anthony Ciavarella
27107 Fraser Highway
Aldergrove, BC V4W 3R2
Bus:604-856-3321
Fax: 604-857-2231
ciavarella@shaw.ca

SECRETARY/ TREASURER
Robert Hauptman
Salvus Family Medical Clinic
62 -143 Liberton Drive
St. Albert, AB T8N 6A7
Bus:780-460-4562
Fax: 780-460-4550
docrob@telusplanet.net

ADMINISTRATION
Glyn Smith
132 Warwick Road
Edmonton AB T5X 4P8
Bus: 866-406-4345
Fax: 780-475-7968
admin@fpagc.com
www.fpagc.com

DIRECTORS

Jacques Bouchard
Clinique de medecine familiale de la Malbaie
515 rue St-Erienne
La Malbaie, PQ G5A 1W7
Bus:418-683-8393
Fax: 418-687-9024
jacques.bouchard@videotron.ca

John Rea
104-348 Muskoka Rd 3 N
Huntsville, ON P1H 1H8
Bus:705 789 2355
Fax: 705-789-1051
reajc2@hotmail.com

Ken Bayly
701 Ave P North
Saskatoon, SK S7L 2W1
Bus: 306-382-5854
Fax: 306-382-7477
ken-nethbayly@sasktel.net

REASEARCH CHAIR

Andrew Cave
1A1 8440 112 Street
Edmonton AV
Bus: 780-433-4211
acave@cha.ab.ca

John Li
1789 Mountain Road, Suite 207
Moncton, NB E1G 1A7
Bus:506-859-8696
Fax: 506-383-8224
drjohnli4@gmail.com

Douglas Tweel
199 Grafton St
Charlottetown, PEI C1A 1L2
Bus:902-629-8843
Fax: 902-628-6024
dt_gcri@hotmail.com

John Kirkpatrick
8 Peppett Street
North Sydney
Nova Scotia, B2A 2M7
Bus: 902-794-2868
Fax: 902-794-4448
jhk@eastlink.ca

Josiah Lowry
Suite 200,
100 Colborne St. W
Orillia, ON L3V 2Y9
Bus:705-327-3330
Fax: 705-327-7675
Jbldr.2381@xplornet.com

Robert Woodland
Major's Path Family Practice
#301, 35 Major's Path
St. John's, NL A1A 4Z9
Bus:709-579-2324
Fax: 709-579-3419
woodlandclinic@nfld.net

Gordon Dyck
Clearspring Medical Clinic
1 – 390 Main Street
Steinbach, MB R5G 1Z3
Bus:(204) 326-6111
Fax: 204-326-6952
gdyck4boys@hotmail.com