What is Clin IQ Program?

Clinical Inquires (Clin IQ) program is based on the evidence based literature search of clinical questions relevant to patient care and helps residents, faculty and community physicians to enhance their knowledge and scholastic activities.

Our program was started in June 2014 under the guidance of program director Dr. Diana Wilkins and core faculty team. UB Family Medicine Clin IQ program is adopted from Clin IQ process of Oklahoma Clinical and Translational Science Institute.

We appreciate the tremendous help and support provided by Primary Care Research Institute (PCRI) especially Drs. Ranjit Singh, Chet Fox and Nikhil Satchidanand.

Purpose

1. Compliance with ACGME residency review committee (RRC) requirement for the residents and faculty participation in scholarly activities.
2. To facilitate and nurture the scholarly activities in the realm of busy clinical practice.
3. Provide evidence based answers to clinical questions and a link between academic and community physicians.

Team

UB Family Medicine class of 2015
Core faculty team

Note: Current issue of Clin IQ is for appreciation of residents hard work and effort and is not intended for CLINICAL or peer reviewed publication purpose.

Influenza vaccine and Pneumonia risk

Dry needling vs. anesthetics for trigger points

Resuming warfarin therapy in Atrial fibrillation

Risk of new onset Diabetes in patients on Statins

Low dose Aspirin and preeclampsia related

Systemic corticosteroids for chronic rhino-sinusitis

 Clin IQ 1: In adults and the elderly who are generally healthy, does administration of the Influenza yearly vaccine reduce the incidence and/or severity of Influenza associated pneumonia?

Authors: Jennifer Yerke-McNamara MD & Kevin C. Lesh MD
Faculty Mentor: David Newberger MD
Residency Program: SUNY Buffalo Family Medicine, Millard Fillmore Suburban/Amherst Track
Answer: Yes
Level of Evidence : B
Search Terms: influenza vaccine, pneumonia

Date Search was Conducted: November 2014 in Pubmed. Assistance received by Medical Librarians at Millard Fillmore Suburban Hospital.

Inclusion Criteria: Published systematic reviews/meta-analyses, clinical trials, cohort studies comparing the development and mortality of influenza associated pneumonia.

Exclusion Criteria: Patients under age 18 years

Summary of the Issues

Worldwide, pneumonia is a common illness affecting all ages, with an estimate of approximately 450 million cases per year.1
Of the varying etiologies, viruses are a common cause of community-acquired pneumonia with an estimated incidence of 49%. Common isolated viruses include RSV (11%) and influenza virus (10%). Typically influenza inoculation is a self-limited upper airway illness, but severe complications include viral pneumonia and/or secondary bacterial pneumonia leading to ICU admissions and death at times. It is estimated that 65,000 deaths per year are attributed to the combination of influenza and pneumonia in the USA. Those affected most severely include the elderly and adults with chronic medical conditions.

The influenza vaccination is an immunization that is recommended annually for all persons over age 6 months old. It induces immunity by leading to the production of antibodies against the specific influenza strains contained within the vaccine. This is true regarding both the typical trivalent vaccine, as well as the quadrivalent vaccine that is also available in adult and pediatric formulations. Trials and studies assessing the efficacy of the vaccines are limited due to ethical considerations. However, of the studies available, results show immunization with the vaccines leads to reductions in both associated pneumonia development and subsequent hospitalizations, morbidity, and mortality.

**Summary of Evidence**

A 2007 cohort study evaluated the impact of prior influenza vaccination on in-hospital mortality and other health outcomes among hospitalized patients with community-acquired pneumonia. Study subjects were adults 18 and older who were admitted to the hospital with a diagnosis of CAP between November to April 1999-2003. A total of 17,393 individual records were analyzed. Vaccination status was available for 8251 study subjects (47%) and 1590 (19%) had a record of current influenza status3. All-cause mortality occurred in 1245 (7%) of individuals3. Those individuals with documented current influenza vaccine were less likely to die during hospitalization compared with documented non-recipients of the vaccine.

A 2006 study examined the effect of annual influenza vaccination on the occurrence of lower respiratory tract infections in elderly, community-dwelling patients. A population-based cohort study was performed using a Primary Care Information database in the Netherlands4. The study was comprised of patients aged 65 years and older, whose individual cumulative exposure to the influenza vaccination was computed. The risk of lower respiratory tract infection (LRTI) in those who were vaccinated or re-vaccinated was compared to the unvaccinated using a multivariable Cox proportional hazard model4. The study looked at the treatment of LRTIs in the primary care setting4. The study consisted of 26,071 subjects, 3,412 of who developed an LRTI. 1,295 of those patients that developed a LRTI developed pneumonia and 455 of those patients were admitted to the hospital for treatment4. Vaccination rates varied the study population and had a range of 64%-74%. Those with co-morbid conditions had a higher vaccination rate of 74-79%. During the influenza epidemic period, a first influenza vaccination was associated with a 71% risk reduction (95% CI, 4%-90%) of hospitalized pneumonia4. No significant association was seen during revaccination during this period4. The data of the study concluded that influenza vaccination reduces the risk of lower respiratory tract infection in specific subgroups during the influenza epidemic period4.

**Conclusion:** From our search of the literature, we can conclude that for adults older than age 65 the influenza vaccine reduces the risk of pneumonia as well as mortality from pneumonia. The influenza vaccine was shown to decrease the incidence of pneumonia during the influenza epidemic period4. A decrease in mortality of those with pneumonia was seen in those who received an influenza vaccine5. This finding does change the way we practice as we can now tell patients that not only is their risk of contracting influenza decreased by receiving a vaccination, but so is their risk of developing pneumonia. This may help encourage people to get an annual influenza vaccine.

**References:**


“Sometimes when you innovate, you make Mistakes. It is best to admit them Quickly and get on with improving your other innovations.”

-Steve Jobs
Clin IQ 2: In patients with myofascial trigger points, can dry needling be just as effective as injections with an anesthetic solution?

**Authors:** Angela Barnes DO, Carlyle Martis MD, Raena Singh MD

**Faculty Mentor:** Priyanka Patnaik MD

**Residency Program:** University at Buffalo, Family Medicine Residency Program. Buffalo General / Jefferson Track

**Answer:** Yes

Our research found that dry needling can be as effective, however it is associated with side effects. These include more pain for the patient during the procedure and needle placement for optimal pain relief is examiner dependent.

**Level of Evidence:** A

**Search Terms:** dry needling, trigger points, dry needling vs wet needling, lidocaine injection.

**Date search was conducted:** May 2015

**Inclusion Criteria:** systematic review of randomized control trials to evaluate whether dry needling is effective.

**Exclusion Criteria:** Studies involving patients with Fibromyalgia.

**Summary of Issues:**

Myofascial trigger points are defined as discrete, focal, irritable spots felt as a nodule or taut band of skeletal muscle. Patients with trigger points experience pain locally, when these points are palpated and their pain will be reproduced on exam. Acute injury or repetitive micro-trauma can also result in the stress on muscle fibers and the formation of trigger points.

Many different techniques are currently used to inactivate trigger points to assist patients with pain relief/control. These include traditional physical therapy, ultrasonography, manipulative therapy and injections. Trigger-point injections have been shown to be one of the most effective treatment options to quickly and effectively treat pain associated with myofascial trigger points.

**Summary of Evidence**

An injectable solution of 1% lidocaine or 1% procaine is usually the solution of choice. Procaine has been found to have the least myotoxic effects. Other solutions such as diclofenac, botulinum toxin type A (Botox), and corticosteroids, have also been used in trigger-point injections, however, these substances have been associated with significant myotoxicity and visible skin defects.

In the systematic review of randomized control trials by Cummings et al., they concluded that when treating myofascial trigger points the nature of the solution injected did not change outcomes. And more importantly, wet needling was not found to be therapeutically superior to dry needling.

Dry needling has been associated with post-injection soreness. In Hong et al. it was concluded that this pain was different from the original myofascial pain. Therefore, that study concluded that to reduce this soreness an anesthetic solution could be injected. However, it did not significantly change the long term outcome of pain relief. Each patient should be re-evaluated however, and they recommended that no reinjection of the trigger points until the post-injection soreness resolves, which typically lasts for 3 to 4 days in length. Providers should encourage patients to stay active even while receiving injections, and this would include various stretches and putting their muscles through a full range of motion to help ensure optimal outcomes.

**Conclusion:**

Pain associated with myofascial trigger points can significantly affect a person’s quality of life. Based on this review, we found that dry needling of myofascial trigger points is just as effective in treating pain as wet needling using an anesthetic solution. Given that some patients can develop myotoxicity from anesthetic solutions, dry needling is a good option for pain relief. However, for those who are able to tolerate these anesthetics wet needling may help minimize post-injection soreness and decrease pain associated with the actual trauma of the needle during injections. After review of the literature, we found that outcomes are usually equivalent when comparing dry needling vs. wet needling, but we suggest always taking into consideration each patient’s individual needs.

**References:**


4. Imamura ST, Fischer AA, Imamura M, Teixeira MJ, Tchia Yeng Lin, Kaziyama HS, et al. Pain management using myofascial approach when other...
Clin IQ 3: In patients with atrial fibrillation (AF) on warfarin and recent gastrointestinal bleed (GIB), should patients resume warfarin to prevent all-cause mortality?

Authors: Nathan Strauss MD, Saman Razzaghi MD, Rachel Larivee MD

Faculty Mentor: M. Ghazi MD

Residency Program: University at Buffalo, Family Medicine Residency Program. ECMC/Clevehill Track

Answer: Yes

Level of Evidence: B (Retrospective cohort studies)

Search Terms: atrial fibrillation, gastrointestinal bleed, warfarin, all-cause mortality

Date Search was conducted: December 2014.

Inclusion Criteria: Published systematic reviews/meta-analysis, cohort studies, and clinical research trials comparing risk of restarting vs not restarting warfarin in patients with AF after any gastrointestinal bleed (GIB).

Exclusion Criteria: Patients other than those with AF as the primary reason for anticoagulation were excluded.

Summary of issues:

AF is one of the most common clinically significant cardiac arrhythmias and is major risk factor for thromboembolism and death. Warfarin has been the anticoagulant agent of choice for the last 3 decades in patients with non-valvular AF, since it prevents thromboembolism and has mortality benefits over the patients who are not treated with warfarin. However, the use of warfarin is not without risks. Patients on warfarin are at risk of hemorrhage. The most common and fatal sites are the gastrointestinal tract and brain. GIB occurs in up to 15% of patients on long-term anticoagulation. The risk of bleeding is increased by the intensity of anticoagulant therapy, age (over 65 years), concurrent use of aspirin and history of GIB.

Therefore, restarting warfarin after GIB is a risky and often difficult decision. In the literature, it appears as though the debate is focused less on whether or not to restart warfarin in patients with AF after any gastrointestinal bleed (GIB).

Summary of Evidence:

Two studies were examined to determine if warfarin should be restarted in patients with AF and previous GIB to prevent all-cause mortality. One study, by Qureshi et al. (2014) hypothesized that warfarin treatment prevents thromboembolism and has mortality benefit when compared with subjects who are not restarted on warfarin after major GIB in patients with AF. They also investigated the various durations of interruption of warfarin therapy and the risk of GIB, thromboembolism, and all-cause mortality. Using a retrospective cohort study, they enrolled 1,329 subjects (mean age 76 years, woman 45%), in which warfarin was restarted after GIB in 653 cases (49.1%). They concluded that warfarin restarted after 7 days was not associated with increased risk of GIB but was associated with decreased risk of all-cause mortality (hazard ratio (HR) 0.67) and thromboembolism compared with resuming after 30 days of interruption.

Also using a retrospective cohort study, the second study by Witt et al. (2012) evaluated the incidence of thrombosis, recurrent GIB, and all-cause mortality, as well as the time to resumption of anticoagulation, during the 90 days following a GIB. Patients were put into a group based on whether they resumed warfarin therapy after GIB and followed up for 90 days. Of those who did not restart warfarin, 2.5% of patients had a thrombotic event compared to 0.4% of patients in the resumption of warfarin group. Regarding recurrent GIB, 10% of patients who restarted warfarin had another episode of GIB, compared to 5.5% of patients who did not restart warfarin and still had a recurrent GIB. This data was not statistically significant and not dependent on dose of Coumadin. All-cause mortality in the group that resumed warfarin was 5.8%, compared to 20.3% of patients that did not resume warfarin. The adjusted analysis confirms that resuming warfarin reduced all-cause mortality (HR 0.31).

Conclusion:

We concluded that for many patients who have experience warfarin-associated GIB, the benefits of resuming anticoagulant therapy outweighs the risks. Qureshi et al. (2014) stratified the duration of warfarin interruption, and conclude that restarting warfarin after 7 days was not associated with increased risk of GIB, but was associated with decreased risk of all-cause mortality and thromboembolism compared with resuming after 30 days of interruption. It has been demonstrated by Witt et al. (2012) that resuming warfarin is best done between days 7 to 90 to decrease TBE and all-cause mortality. Based on these two studies, the overall recommendation is to restart warfarin between days 7 to 90 to reduce not only all-cause mortality, but also risk of TBE.

Limitations: For this topic to be relevant to current practice, using warfarin as the only anticoagulant is limiting, since there are other newer anticoagulants, such as Apixaban (Eliquis) and Dabigitran (Pradaxa) that need to be studied.

Future studies need not only address other types of anticoagulation, but also all-cause mor-
tality, since is one of the most important outcomes of restarted warfarin after GIB. Randomized controlled trials are needed in this area, since most of the current studies involve cohort studies.

References:

Table 1: Summary of key research findings.

<table>
<thead>
<tr>
<th>Reference number</th>
<th>Objective</th>
<th>Type of Study</th>
<th>Number of Subjects</th>
<th>Intervention</th>
<th>Outcomes &amp; Statistical Significance</th>
</tr>
</thead>
</table>
| 7                | Determine whether warfarin treatment prevents TBE & has all-cause mortality benefit over subjects not restarted on warfarin. | retrospective cohort study | 1329 mean age 76 years old 45% women | Restarting warfarin | Decision to restart warfarin after an episode of major GIB is associated with:  
Mortality: Decreased all-cause mortality (HR 0.67, 95% CI 0.56-0.81)  
TBE: Decreased TBE (HR 0.71, 95% CI 0.54-0.93)  
Recurrent GIB: No increased risk of GIB (HR 1.18, 95% CI 0.94-1.10).  
Restart Warfarin: > 7 days. |
| 8                | Determine the incidence of thrombosis, GIB or all-cause mortality and when to restart on warfarin in a 90-day interval following a warfarin associated GIB. | retrospective cohort study | 442 mean age 74.2 years old 49.8 women | Restarting warfarin | Warfarin therapy resumption after GIB was associated with:  
Mortality: Decreased all-cause mortality (HR 0.31, 95% CI 0.15-0.62)  
TBE: Decreased TBE (HR 0.05, 95% CI 0.01-0.58)  
Recurrent GIB: No increased risk of GIB (HR 1.32; 95% CI 0.50-3.57).  
Restart Warfarin: > 7 days, but < 90 days. |

Abbreviations: HR: hazard ratio, CI: confidence interval
Clin IQ 4: In a patient with hypercholesterolemia, does statin use increase the risk of developing new onset diabetes?

**Authors:** Samad Khan MD, Enaame Farrell

**Faculty Mentor:** Masashi Ohira MD, M. Ghazi MD

**Residency Program:** University at Buffalo, Family Medicine Residency Program. ECMC/Clevehill Track

**Answer:** Yes

**Level of Evidence:** A

**Search Terms:** statin therapy, hyperglycemia, new onset Diabetes

**Date Search was conducted:** January 2015

**Inclusion Criteria:** Published systematic reviews/meta-analysis, cohort studies, and clinical research trials looking at the use of statin therapy on development of Diabetes Type 2.

**Exclusion Criteria:** Patients who were on statin therapy for indications other than hyperlipidemia

**Summary of issues:** Recently the centers for disease control and prevention (CDC) released statistical data on the ever-growing epidemic of diabetes which pose a threat to our society. As supported by the CDC the cost in billions of dollars in 2014 is estimated at approximately $245 billion in total medical costs and lost work and wages, in addition, the numbers have been rising steadily to approximately 29 million people in the United States. One out of three Americans are at risk of getting diabetes.

The fight against metabolic syndrome and the early onset of cardiovascular disease, has prompted many clinicians to prescribe statin medications. The use of statins in modern evidence based treatment regimens is known to reduce the relative risk of occurrence of coronary event, cardiovascular disease mortality, non-fatal strokes and all-cause mortality. But what if the treatment implemented to stave off cardiovascular disease is now implicated in causing the early onset of type two diabetes? A recent article found that statin therapy is associated with a slightly increased risk of development of diabetes, but the risk is low both in absolute terms and when compared with the reduction in coronary events. Clinical practice in patients with moderate or high cardiovascular risk or existing cardiovascular disease should not change.

**Summary of the Evidence:**

Recently, there have been clinical trials of statin therapies that have conflicting findings on the risk of developing diabetes mellitus in patients who were given statins. In a 2009 study it was investigated whether Atorvastatin might decrease insulin sensitivity and hyperglycemia in patients with hypercholesterolemia. This was a randomized, single-blind, placebo-controlled parallel study. Atorvastatin 10, 20, 40, and 80mg significantly increased fasting plasma insulin with mean changes of 25%, 42%, 31%, and 45% respectively and hemoglobin A1C levels (2%, 5%, 5%, an 5%, respectively when compared to baseline or placebo. This rise in HgA1c levels were evident after only 2 months of treatment. Atorvastatin also decreased insulin sensitivity (mean changes 1.3,3,4 % respectively). The study’s primary outcome of higher HgA1c levels with Atorvastatin was statistically significant. This was also associated with increased fasting insulin levels, lower adiponectin and reduced insulin sensitivity. This reduction in insulin sensitivity is the strongest evidence for why there is glucose intolerance with Atorvastatin.

In a meta-analysis 2 of published and unpublished trials from 1994 to 2009, study was done on the relationship between statin use and development of diabetes. This analysis included trials with more than 1000 patients only with identical follow-up and duration of more than 1 year. The study showed that in 13 statin trials, out of 91,140 participants, 4278 developed diabetes during a 4 year period. Statin therapy

<table>
<thead>
<tr>
<th>Study name</th>
<th>Total number (n)</th>
<th>New DM Assigned Statin</th>
<th>New DM in Control Group</th>
<th>Level of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASCOT-LLA (Anglo-Scandinavian Cardiac Outcomes Trial -Lipid Lowering Arm) Atorvastatin 10mg or placebo (double blind)</td>
<td>3863</td>
<td>154 (3.9%)</td>
<td>134 (3.5%)</td>
<td>A</td>
</tr>
<tr>
<td>HPS (Heart Protection Study of cholesterol lowering with simvastatin in 20 536 high risk individuals: a randomized placebo controlled trial) Simvastatin 40 mg or placebo (double blind)</td>
<td>7282</td>
<td>335 (4.6%)</td>
<td>293 (4.0%)</td>
<td>A</td>
</tr>
<tr>
<td>JUPITER (Justification for the Use of Statins in Primary Prevention: An Intervention Trial Evaluating Rosuvastatin trial) Rosuvastatin 20mg or placebo (double blind)</td>
<td>8901</td>
<td>270 (3.0%)</td>
<td>216 (2.4%)</td>
<td>A</td>
</tr>
</tbody>
</table>

Table 1 Association between Statin Therapy and New Onset DM (Diabetes Mellitus)
Clin IQ 4 (Contd.)

was associated with a 9% increased risk for incident diabetes (odds ratio [OR] 1.09; 95% CI 1.02–1.17). Meta-regression showed that risk of development of diabetes with statins was highest in trials with older participants, but neither baseline body mass index nor change in LDL-cholesterol concentrations accounted for residual variation in risk. Treatment of 265 (95% CI 150–852) patients with statins for 4 years resulted in one extra case of diabetes. Heterogeneity between the trials was low meaning that most variation was due to chance alone. The results showed that individual assigned statins were at a slight increased risk of diabetes compared with those assigned placebo or standard care. Another explanation for the relationship between statin therapy and incidental diabetes is due to residual confounding factors. Some of these factors may be improved survival with statin therapy, or a change to a healthy lifestyle (i.e., weight loss) after cardiovascular events, which are more likely in placebo than statin groups. Overall survival with statins is very similar to survival with control therapy.

In a meta-analysis of 6 large randomized trials, there have been conflicting results. In the Jupiter trial, more than 17000 adults included in a double blind study using Rosuvastatin and its effect on blood sugar. All of these trials were double blind studies and painted a clinical picture of how statins affect patient’s blood sugars. The major issue in determining whether or not statins raised the risk of diabetes was, what would be done with the results. The fact is statins are mostly well tolerated drugs that significantly reduce cardiovascular events. When stating the ill effects of statin therapy on a subgroup of participants, statin therapy has an associated 9% increased risk for incident Diabetes. The authors go on to say that the risk of development of diabetes with statin drugs was highest in trials with older participants. In the article it is stated that the body mass index as well as LDL-cholesterol concentrations in these participants showed no direct correlation to increasing residual variation in risk. It is known that one in four Americans ages 45 and older are taking a Statin. Based on that assumption, that equates to approximately 32 million Americans currently taking a Statin. With these numbers in mind, the implications can have lasting effects on the common practice of how these relatively safe drugs are prescribed.

Conclusion:

In view of the overwhelming benefit of statin for reduction of cardiac events, the small risk of development of Diabetes is outweighed by cardiovascular benefit in most patients. Taking a Statin. With these numbers in mind, the implications can have lasting effects on the common practice of how these relatively safe drugs are prescribed.

References:


Clin IQ 5: In pregnant women at increased risk for preeclampsia, dose low-dose aspirin prevent morbidity and mortality associated with preeclampsia?

**Answer:** Yes

**Level of Evidence:** A

**Search Terms:** Preeclampsia.

Low dose aspirin

**Date search was conducted:** January 2015

**Inclusion Criteria:** Randomized controlled trials and meta-analyses on Aspirin use for pregnant patients with preeclampsia

**Exclusion Criteria:** Non-pregnant females

**Summary of Issues:**

Preeclampsia is a leading cause of maternal death and affects 2-8% of pregnancies throughout the world. The rate of severe preeclampsia continues to rise and perinatal mortality is two times higher in pregnancies affected by preeclampsia. Of all maternal deaths, 12% are related to preeclampsia.

**Authors:** Stacey Shaw-Gugino MD, Sarah Morris MD

**Faculty Mentor:** David Newberger MD

**Residency Program:** SUNY Buffalo Family Medicine, Millard Fillmore Suburban/Amherst Track

**Inclusion Criteria:**

-Participants, statin therapy has an associated 9% increased risk for incident Diabetes.
-When stating the ill effects of statin therapy on a subgroup of participants, statin therapy has an associated 9% increased risk for incident Diabetes.
-Low dose aspirin.
-Summary of Issues:

Preeclampsia is a leading cause of maternal death and affects 2-8% of pregnancies throughout the world. The rate of severe preeclampsia continues to rise and perinatal mortality is two times higher in pregnancies affected by preeclampsia. Of all maternal deaths, 12% are related to preeclampsia.
Preeclampsia is defined as hypertension (blood pressure >140/90) and proteinuria (presence of at least 0.3 grams of protein in 24 hour period) observed during the second half of pregnancy (>20 weeks gestation). Preeclampsia is considered severe when any of the following occur: blood pressure above 160/110, thrombocytopenia, impaired liver function, renal insufficiency, pulmonary edema or cerebral or visual disturbances. Preeclampsia, with or without severe features, can evolve into eclampsia with systemic complications and death. Once preeclampsia develops, the only effective treatment is delivery.

Previous comprehensive systematic reviews and meta-analysis studies have suggested that prophylactic use of low-dose aspirin is associated with a significant reduction in prevalence of severe preeclampsia, fetal growth restriction and preterm birth. These are all placenta-related complications of pregnancy and although the exact etiology of preeclampsia remains unknown, it has been observed that low-dose aspirin may improve maternal and fetal outcomes. One proposed mechanism is that aspirin inhibits thromboxane more than prostacyclin production and protects against vasoconstriction and resulting pathological blood coagulation in the placenta. Another proposed mechanism is based on the concept that preeclampsia is a consequence of impaired trophoblastic invasion of maternal spiral arteries. Low-dose aspirin has been shown to cause improvement of uterine artery blood flow resistance and therefore a greater remodeling and transformation of uterine spiral arteries. The spiral arteries are usually completely developed by 16-18 weeks and therefore the timing of aspirin initiation has been suggested to be a critical factor. Most previous large randomized trials have only evaluated the effect of aspirin given in the second half of pregnancy and therefore further investigation into early initiation (<16 weeks gestation) of low-dose aspirin would be beneficial.

**Summary of Evidence:**

It has been suggested by meta-analyses of randomized studies that prophylactic use of low-dose aspirin initiated at or before week 16 of pregnancy is associated with significant reduction in prevalence of severe preeclampsia, fetal growth restriction & preterm birth. In one such meta-analysis, 42 studies including 27,222 women who had risk factors for preeclampsia were included. These risk factors included: nulliparity, multiple pregnancy, chronic hypertension, cardiovascular or endocrine disease, prior gestational hypertension or FGR, and/or abnormal uterine artery Doppler. All studies examined women who initiated treatment at ≤16 weeks of gestation and at >16 weeks of gestation, and all included a control or placebo group. The outcome of interest was perinatal mortality defined as, fetal death after 16 weeks’ gestation or neonatal death before 28 days of age. Secondary outcomes included preeclampsia, severe preeclampsia, FGR, preterm birth, placental abruption, birth weight & gestational age at delivery. When compared with controls, low-dose aspirin started at ≤16 weeks’ gestation compared with low-dose aspirin started after 16 weeks’ gestation was associated with a greater reduction in perinatal death (P = 0.02), preeclampsia (P <0.01), severe preeclampsia (P <0.01), FGR (P <0.001) and preterm birth (P <0.001). This is in agreement with a second similar meta-analysis which studied the effects of low-dose aspirin started in early pregnancy on incidence of preeclampsia and IUGR. In the second meta-analysis, pregnant women at moderate to high risk of preeclampsia received either aspirin or placebo; these were then analyzed by gestational age at initiation of either aspirin or placebo (≤16 weeks or 16 weeks gestation). 34 randomized controlled trials were included (11,348 women), 12 of those being ≤16 weeks of gestation. Low-dose aspirin initiated at ≤16 weeks was associated with a significant reduction in preeclampsia (RR = 0.47) and IUGR (RR 0.44) whereas aspirin started after 16 weeks was not. Low-dose aspirin initiated ≤16 weeks was also associated with reduction in severity of preeclampsia (RR = 0.47) and IUGR (RR 0.44) whereas aspirin started after 16 weeks was not. Low-dose aspirin initiated ≤16 weeks was also associated with reduction in severe preeclampsia (RR 0.47) and IUGR (RR 0.44) whereas aspirin started after 16 weeks was not.

**Conclusion:**

In conclusion, preeclampsia is a leading cause of maternal death and the prevalence continues to rise. After review of two large meta-analysis studies, we can conclude that in pregnant women, with increased risk for preeclampsia, low-dose aspirin initiated at <16 weeks (when compared with initiation after 16 weeks) is associated with reduction in severity of preeclampsia. However, due to limitations and bias noted above, further larger scale studies are needed before we would change our practice to initiate Aspirin prior to 16 weeks gestation. Early identification of women with risk factors for pre-eclampsia will remain the first crucial step in prevention of pre-eclampsia associated morbidity and mortality.

**References:**


“Further larger scale studies are needed before we would change our practice to initiate Aspirin prior to 16 weeks gestation.”
Clin IQ 6: In patients with nasal polyps, do systemic corticosteroids provide equal or better efficacy than nasal corticosteroid therapy in treating chronic viral rhino-sinusitis?

Authors: Inderjit Bolla, MD, Anitha Kumaaravel, MD  
Faculty Mentor: Priyanka Patnaik MD  
Residency Program: University at Buffalo Family Medicine Buffalo General/ Jefferson Track

Answer: Yes. An initial 2 weeks of oral prednisolone therapy significantly improves polyp size and olfaction in those with Chronic rhino-sinusitis with nasal polyposis (CRSwNP).

Level of Evidence : A

Search Terms: Chronic rhino-sinusitis, corticosteroid therapy, nasal polyposis.

Date Search was Conducted: May 2015.

Inclusion Criteria : Presence on nasendoscopy of bilateral moderate-sized to large nasal polyps according to the Lildholdt scale and at least 2 of anterior or posterior nasal discharge, nasal obstruction, or decreased sense of smell for more than 12 weeks,

Exclusion Criteria: Treatment with an oral corticosteroid in the past 3 months, sinus surgery in the past year, recent upper respiratory tract infection, mechanical nasal airway obstruction of more than 50% due to septal deviation, or pregnancy or lactation.

Summary of Issues:

Chronic rhino-sinusitis accounts for substantial health care expenditures including office visits, antibiotic prescriptions filled, missed work and school days 2. Approximately 20% of patients with chronic rhino-sinusitis have nasal polyposis, which is a common indication for nasal surgery.

There is a high recurrence rate of disease in such patients. According to national surveys, chronic rhino-sinusitis has been a significant chronic health condition affecting more than 31 million patients in the United States each year. Studies looking at initial oral steroid therapy followed by topical steroid therapy seem to suggest greater effectiveness over 6 months than topical steroid therapy alone in decreasing polyp size and improving olfaction in patients referred for specialty care of chronic rhino-sinusitis with at least moderate nasal polyposis (CRSwNP).

Summary of the Evidence:

In 2013, a comprehensive systematic review was done of 30 studies with chronic rhino-sinusitis without polyposis (CRSsNP) and 3 studies on allergic fungal sinusitis. Two retrospective and one prospective study used oral steroids in combination with antibiotics and nasal steroids. The systematic evaluation was done of oral steroid use in CRSwNP, which has not been previously conducted. The objective of this study was to assess evidence on oral steroid therapy in CRSwNP via a literature review. A potential downside to this review is that the authors did not include any randomized control trials or any clinical study that employed oral systemic corticosteroids alone and in those with Chronic Rhinosinusitis with nasal polyps (CRSwNP).

A 2011 trial assessed treating chronic rhino-sinusitis with nasal polyposis (CRSwNP) with oral steroids followed by topical steroids. This Parallel randomized trial studied 60 adults with CRSwNP (moderate to large sized polyps) who were referred by primary physicians for specialty care. The mean decrease in polyp grade from baseline to 2 weeks was 2.1 units (SD, 1.1) in the prednisolone group and 0.1 unit (SD, 1.0) in the placebo group (mean difference between groups, -1.8 units [95% CI, -2.4 to -1.2 units]; P < 0.001). Patients were randomly assigned in a 1:1 ratio to receive oral prednisolone, 25 mg/day, or placebo for 2 weeks, followed in both groups by fluticasone propionate nasal drops, 400 µg twice daily, for 8 weeks followed by fluticasone propionate nasal spray, 200 µg twice daily, for 18 weeks. Initial oral steroid therapy followed by topical steroid therapy seems to be more effective over 6 months than topical steroid therapy alone in decreasing polyp size and improving olfaction in patients referred for specialty care of chronic rhino-sinusitis with at least moderate nasal polyposis. A possible limitation here may be that patients were referred from primary care to a single-center rhinology clinic, which limits the generalizability of results. Serial measurements of surrogates of nasal inflammation (such as nitric oxide or cytokine levels) were not performed.

Conclusion:
Based on our research in literature, we concluded that in patients with CRS with nasal polyposis an...
initial 2-week course of oral prednisolone in a single once daily dose of 25mg can significantly improve polyp size and reduce the burden of symptoms as well as prevent the high relapse rates seen in this population.

This study provides clear strong evidence to guide practitioners on initiation of maintenance therapy in such patients with CRSwNP, a condition that carries a high prevalence rate and significant morbidity in our community.

References:

Algorithm for determining level of evidence for an individual study

Levels of Evidence
A = Consistent level 1 studies
B = Consistent level 2 or 3 studies or extrapolations from level 1 studies
C = Level 4 studies or extrapolations from level 2 or 3 studies
D = Level 5 studies or troubling inconsistent or inconclusive studies of any level