VOLUME 2 | ISSUE 3 | JULY 2012

L|E|C|O|M Point

WELCOME TO LECOM POINT, A DRUG INFORMATION SOURCE THAT IS DIRECT AND TO THE POINT

New Health Info Resources Available

LECOM SOP partners with AHRQ's Effective Healthcare Program

LECOM School of Pharmacy has developed a partnership with the Agency for Healthcare Research and Quality (AHRQ) to allow access to an information resource for healthcare professionals. The Effective Healthcare Program is designed to help providers make evidence-based treatment decisions. Research summaries, reports and reviews are offered to evaluate risks and benefits with various treatment options. The program is focused on comparative-effectiveness research which aims to compare efficacy, risks and benefits of therapy and procedures. Visitors to the website can also suggest research questions and comment on current research topics. Click here to access the site or go to the LECOM web page under Where to Find More Healthcare Information under the Links list on the Affiliates page.

ADA-EASD publishes new diabetes management algorithm

The American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) have combined to offer patient-focused recommendations for Type 2 diabetes management. Previous guidelines have been criticized for being too 'cookbook' but these new recommendations offer more options based on specific patient characteristics. Goals for A1c are relaxed as well, offering options for less stringent glycemic control in patients at risk for hypoglycemia or who are non compliant. Handy charts on medications, treatment suggestions and goal management are also available here.

Feel free to contact us with drug information questions, general questions or comments at cdir@lecom.edu.

FDA Reviews Risk of Cardiotoxicity with Azithromycin

The U.S. Food and Drug Administration (FDA) issued a statement regarding a study recently published in the New England Journal of Medicine (NEJM) that indicates an increased risk of mortality in patients taking azithromycin. Azithromycin is a macrolide antibiotic, related to clarithromycin and erythromycin which have known associations with cardiotoxicity. All macrolides currently carry a warning for the possibility of prolonged Qt intervals during a course of treatment.

This new study published in the May 17, 2012 issue analyzed Tennessee Medicaid records for patients prescribed azithromycin from 1992 to 2006. Patients were age 30 – 74 and generally healthy with no history of life-threatening disease or recent hospitalization.

The primary outcomes measured were cardiovascular and all-cause mortality. Patients receiving azithromycin prescriptions were compared with patients who received prescriptions of amoxicillin/amoxicillin with clavulanate, ciprofloxacin or levofloxacin.

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More than 3.5 million prescriptions were reviewed. Five days of treatment with azithromycin was compared to a ten-day course with other antibiotics and a control group of patients not taking an antibiotic.

Deaths due to cardiovascular reasons occurred in nearly three times the number of patients taking azithromycin as compared to those taking amoxicillin or no antibiotic. Deaths were similar in patients taking amoxicillin or no antibiotic. Total numbers included approximately 30 deaths per 1 million treatment courses in the control group and amoxicillin group with 85.2 deaths per 1 million treatment courses in the azithromycin group. Deaths in patients on azithromycin were determined to be statistically significant with a p value of < 0.001. Sudden cardiac death and mortality due to other cardiac reasons in patients taking azithromycin were similar. Total deaths were nearly twice as high in the azithromycin group with an odds ratio of 1.85 (95% CI 1.25-2.75).

Patients taking ciprofloxacin did not show any difference in mortality as compared to patients taking amoxicillin whereas azithromycin was associated with 3.5 times more deaths than ciprofloxacin. When compared with levofloxacin, there was no significant difference in mortality for azithromycin. Both ciprofloxacin and levofloxacin have been associated with prolongation of the QT interval.

The FDA is reviewing information and has not issued any new warnings for cardiovascular risk during azithromycin use. The benefits of this medication may still outweigh the risks for most patients. This new study indicates only a small absolute risk of mortality of 0.01% with the use of azithromycin when compared with a risk of 0.006% in patients not using antibiotics. This translates into a number needed to harm (NNH) of 21400 where one death would be expected for approximately every 21400 courses of treatment. Until more information is available, consider caution when prescribing azithromycin to patients with known cardiac problems.

Click for References

Reader Question: NSAIDs and fracture healing

Reader Question:

Do NSAIDs delay healing of bone? Do they increase the risk of nonunion of fractures?

Response:

Adina Solis, PharmD Candidate

Prostaglandins play a role in both bone resorption and bone formation. Prostaglandins are potent stimulators of cytokines and growth factors which mediate bone resorption. The inflammatory response to trauma leads to resorption of necrotic tissue and the production of bone forming cells, eventually leading to new bone. Without this primary inflammatory response, bone repair may not completely occur.

Nonsteroidal anti-inflammatory drugs (NSAIDs) decrease inflammation by inhibiting the synthesis of prostaglandins. They are proven to decrease pain and average length of hospital stay, allowing earlier mobilization, decreasing opioid consumption, and increasing patient satisfaction. Because prostaglandins play a role in bone repair, researchers have attempted to prove whether NSAIDs cause delay in fracture healing or an increase in nonunion.

In numerous animal studies, the use of NSAIDs has been shown to impede the healing of fractures. In 1976, Ro et al. compared the effects of indomethacin 2mg/kg/day given to rabbits with femur fractures. The researchers made a closed, standardized fracture of 129 rabbit femurs and randomly assigned the rabbits to either receive indomethacin via stomach tube or placebo. The rabbits were sacrificed at 6, 9, 12, 18, and 24 days after the fracture. The bones of the two groups were compared using mechanical strength testing, radiological examination, and histological examination. Researchers discovered that the treatment group had significantly less mineralization, cartilage, and bone bridging than the placebo group. This effect has been repeated in numerous studies with rats and rabbits, using indomethacin, ibuprofen, and ketorolac.

The question is whether the inhibitory action upon bone healing will be seen in humans. Unfortunately, there are very few quality studies, and of those there are conflicting data. In a randomized, double-blind study by Adolphson et al., there was no effect of piroxicam on bone mineral density or fracture healing. Researchers in this study randomly assigned 42 healthy postmenopausal women with displaced Colles' fractures to either start taking 20 mg oral piroxicam daily within 48 hours of injury or to the placebo group. The fractures were analyzed radiographically initially, after reduction, 11 days, 4 weeks, and 8 weeks post-trauma. Although not significant, patients assigned to the treatment group experienced less bone mineral decrease when compared to placebo. Although this randomized controlled trial showed that NSAIDs may not have contributed to nonunions in humans and may have bone-sparing effects, several retrospective studies have suggested otherwise.

In a retrospective study by Burd et al., patients given indomethacin after the surgical treatment of acetabular fractures developed significantly more nonunions than those who did not receive indomethacin.

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Researchers involved in this study evaluated 112 patients who had open reduction and internal fixation of an acetabular fracture and who were at risk for heterotopic ossification. Of these patients, 36 patients needed no prophylaxis, 38 received focal radiation, and 38 received indomethacin. A total of fifteen patients developed nonunions, but the rate of nonunion in patients receiving indomethacin was significantly higher versus those the who did not (26% v 7%; p = 0.004). In another retrospective study investigating the effects of posterior spinal fusion, patients given ketorolac 60mg IM loading dose followed by 30mg every 6 hours as needed, there was an odds ratio of 4.9 with a dose-dependent relationship between nonunion rates.

Researchers looked at the records of 288 patients who received spinal fusion. Nonunion was identified in five of the 121 patients (4%) who received no NSAID. In contrast, nonunion was identified in 29 of 167 patients (17%) who received ketorolac after surgery, demonstrating an approximately five times greater likelihood of developing nonunion after ketorolac consumption. Unfortunately, because ketorolac was given to patients for pain control, those who requested ketorolac might have been selected preferentially for further surgical exploration, possibly introducing confounding. Finally, in a 2010 meta-analysis of cohort and case-control studies looking at the effect of NSAIDs on bone union, a pooling of all studies showed an increased risk of nonunion with NSAID exposure; however, when only the high quality studies were used, there was no increased risk. Quality of the studies was assessed using the Newcastle-Ottawa Scale. After screening 158 studies for inclusion, researchers used a total of 11 studies for the initial pooling of results which showed odds ratio for nonunion of 3.0 (95% CI 1.6-5.6). However, metaregression showed a significant association between lower study quality and increased reported risk of nonunion (p = 0.0009). When only higher quality spine studies were considered, there was no increased risk of nonunion demonstrated (OR = 2.2, 95% CI 0.8-6.3).

A need still exists for more prospective trials investigating the effects of NSAIDs on bone healing. Although several retrospective cohort and case-control studies have found an association between NSAID use and effects on bone healing, no conclusive, causal relationship has been firmly established. Current evidence is not strong enough to advocate avoiding NSAIDs in patients with fractures.

Click for references

May New Drug Approvals

- Taliglucerase alfa (Elelyso) for treatment of Type 1 Gaucher disease
- Azelastine hydrochloride/fluticasone proprionate (Dymista) nasal spray for seasonal allergic rhinitis
- Clopidogrel generic for Plavix
- Nevirapine generic for Viramune
- Lansoprazole generic OTC for Prevacid 24 hr

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LECOM SCHOOL OF PHARMACY
CENTER FOR DRUG INFORMATION AND RESEARCH

LECOM is a single school of pharmacy operating out of two locations. Consistent with LECOM's core value of creating student-centered education, two distinct learning pathways are offered for the Pharm.D. degree providing students the option of choosing a pathway most suited to their learning needs. In Erie, PA, an accelerated three-year pathway is offered enabling students to complete the Pharm.D degree in three calendar years; in Bradenton, FL, a traditional four-year pathway is offered. Both curricula offer the same spectrum of didactic courses, credit hours, and experiential education and experiences. The full array of supporting services exists at both campuses. Physical facilities, at each campus, are state-of-the art and of sufficient volume to meet all educational and administrative functions.

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