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Continuous Quality Improvement Pre-Conference to NEO

Feb. 10, 2010; Orlando, FL USA
www.neoconference.com

NEO - The Conference for Neonatology

Feb. 11-14, 2010; Orlando, FL USA
www.neoconference.com

Speciality Review in Neonatology/Perinatology 2.0

Feb. 12-16, 2010; Orlando, FL USA
www.pediatrics.com/specialtyreview

Recruitment Ads: Pages 2 and 7

Epocrates....Is It Useful at the Neonatal Bedside?

By Bob Miller, MD, FAAP

Most physicians, including residents and medical students have heard of, and many use, a mobile drug database called Epocrates. The purpose of this review is to evaluate Epocrates as a bedside tool from the perspective of a neonatologist on a busy teaching service.

Epocrates, Inc. was privately founded in 1998 and is currently headquartered in San Mateo, California. According to their website (www.epocrates.com), "Epocrates, Inc. develops clinical information and decision support tools that enable healthcare professionals to find answers more quickly and confidently at the point-of-care," (Epocrates Company Overview, 2009). The company currently employs more than 200 individuals including physicians and pharmacists who continuously review and update clinical content. They proudly state on their website that "more than 900,000 healthcare professionals, including more than one in three U.S. physicians, use Epocrates' innovative mobile and web-based products to help them reduce medical errors, improve patient care and increase productivity," (Epocrates Company Overview, 2009).

Epocrates offers several levels of service for various fees. However, for this review I will focus on the free version called Epocrates Rx. The website describes Epocrates Rx as "free comprehensive handheld drug guide for Palm, Windows Mobile, iPhone, and BlackBerry," (Epocrates Company Overview, 2009). This free version includes a drug guide, formulary information, drug interaction checker, continual free updates, and medical news. Of note, Epocrates also offers other free mobile tools, most of which

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are related to adult medicine, but I will include a discussion about MedMath which provides the user with some common medical equations for use at the point-of-care.

I am using Epocrates on an iPhone 3G. It downloads easily through the iTunes App Store but does take several minutes to update, most likely related to the large database required for the drug guide. The software publisher requires some personal information, such as your date of birth and what medical school you attended, to confirm your status as a physician, and this information can be filled out on the device. Once loaded on the iPhone, it is easy to access by simply touching the Epocrates icon. It loads quickly and is ready to use in just over one second. Updates can be done wirelessly over the

Do you or your colleagues have interesting research results, observations, human interest stories, reports of meetings, etc. that you would like to share with the neonatology community?

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Figure 1. Home Page. Pressing the search bar at the top brings up keyboard so the user can begin searching the drug database.



Figure 2. Drug Specific Tabs. Not all tabs fit on the screen but one can easily scroll through them.



Figure 3. Dosing Calculator Tab. Pressing the circled tab takes the user to the default pediatric dosing calculator.

connection with your service provider, or by syncing with iTunes on your computer.

When you open Epocrates on the iPhone, the initial home page (Figure 1) has a search bar prominently displayed at the top. Immediately below this is a button to "Browse Drugs, Diseases, Labs..." which takes the user to a menu to select: drugs by class, drugs by name, disease by name, disease by system, labs by specimen, etc. Only the drug content is accessible in the free version, the other categories require upgrading to a purchased product.

In the middle of the home page you will find DocAlert Messages (Figure 1). A set of new DocAlert Messages are presented with each update of the drug database. For wireless devices that have a data plan through a service provider, updates occur automatically every couple of days. If you designate your specialty with Epocrates, such as a pediatrician, you will receive timely and topical news alerts for that specialty. If you want a brief synopsis of the DocAlert topic you select "Read More". This provides a 3 to 4 sentence

overview of the topic. If you want additional details, select "Email More Info" and at your next sync, Epocrates will email you a brief of the topic and a reference to the article(s) being discussed. I have been monitoring these topics for the last six weeks to determine how many were pediatric-related. The pediatric specific DocAlert Channel produces about one message per week, although none thus far have specifically touched upon neonatology.

Now to the important stuff....the drugs. From the Epocrates home page you merely have to tap the search bar and the keyboard pops up. You begin typing the name of the drug and the program immediately begins providing a list using the letters typed into the system. When you see the name of the drug you are looking for, simply tap it and a new screen specific to the drug comes up (Figure 2). This screen includes numerous options specific to the drug selected including: Adult dosing, Peds dosing, Black Box Warning, Contraindications/Cautions, Adverse Reactions, Drug Interactions, Safety/monitoring, Pharmacology, Pricing, and Pill Pictures. The last category is labeled "Notes" and allows the

user to enter personal notes about the medication that are saved for later reference if needed.

Of note for the neonatologist, the safety/monitoring information includes pregnancy and lactation information. In terms of the educational aspects of my job, the Pharmacology tab provides data on metabolism, half-life, excretion route, and mechanism of action which I have found useful for bedside teaching.

In an attempt to determine the accuracy of the dosing regimens described in Epocrates, I chose to compare the Epocrates doses with other fairly well accepted drug references used by neonatologists. Table 1 shows a list of commonly used neonatal drugs and the recommended doses provided in the "Neofax" (Young & Mangum, 2009) and "The Harriet Lane Handbook" (Custer & Rau, 2009) alongside the dosing regimens described by Epocrates. As one can tell by looking over the table, the dosing regimens are similar between the different sources, with only slight



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Name	Epocrates	Neofax	Harriet Lane																																																																																																		
Poractant-alfa	Initial Dose 2.5 ml/kg followed by up to 2 subsequent doses of 1.25 ml/kg at 12 hour intervals	Initial Dose 2.5 ml/kg followed by up to 2 subsequent doses of 1.25 ml/kg at 12 hour intervals	Initial Dose 2.5 ml/kg followed by up to 2 subsequent doses of 1.25 ml/kg at 12 hour intervals																																																																																																		
Beractant	100 mg/kg intratracheal q 6 hrs x 1 - 4 doses	4 ml/kg per dose given up to 4 times in the first 48 hours of life, no more frequently than every 6 hours	4 ml/kg per dose given up to 4 times in the first 48 hours of life, no more frequently than every 6 hours																																																																																																		
Caffeine Citrate	Load: 10 to 20 mg/kg Maintenance: 5 mg/kg q 24 hours	Load: 20 to 25 mg/kg Maintenance: 5 to 10 mg/kg q 24 hours	Load: 10 to 20 mg/kg Maintenance: 5 to 10 mg/kg q 24 hours																																																																																																		
Ibuprofen	First dose: 10 mg/kg Second & Third dose: 5 mg/kg q 24 hrs	First dose: 10 mg/kg Second & Third dose: 5 mg/kg	First dose: 10 mg/kg Second & Third dose: 5 mg/kg																																																																																																		
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Table 1. A comparison of dosing regimens between Epocrates, the "Neofax" (Young & Mangum, 2009), and "The Harriet Lane Handbook" (Custer & Rau, 2009).



Figure 4. Default Pediatric Dosing Calculator

variations between the three sources. I found this exercise to be reassuring in that Epocrates provides acceptable dosing regimens for the commonly used neonatal drugs.

Of note, when looking up complex dosing regimens, such as vancomycin, Epocrates provides a dosing calculator in the upper right hand corner (Figure 3). However, when one pushes the button it comes up with a default pediatric dosing calculator (Figure 4). While I can see where this calculator would be useful in the outpatient setting, for suspensions or pills, it has limited usability in the neonatal setting. I would like to see a simplified neonatal dosing calculator which requests the day of life, the post-menstrual age, and the weight, and then Epocrates would select the correct dose and dosing interval based on the information provided by the neonatologist.

Across the bottom of the home screen (Figure 1), there are 5 navigation tabs: Home, Interactions, Pill ID, MedMath, and More. The Home tab is straight forward and returns the user to the home page. The Interactions tab takes you to a screen that allows one to check for potential drug-drug interactions. To test this function, I checked for interactions between gentamicin with indomethacin and

vancomycin with indomethacin, both reported no known or significant interaction. When I checked interactions between gentamicin and vancomycin, Epocrates did report "avoid combo or monitor renal fxn: combo may incr. risk of nephrotoxicity (additive toxicity)". I received the exact same result when checking for interactions between amphotericin with vancomycin or gentamicin.

The Pill ID tab allows one to identify tabs based on shape, color, score, coating, and imprinting on the pill. Epocrates then provides well done full-color pictures that include both sides of the pill and details about the imprinting. While I can see that this would be quite useful in an outpatient setting or in the emergency department when dealing with overdoses, it is of little use to the neonatologist, unless treating pediatric patients as well.

The MedMath tab takes one to a listing of commonly used yet sometimes difficult to recall mathematical formulas such as A-a O2 gradient, Cardiac Output (Fick equation), Creatinine clearance, Fractional Excretion of sodium, etc. All told, my version included approximately 41 equations. Once selected the equation takes you to a fill-in-the-blank screen where you simply input the lab values and hit



Figure 5. Fractional Excretion of Sodium Calculator. Simply fill in the lab values and Epocrates calculates the value of the test. Pressing the circled "i" button take the user to the information page.

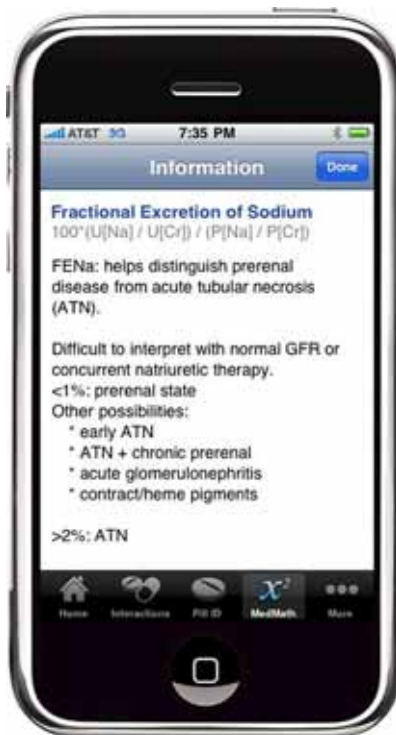


Figure 6. FENA information page which helps user interpret results of the calculation.

Calculate (CA) (Figure 5). In the top right corner there is an information button which when pressed will show you details about the particular test you are doing (Figure 6). While a fair number of the equations are adult specific (cholesterol, for example), I find some quite useful for driving home a teaching point at the bedside. Additionally, some of the formulas are statistic-type tests (such as numbers needed to treat, or post-test probability) which I have found useful at times for discussing articles during rounds and at journal club.

The More tab takes the user to a list of additional resources. The first is the Resource Center that has specific topics reviewed by an appointed expert in the area. The current topics include Alzheimer Disease, Diabetes, Epilepsy, Infection Management, Pain Management, and Venous Thromboembolism. A quick look at these areas reveals that while they are very resource rich, they apply almost exclusively to adult medicine. They are supported by commer-

cial interests whose ads are displayed clearly on the topic specific home page, but Epocrates has confirmed there is no commercial influence in the content. I will say this has been the only place I have seen commercial advertising in the free version of Epocrates.

In summary, I found the free Epocrates Rx to be a good resource for the practicing neonatologist and recommend its use to residents and neonatal nurse practitioners at my institution. The drug database includes dosing regimens comparable to those found in other commonly used neonatal references; however Epocrates presents the information in a more easily accessible manner to the user. I found some of the extra information to be more quickly accessible and easier to incorporate in a teaching environment. Epocrates is developed and marketed to the larger target audience of adult medical providers, but with some focused changes in the neonatal category, I would consider it worth the extra money to purchase an Epocrates premium product with disease content.

"In summary, I found the free Epocrates Rx to be a good resource for the practicing neonatologist and recommend its use to residents and neonatal nurse practitioners at my institution."

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Medical News, Products and Information

Heartburn Drugs Deemed Safe for Fetuses According to Ben-Gurion University Researchers

H2 Blocker drugs, such as Famotidine, Cimetidine and Ranitidine, approved in the US for acid reflux (heartburn), pose no significant risks for the fetus according to a large collaborative cohort study by researchers at Ben-Gurion University of the Negev.

The study published in the *Journal of Clinical Pharmacology* provides significant reassurance for the safety of the fetus when H2 blocker drugs are given to women to relieve acid reflux during pregnancy.

H2 blockers are among the most frequently recommended drugs for acid reflux symptoms of heartburn, regurgitation and trouble swallowing, which are common in pregnant women. The findings are from a large cohort study examining infants born to mothers who were exposed to H2 blockers, particularly Famotidine, during pregnancy. Usually symptoms of acid reflux are more frequent and more severe in the latter months of gestation. It has been estimated that between 30% to 80% of pregnant women are affected.

The study was a collaboration between Ben-Gurion University of the Negev, Soroka University Medical Center and Clalit Health Services -- all in Beer-Sheva, Israel -- along with the Division of Pharmacology, Hospital for Sick Children in Toronto, Canada. It was part of the doctoral thesis of Ilan Matok under the supervision of principal investigators epidemiologist Dr. Amalia Levy and pediatrician and clinical pharmacologist Professor Emeritus Rafael Gorodischer. The study was conducted by the three Israeli entities as part of the BeMORE collaboration (Ben-Gurion MotheRisk Obstetric Registry of Exposure). The investigation of the safety of other medications commonly used off-label in pregnancy is an ongoing project of BeMORE investigators in large cohorts of women in Southern Israel.

"Of the vast majority of medications approved for use, there is insufficient data from human studies to determine whether the benefits of therapy exceed the risk to the fetus," according to the pediatrician and clinical pharmacologist, principal investigator Dr. Rafael Gorodischer, Professor Emeritus at Ben-Gurion University of the Negev. "Medicines are approved for use only after there is sufficient scientific evidence demonstrating the drug safety and effectiveness for its intended uses."

The safety of H2 blockers used during the first trimester of pregnancy was investigated by linking a database of medications dispensed over 10 years to all women registered in Clalit Health Services in the Southern District of Israel, with databases containing maternal and infant hospital records, and with therapeutic abortion records of Soroka University Medical Center, during the same period. In the study, 1,148 (or 1.4%) were exposed to H2 blockers during the first trimester of pregnancy of the 84,823 infants born to mothers during the study period.

The rate of major congenital malformations identified in the group that was exposed to H2 blockers during the first trimester was 5.7% (65 of 1,148 infants), as compared with a rate of 5.3% (4,400 of the 83,675 infants of the 84,823 infants born to mothers during the study period were exposed to H2 blockers during the first trimester of pregnancy).

According to principal investigator epidemiologist Dr. Amalia Levy of the BGU Faculty of Health Sciences, and Chairwoman of the BeMORE collaboration, "Exposure to H2 blockers among this group was not associated with significantly increased risks of major congenital malformations. The results were unchanged when therapeutic abortions of exposed fetuses were included in the analysis. Also, infants exposed in utero had no increased risk of perinatal mortality, low birth weight or premature birth."

Journal of Clinical Pharmacology: "The Safety of H2Blockers Use During Pregnancy"(J Clin Pharm OnlineFirst, doi: 10.1177/0091270009350483).

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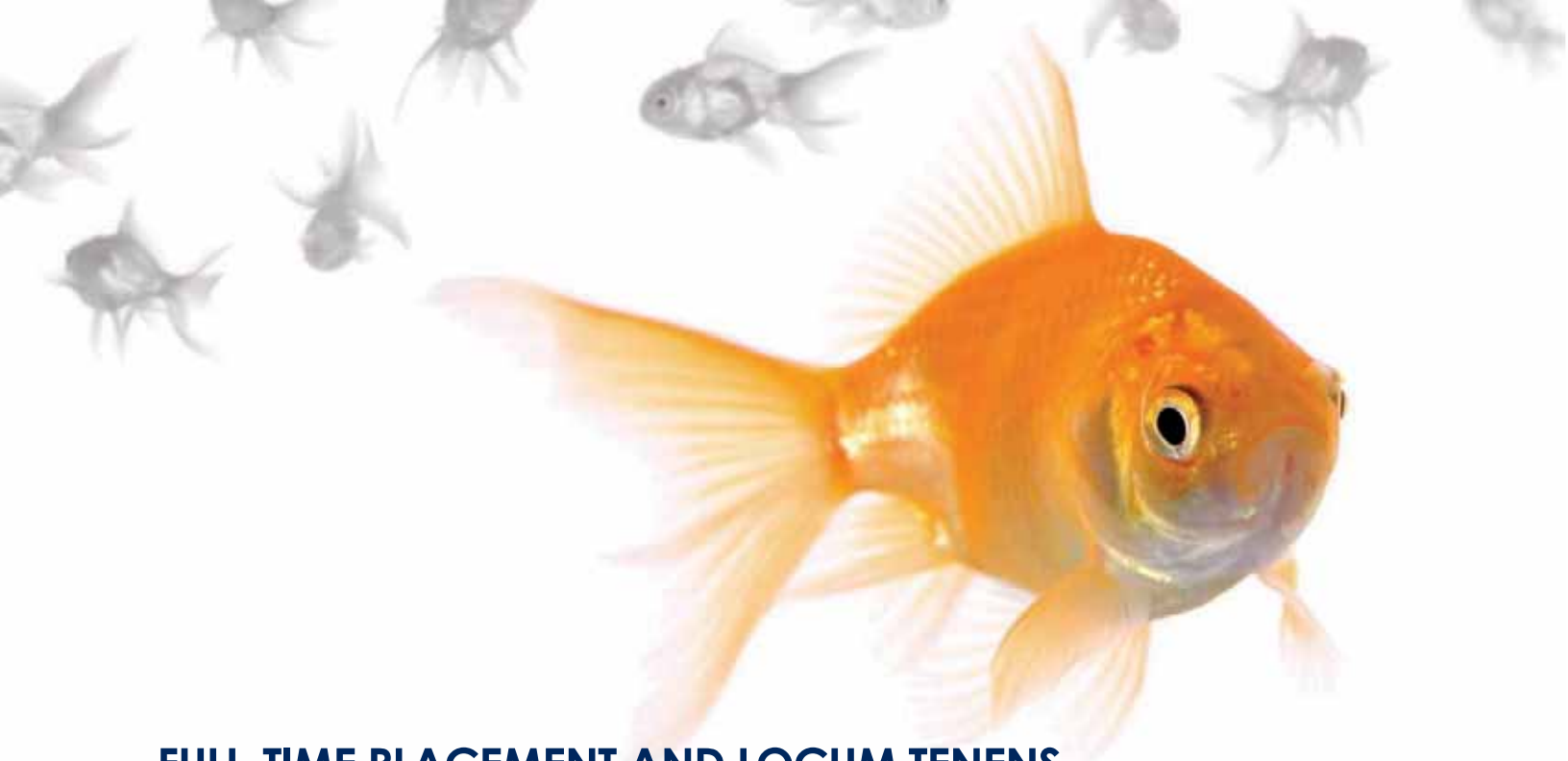
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