About the KDIC

*Our Vision:*
The pharmacist working in Kasr Alainy Drug Information Center provides accurate, unbiased, relevant, evidenced based, and timely information about drugs and drug related problems to assist the centre users in optimizing health outcomes.

*Our mission:*
Pharmacists in Kasr Alainy Drug Information Center are part of the health care team working through the Clinical Pharmacology and Pharmacy committee, to provide useful service and the pharmaceutical information needed for the hospitals’ patients.

---

**In this issue:**
*Paracetamol...pg1*
*Bisphosphonates updates...pg3*
*LABAs update...pg4*
*From our answered questions...pg4,5*

---

**A Drug Overview**

**PARACETAMOL....**

1) Safety Controversy!!!

Paracetamol (Acetaminophen) was considered as one of the safest and most frequently used analgesic and antipyretic drug all over the world. However, many problems and concerns associated with its use appeared by time.

- Paracetamol during pregnancy and risk of male fetus infertility
  A controversial issue suggested by a new European study (2010) about paracetamol and other mild analgesics that women who use these drugs during pregnancy may increase the risk
that their male children will grow up to be infertile. The prospective cohort study included 2297 Danish and Finnish pregnant women reporting on their use of mild analgesics during pregnancy. The testicular position of newborns was assessed by trained pediatricians. The study concluded that there was an association between the timing and the duration of mild analgesic use during pregnancy and the risk of cryptorchidism. These findings were supported by anti-androgenic effects in rat models leading to impaired masculinization. The results suggest that intrauterine exposure to mild analgesics is a risk factor for development of male reproductive disorders. (1)

In a new release from the European Society of Human Reproduction and Embryology that the second trimester seemed to be the most vulnerable time. Use of painkillers during this period doubles the risk. (2)

✧ Paracetamol during pregnancy and Asthma

The conclusion from several clinical studies is:

As paracetamol is the most commonly used analgesic in young children, some evidence suggests that ingestion of paracetamol in early life may cause asthma, eczema, and allergic rhinitis in some children. Exposure to paracetamol may increase respiratory oxidative stress by depleting glutathione in the lungs, thereby enhancing airway inflammation and bronchoconstriction. Decreased glutathione concentrations may favor the development of allergic disease. (3) Given the current global burden of asthma, if paracetamol is a cause of asthma its use needs to be urgently re-evaluated, particularly in the first two years of life during pulmonary development. The frequent use of paracetamol in late pregnancy may increase the risk of wheezing in the offspring, although such an effect could explain only about 1% of the population prevalence of wheezing in early childhood. (4)

However, a prospective birth cohort study (Melbourne Atopy Cohort Study, Published 2010) was conducted to determine if the use of paracetamol in early life is an independent risk factor for childhood asthma. The study concluded that in children with a family history of allergic diseases, no association was found between early paracetamol use and risk of subsequent allergic disease after adjustment for respiratory infections or when paracetamol use was restricted to non-respiratory tract infections. These findings suggest that early paracetamol use does not increase the risk of asthma. (5)

✧ Paracetamol and congenital abnormalities

Single-ingredient-acetaminophen use during the first trimester does not appear to increase the risk of major birth defects and it may decrease the risk of selected malformations when used for a febrile illness. (6)

2) Paracetamol Intravenously

(Available as Perfalgan and the newly approved drug by the FDA Ofirmev)

IV Paracetamol is indicated only for the short-term treatment of moderate pain, especially following surgery, and for the short-term treatment of fever, when administration by IV route is clinically justified and/or when other routes of administration (e.g. oral, rectal) are not possible.
Patients should be switched to an oral analgesic as soon as this route of administration is possible.

**Adult or adolescent dosing advice**

- **Patients weighing less than 50 kg:**
  The dose of IV paracetamol should be 15mg/kg per dose with a minimum of 4 hours between doses, up to a maximum of 4 times a day. The daily dose mustn’t exceed 60mg/kg/day (maximum daily dose not more than 3 gm).

- **Patients with renal insufficiency:**
  In patients with renal impairment and an estimated creatinine clearance less than or equal to 30ml/minute, the interval between IV paracetamol doses should be at least six hours.

Please note that paracetamol should be used with caution and the dose reduced appropriately in patients with hepatocellular insufficiency, chronic alcoholism, chronic malnutrition or dehydration. (7)

**References:**
1) Intrauterine exposure to mild analgesics is a risk factor for development of male reproductive disorders in human and rat by David Møbjerg Kristensen, Ulla Hass, Laurianne Lesné, Grete Lottrup, Pernille Rosenskjold Jacobsen, Christele Desdoits-Lethimonier, Julie Boberg, Jørgen Holm Petersen, Jorma ToppariS, Tina Kold Jensen, Søren Brunak, Niels E. Skakkebaek, Christine Nelleman, Katharina M. Main, Bernard Jégou and Henrik Leffers.
2) Drugs.com
4) “Paracetamol use in pregnancy and wheezing in early childhood” by S O Shaheen, R B Newson, A Sherriff, A J Henderson, J E Heron, P G J Burney, JGolding, the Alspac Study Team).
5) Paracetamol use in early life and asthma: prospective birth cohort study by Adrian J Lowe, research fellow, John B Carlin, director of Clinical Epidemiology and Biostatistics Unit, Catherine M Bennett, associate professor, Clifford S Hosking, paediatric allergist, Katrina J Allen, paediatric gastroenterologist/allergist, Colin F Robertson, respiratory physician, Christine Axelrad, research nurse, Michael J Abramson, deputy head of department, David J Hill, senior consultant allergist, Shyamali C Dharmage, principal research fellow.
6) Acetaminophen use in pregnancy and risk of birth defects: findings from the National Birth Defects Prevention Study. Feldkamp ML, Meyer RE, Krikov S, Botto LD.Division of Medical Genetics, Department of Pediatrics, University of Utah Health Sciences Center, Salt Lake City, Utah, USA.
7) National Health Service.UK

---

**FDA News and Alerts**

Two of 2010 drug-Safety label changes Approved by FDA Center for Drug Evaluation and Research

1- **Bisphosphonates (Osteoporosis Drugs) ...Atypical Fractures Update**

(Available as Fosamax, Actonel, fosavance, miacalcic, bonefos, Evista, aredia, protelos and their generic products)

- FDA is updating the public regarding information previously communicated describing the risk of atypical fractures of the thigh, known as subtrochanteric and diaphyseal femur fractures, in patients who take bisphosphonates for osteoporosis.
• Diaphyseal femur fractures occur in the long part of the thigh bone. These fractures are very uncommon and appear to account for less than 1% of all hip and femur fractures overall. Although it is not clear if bisphosphonates are the cause, these unusual femur fractures have been predominantly reported in patients taking bisphosphonates.

• **Recommendations:** Patients should continue to take their medication unless told to stop by their healthcare professional. FDA recommends that healthcare professionals should discontinue potent antiresorptive medications (including bisphosphonates) in patients who have evidence of a femoral shaft fracture.

---

### 2- Long-Acting Beta Agonists (LABAs)

(Available as Metrovent (Salmeterol), Serevent (Salmeterol), Salmeterol, Foradil (Formeterol), Oxis (Formeterol), Bambec (bambuterol) and their generic products)

✓ FDA notified healthcare professionals and consumers that, due to safety concerns, FDA is requiring a risk management strategy (REMS) and class-labeling changes for all **Long-acting beta2-adrenergic agonists (LABAs)**. These changes are based on FDA’s analyses of studies showing an increased risk of severe exacerbation of asthma symptoms, leading to hospitalizations in pediatric and adult patients as well as death in some patients using LABAs for the treatment of asthma.

The new recommendations in the updated labels state:

• Use of a LABA alone without use of an inhaled corticosteroid, is **contraindicated** in the treatment of asthma.

• LABAs should not be used in patients whose asthma is adequately controlled on low or medium dose inhaled corticosteroids.

• Pediatric and adolescent patients, who require the addition of a LABA to an inhaled corticosteroid, should use a combination product containing both an inhaled corticosteroid and a LABA, to ensure adherence with both medications.

---

### From Our Answered Questions

1-Potassium content in a sachet of Fawarem versus a tablet of slow K:

• **Slow-K:** potassium chloride extended-release tablets USP contain 600 mg of potassium chloride (1,2). Potassium content in one tablet of slow-K contains 314 mg.

• **Fawarem K (KHCO3):** Potassium content in one sachet of Fawarem is 934.44mg (3)

**Conclusion:** The Potassium content of the **THREE** times daily Slow k tablets matches with **ONCE** daily sachet of Fawarem.

**References:**
3. Manufacturer of Fawarem.
2- Stability of Nitroglycerin

(Available as Tridil, Nitronal)

- Dilution of Nitroglycerin injections with dextrose 5% in water or sodium chloride 0.9% in glass containers resulted in physically and chemically stable solutions for 48 hours at room temperature and seven days under refrigeration.(1)
- Non-polyvinyl chloride (Non-PVC) tubing is recommended for administration since 40% to 80% of the calculated final concentration of nitroglycerin can be adsorbed by PVC sources, substantially affecting the actual delivered dose.(2,3)
- For the infusion of NITRONAL® aqueous polyethylene or polytetrafluoroethylene tubings proved to be not contraindicated.(4)

References:
2. Micromedex Database
3. www.uptodate.com
4. Manufacturer of Nitronal® aqueous

To contact us
Internal line: 1260 ☎
External line & Fax: 23687397 ☎
Email: kdic@kasralainy.edu.eg

Advisory Board
Prof. Dr. Magda Zaki
Professor of Pharmacology,
Ex Head of Pharmacology department,
Faculty of medicine, Cairo University.

Dr. Samia Rashid
Ex Head of Pharmacy department,
Technical director of KDIC,
Cairo University Hospitals.

Editorial Board
Chief Editor
Pharmacist Rania Ramzi
Director of KDIC,
Drug information specialist,
Cairo University Hospitals.

Editors
Pharmacist Doaa Bazan
Drug information pharmacist,
Cairo university Hospitals.

Pharmacist Samar Samy
Drug information pharmacist,
Cairo university Hospitals.

Pharmacist Maha Ollaek
Drug information pharmacist,
Cairo university Hospitals.