SFDA SAFTEY COMMUNICATION

Aug 26th , 2012

Saudi Food and Drug Authority (SFDA) PRESS RELEASE- Safety of Codeine Use in Children Following Tonsillectomy and/or Adenoidectomy

The Saudi Food and Drug Authority (SFDA) would like to share some recent information regarding use of codeine in children as post-operative pain killer. On 2009 and 2012, three pediatric deaths and one life threatening case of respiratory depression were reported in the medical literature after taking codeine for relieving pain following tonsillectomy and/or adenoidectomy for obstructive sleep apnea syndrome.[1,2] These cases were for children who have genetic ability to convert codeine into fatal amounts of morphine in the body. The age of those children were between two and five years.

Codeine is converted inside the body to morphine in the liver by a cytochrome P450 2D6 enzyme (CYP2D6). Moreover, codeine is converted to morphine faster and more completely in some people who have DNA variations due to the fact that CYP2D6 is more active. Those patients who have this condition are called “ultra-rapid metabolizers” and they usually have higher amounts of morphine than normal in blood after taking codeine (table 1). Subsequently, the high levels of morphine may lead to breathing difficulty which may be fatal.

Table 1. Prevalence of Ultra-rapid Metabolizers in Different Populations (Adopted from the FDA website[3])

Population	**UM Genotypes/Phenotypes (↑ Activity)**	**Prevalence % (UM/Total n)**
African/Ethiopian	UM (active duplicate genes)	29% (35/122)
African American	UM (three active duplicate genes)	3.4% (3/87) 6.5% (60/919)
Asian	UM (active duplicate genes)	1.2% (5/400) 2%
Caucasian	UM (three active duplicate genes)	3.6% (33/919) 6.5% (18/275)
Greek	CYP2D6*2xN/UM	6.0% (17/283)
Hungarian	UM (active duplicate genes)	1.9%
Northern European	UM (active duplicate genes)	1-2%

UM = ultra-rapid metabolizer; CYP2D6 = cytochrome P450 2D6

In the meantime, SFDA is reviewing all data on this safety concern and will release the results of this review when it finished. SFDA advises all healthcare professionals to prescribe codeine-containing drugs in the lowest effective dose for the shortest period of time and should be used on an as-needed basis not exceeding six doses/day. All healthcare professionals should be aware of the risks of using codeine in children, particularly in those who have undergone tonsillectomy and/or adenoidectomy for obstructive sleep apnea syndrome.

Report Adverse Drug Reactions (ADRs) to the Saudi FDA

The SFDA urges both healthcare professionals and patients to report ADRs resulted from using such a medication and other medications to the SFDA either online, by regular mail or by fax, using the following contact information:

National Pharmacovigilance and Drug Safety Center (NPC)
Saudi Food and Drug Authority-Drug sector
3292 Northern Ring Road
Al Nafal District
Riyadh 13312 – 6288
Kingdom of Saudi Arabia
Toll Free: 8002490000
Tel: 012038222 ext. 2354, 2317
Fax: 012057662
Email: NPC.Drug@sfda.gov.sa
Website: www.sfda.gov.sa/NPC

References

1. Ciszkowski C, Madadi P, Phillips MS, Lauwers AE, Koren G. Codeine, ultrarapid-metabolism genotype, and postoperative death. N Engl J Med 2009;361:827-8.
2. Kelly LE, Rieder M, van den Anker J, Malkin B, Ross C, Neely MN, et al. More codeine fatalities after tonsillectomy in North American children. Pediatrics 2012;129:e1343-7.
3. U.S. Food and Drug Administration. FDA Drug Safety Communication: Codeine use in certain children after tonsillectomy and/or adenoidectomy may lead to rare, but life-threatening adverse events or death. 2112; http://www.fda.gov/Drugs/DrugSafety/ucm313631.htm#data. Accessed on Aug 25th, 2012.