Acute epigastric pain and liver toxicity associated with acetaminophen-codeine use in cholecystectomized patients

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Introduction: Acetaminophen-codeine (AC) fixed association represents the standard medication in the second step of the World Health Organization analgesic ladder and is the most commonly used opioid analgesic for a variety of pain conditions. Side effects of AC consisting of nausea, vomiting, and constipation, may be considered minor when compared to those of NSAIDs. Cholecystectomized patients may present disorders on gastrointestinal tract. In fact, these patients have a high predisposition to develop spasms of the sphincter of Oddi and have an increase of the surface area of Vater's Papilla. This variation may represent an obstruction to the normal biliary-pancreatic flow and the drugs excreted through the bile may remain for a longer time in the liver, especially in the bile duct. Morphine (codeine metabolite) has a biliary excretion.

Aim: To investigate the incidence of acute epigastric pain and the association between this side effect and AC use, from September 2012 to September 2013, we collected data on patients admitted to Prato Hospital Emergency Department (ED) and identified those admitted for acute epigastric pain and hepatic enzymes increase. To quantify the association we calculated Odds Ratios (ORs) and corresponding 95% Confidence Intervals (CIs) using multivariable logistic regression models.

Results: During a period of one year, 76761 patients were admitted to Prato ED and among them 2339 (3%) were diagnosed with acute epigastric pain. OR for AC use was 3.57 (95% CI: 2.64-4.82) compared to non-use. This association was higher in cholecystectomized patients (OR 11.38; 95% CI: 5.06-25.62). In the majority of cases (64.7%), we observed an increase of liver enzymes related to the onset of acute epigastric pain after AC administration.

Conclusions: Although in cholecistectomized patients use of AC is not strictly contraindicated, data from present research quantify the risk of acute epigastric pain and identify the liver toxicity in this population. We could assume that, if the results of this study were confirmed, the use of AC could be considered contraindicated in this specific population. However, further studies are necessary to confirm and extend results here reported.