Therapeutic consequences of dextropropoxyphene withdrawal in France

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BACKGROUND
- Dextropropoxyphene (DXP) is a step-2 opioid analgesic, commonly used in France to treat mild pain.
- Was removed from the French market in March 2011, given the European decision of its withdrawal due to concerns of fatal overdoses and arrhythmias.
- Therapeutic consequences of this withdrawal little investigated in France.

OBJECTIVES
Main objective
- To determine which analgesic drugs have replaced DXP in France after its withdrawal.

Secondary objectives
- To document how DXP withdrawal occurred, in terms of level and kinetics of dispensing.
- To describe the impact of DXP withdrawal on the dispensing level of acetaminophen.

METHODS

Data sources
An extraction of aggregated dispensing data from 2009 to 2012 obtained from claims data from the French Rhône-Alpes Region (6 million inhabitants).

Analyses
- Description of dispensing levels of DXP during withdrawal period, from 2009 to 2011.
- Changes in dispensing levels of the different analgesic molecules studied between 2009 and 2012, in order to encompass DXP withdrawal period in France (March 2011). Time-series analyses approach used.
- Modeling of the impact of DXP withdrawal on dispensing levels of acetaminophen.

RESULTS

DXP dispensing levels during withdrawal period (Fig. 1)
A 2-stage downward trend identified for DXP use:
- Initial drop during summer 2009 (EMA decision),
- 16-month plateau before complete dispensing cessation in spring 2012 (effective withdrawal in France).

Changes in dispensing levels of analgesic molecules after DXP withdrawal (Fig. 2)
- Increase in the annual parts of acetaminophen, codeine and tramadol, in parallel to a decreasing use of DXP.
- DXP mainly replaced by acetaminophen (71% to 79%) and, to a lesser extent by codeine (4% to 7%) and tramadol (8% to 11%).
- Trend & Level test p<0.0001.

Relative changes in dispensing levels over time for main analgesic molecules
- Nearly a 20% increase in acetaminophen dispensing level observed in 2012 compared to 2010 (Fig. 3).
- Higher relative increases observed for tramadol and codeine (Fig. 3), even though their relative weight in analgesic dispensing remain modest (Fig. 2).

Impact of DXP withdrawal on dispensing levels of acetaminophen
- A change in acetaminophen dispensing pattern observed after DXP withdrawal.
- Dispensing levels of acetaminophen can be in part predicted by the withdrawal pattern of DXP (Fig. 4).

CONCLUSION - DISCUSSION
DXP was mainly replaced by acetaminophen and partially by tramadol and codeine. These preliminary results will be confirmed from the national claims data (EGB database, a 1/97th sample of the French population) on an extended study period (2003-2013), and using more elaborated analyses (including prescriber and patient-related data).

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