Evaluating the Impact of Flow Restrictors on Pediatric Exposures to Liquid Single-Ingredient Acetaminophen and Cough/Cold Products

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Project Duration: 9/09/16 – 4/30/18

Regulatory Science Challenge

Each year, approximately 1 million exposures are reported to U.S. poison centers involving children aged ≤5 years.[1] These exposures commonly involve both non-pharmaceutical products like cleaning agents (55%), as well as pharmaceutical products like over-the-counter and prescription medications (45%). Pediatric unintentional exposures most often involve accidental unsupervised ingestions (AUIs). Annually, AUIs involving medications result in more than 70,000 visits to U.S. emergency rooms. AUIs are the most common exposure reason associated with pediatric fatalities reported to poison centers.

Flow restrictors are intended to limit the unintended access of drug products to children and other vulnerable populations. An example of a flow restrictor is an insert that fits into the mouth of a bottle. With a flow restrictor in place, the medicine may be pulled out using a syringe. Despite evidence of their effectiveness, there has been no systematic evaluation of the impact of flow restrictors on the morbidity and mortality associated with AUIs.

Project Description

The proposed study will evaluate the rate of change before and after implementation of flow restrictors among single-ingredient liquid pediatric acetaminophen AUI exposures, as reported to US poison centers. This evaluation will be conducted in the context of product sales and would be performed in terms of both reported exposures and associated outcomes. The calculated rates of change for acetaminophen products will be used to predict the potential impact of implementing flow restrictors on liquid cough/cold medications.

Project Goals

- Evaluate the impact of flow restrictors on exposures to pediatric liquid single-ingredient acetaminophen products as reported to United States poison centers.
- Predict the potential impact of implementing flow restrictors on pediatric liquid cough/cold medications.

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[1] Mowry JB, Spyker DA, Cantilena LR, Jr., McMillan N, Ford M. 2013 Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 31st Annual Report. Clinical Toxicology 2014; 52: 1032-1283.

- Predict the potential impact of implementing flow restrictors on pediatric liquid ibuprofen products.

Project Results

The final report of the researchers to the FDA included the following results:

- The rate of AUI for single ingredient acetaminophen products was significantly lower (325.6 exposures/ million units sold) after flow restrictors were introduced compared to before (507.2 exposures/ million units sold).
- The researchers estimated 19,836 exposures and 115 clinically significant outcomes were prevented.
- The researchers applied the reduction observed in pediatric single-ingredient acetaminophen exposures to estimate the rate of exposures involving pediatric liquid single-ingredient ibuprofen, cough/cold medications, and single-ingredient diphenhydramine products. Based on the researchers' calculations, all exposures would be reduced by an estimated 35.8% and exposures with a clinically significant outcome would be reduced by an estimated 27.2%.
- This work established that flow restrictors were associated with decreases in exposures.

  Note: Flow restrictors were recommended in an August 2015 FDA Guidance (Over the Counter Pediatric Oral Liquid Drug Products Containing Acetaminophen),

Publications

- Paul IM, Reynolds KM, Delva-Clark H, Burnham RI, Green JL. Flow Restrictors and Reduction of Accidental Ingestions of Over-the-Counter Medications. Am J Prev Med. 2019 Jun;56(6):e205-e213. doi: 10.1016/j.amepre.2018.12.015. Epub 2019 Apr 17.