619 | Comparative risk of respiratory depression in patients treated with opioids for non-malignant pain

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Background: Opioid use for non-cancer pain has increased considerably and has been associated with fatal overdoses, the majority being unintentional. The most serious opioid-related adverse event is respiratory depression (RD).

Objectives: To assess the comparative risk of RD in new users of opioids for non-malignant pain using routinely-collected hospital electronic patient records (EPR).

Methods: Opioid users from Salford hospital EPR were identified (2014-2017). Patients with prior malignancy were excluded using ICD-10 codes. Electronic National Early Warning Scores were used to define an RD event as any one of the following: respiratory rate (RR) ≤8/min, RR ≤10/min and O2 saturations<94%, RR≤10/min and altered consciousness, or dispensed naloxone use. Administered medication was categorised as opioid monotherapy or combination of opioids. Primary analysis attributed RD to opioids during a risk window of "on drug+1 day," unless patients switched to another opioid. Patients contributed follow-up time from dispensed drug start date until day after discontinuation, first RD event, death or end of hospital admission. Crude rates/1000 person-years (pyrs) and Cox proportional hazards models were used to examine comparative risk of administered opioids and RD, adjusted using propensity scores derived using inverse probability of treatment weights. Daily dose converted to MME was entered as an interaction term.

Results: 33 341 opioid users were included: 18 325 female (55%); mean age (SD) 53(20) years. There were 515 RD events on treatment. The highest crude rates (95% CI) were on fentanyl (222 [106, 465]), oxycodone (221 [182, 270]) and combination opioids (260 [224, 300]). Compared with codeine the highest unadjusted risk was observed in combination opioid (HR 3.1 [95% CI 2.4, 4.0]) and fentanyl groups (HR 3.5 [95% CI 1.6, 7.7]). Patients experienced RD on opioid doses as low as codeine 30 mg PRN; fentanyl patch 50 mcg/hr per 72 hours; oxycodone 1.25 mg QDS; tramadol 50 mg PRN. In the adjusted model using MME, compared with codeine, the adjusted HR of of other opioids did not reach statistical significance.

Conclusions: Fentanyl, oxycodone, and combination opioids have the highest risk of RD; following adjustment the risk no longer remained significant. The study's strengths include physiological parameters to define RD and dispensed medications to define exposure. Access to this rich, novel data source for pharmacoepidemiological research will deliver an improved understanding of how opioids can affect patient safety.

620 | Prevalence of hospital admissions related to medication in the Netherlands between 2008 and 2013

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Background: The significant impact of hospital admissions related to medication (HARMs) in the Netherlands was shown by the HARM study. A Dutch consensus guideline containing recommendations to reduce HARMs was published in 2009.

Objectives: The aim of this study was to examine time-trends of potential HARMs and its potential preventability in the Netherlands between 2008 and 2013.

Methods: A population-based cohort study was conducted using the Dutch PHARMO Database Network. The QUADRAT computerized pre-selection was used to make a crude identification of admissions with possible HARMs in four samples (2008, 2009, 2011, and 2013). A physician and a pharmacist independently assessed these admissions with respect to causality and preventability using discharge hospital letters and drug dispensing data. Consensus was reached in case of disagreement. The net percentage of potentially preventable medication related hospital admissions for the years 2008 to 2013 was calculated. Results were stratified by age: 18-65 years (age-group 1) and 65 years and older (age-group 2).

Results: Four samples of 467 (2008), 447 (2009), 446 (2011), and 408 (2013) hospital admissions were assessed. The mean prevalence of HARMs in age-group 1 was 2.7% (95% confidence interval [CI]:2.4-3.0%), which was approximately four times lower than in age group 2 with a mean prevalence of 10.2% (95% CI: 9.7-10.7%). The associated preventability was also lower in age-group 1 with 25.1% (18.4-31.8%) and 48.3% (95% CI: 44.8-51.8%) in age-group 2. The majority of these preventable admissions were related to fractures (29.1%), syncope's (17.0%), and gastro-intestinal (GI) complications (13.6%). The prevalence of HARMs in both groups showed a non-significant increase between 2008 and 2013 of 2.4% (95% CI: 1.9-3.0%) and 10.0% (95% CI: 9.0-11.0%) in 2008 to 3.1% (2.7-3.5%) and 10.4% (95% CI: 9.4-11.4%) in 2013.

Conclusions: The number of HARMs in the Netherlands did not decrease between 2008 and 2013 despite efforts to reduce it. Especially in the elderly population, additional measures focusing on the prevention of fractures, syncope's and GI complications are necessary.

621 | Trends in US Emergency Department visits for zolpidem-related adverse events before and after FDA Drug Safety Communications, 2010-2016

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Background: Zolpidem is a prescription medication used to treat insomnia. Based on new data, the Food and Drug Administration (FDA), in two Drug Safety Communications (DSCs) issued in 2013, recommended lowering the bedtime dose of zolpidem, especially when prescribed for women.

Objectives: To describe time trends in emergency department (ED) visits for zolpidem-related adverse events (AEs) in the United States, before and after FDA zolpidem DSCs.

Methods: We used data from an active, nationally representative sample of 59 hospital EDs participating in the National Electronic Injury Surveillance System—Cooperative Adverse Drug Event Surveillance (NEISS-CADES) project to estimate national ED visits due to zolpidem in 2010-2016. We estimated the rates of ED visits using IMS National Prescription Audit data (2010-2016). We employed piecewise (segmented) regression to calculate average change in estimated 6-month rates of ED visits from zolpidem per 10 000 prescriptions dispensed from retail and long-term care pharmacies and used Joinpoint Regression (National Cancer Institute, Bethesda MD) to identify potential inflection points.

Results: We estimate an annual average of 9578 (95% confidence interval [CI], 7108-12 048) ED visits for zolpidem-related AEs during 2010-2016. We observed a decrease in prescription-adjusted estimated rates from 3.0 ED visits per 10 000 prescriptions in 2010 (CI, 2.0-3.9) to 1.4 per 10 000 prescriptions in 2014 (CI, 0.8-2.0); then an increase to 3.2 per 10 000 prescriptions in 2016 (CI, 2.0-4.5). The bestfit regression model of ED visits by 6-month intervals identified a single inflection point in the second half of 2014 (p = 0.018) with a significant decrease of 7.7% biannually from 2010 to 2014 and a non-significant increase of 20.7% biannually from the second half of 2014 through 2016. A model with 2 inflection points did not reach statistical significance (p = 0.07); the first segment decreased 5.6% biannually (2010 to the first half of 2013), the second segment decreased 12.8% biannually (to the second half of 2014), and the third segment increased 24.5% (to the second half of 2016). Females accounted for approximately 60% of zolpidem-related ED visits. Estimated annual rates of ED visits for males and females were similar.

Conclusions: The 2013 zolpidem DSCs and changes in prescribing practices may have either led or contributed to a short-term decline in zolpidem-related AE ED visits in 2014. However, because the decrease in ED visit rates was not sustained, questions remain concerning the long-term impact of the FDA zolpidem DSCs.

622 | Predisposing factors, incidence, and severity assessment of antibiotic-induced hypersensitivityreactions in inpatients of a tertiary care hospital in India

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Background: Antibiotics are extensively used drugs globally including Indian hospital settings and are associated with various Adverse Drug Reactions (ADRs) including dermatologic-hypersensitivity reactions. Antibiotics-induced hypersensitivity reactions constitute nearly 6-10% of all reported ADRs.

Objectives: The aim of this study was to identify and evaluate predisposing factors, incidence, and severity assessment of antibiotic-induced hypersensitivity in hospital admitted patients receiving antibiotics in departments of Medicine, Surgery and Pulmonology of an 1800-bed tertiary-care hospital.

Methods: A prospective observational study was conducted for a period of 9 months in selected inpatient departments of a tertiary care teaching hospital. Hypersensitivity reactions were assessed for its severity, preventability, and predictability causality by using various standard causality assessment scales.

Results: A total of 25 293 patients who had received aminoglycosides (n = 650), penicillin (n = 2207), tetracyclines (n = 5389), quinolones (n = 6464), and cephalosporins (n = 10583) antibiotics in 9 months of study period were observed for hypersensitivity by prescription event monitoring. Sixty-two patients developed antibiotic-induced hypersensitivity, 58% were male. The most common hypersensitivity reactions were rashes (43.5%) followed by itching (20.9%) and moderate severity (89%). Incidence rates found were aminoglycosides (0.46), penicillin (0.4), cephalosporins (0.3), quinolones (0.21), and tetracyclines (0.07). There were cases who had allergic history but no alert-card resulted in same drugs being used again unknowingly and hypersensitivity reactions. Numerous other possible factors for hypersensitivity including age, gender, multiple drugs, genetic, and disease state were observed.

Conclusions: Aminoglycosides, penicillin, and cephalosporins were found to be the most commonly implicated classes of antibiotics associated with hypersensitivity. Alert-cards and medication history databases are needed for better monitoring and care of cases of hypersensitivities.

623 | Risk of cardiovascular events among COPD patients using roflumilast

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