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234. Pharmacokinetics and pharmacodynamics of two doses of oral LSD in healthy subjects

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Objective: Lysergic acid diethylamide (LSD) is used recreationally and in clinical research. The aim of the present study was to characterize the pharmacokinetics and exposure-response relationship of representative oral doses of LSD.
Methods: We conducted two placebo-controlled, double-blind, cross-over studies using oral administration of 100 and 200 µg LSD in 24 and 16 subjects, respectively. Plasma concentrations of LSD, subjective effects and vital signs were repeatedly assessed. Pharmacokinetic parameters were determined using compartmental modeling. Concentration-effect relationships were described using pharmacokinetic-pharmacodynamic modeling.
Results: Geometric mean (95% confidence interval) C_{max} values of 1.3 (1.2–1.9) and 3.1 (2.6–4.0) ng/mL were reached 1.4 and 1.5 hours after administration of 100 and 200 µg LSD, respectively. The plasma half-life was 2.6 hours (2.2–3.4). The subjective effects lasted (mean ± SD) 8.2 ± 2.1 and 11.6 ± 1.7 hours for the 100 and 200 µg LSD doses, respectively. Subjective peak effects were reached 2.8 and 2.5 hours after administration of 100 and 200 µg LSD, respectively. A close relationship was observed between the LSD concentration and subjective response within-subjects, with moderate counter clockwise hysteresis. The half maximal effective concentration EC_{50} values were in the range of 1 ng/mL. No correlations were found between plasma LSD concentrations and its effects across subjects.
Conclusion: The present pharmacokinetic data are important for the interpretation of LSD intoxication. Oral LSD presented dose-proportional pharmacokinetics and first-order elimination up to 12 hours. The effects of LSD were related to changes in plasma concentrations over time, with no evidence of acute tolerance.

235. Relationship between poison center opioid exposure data and mortality rates and National Vital Statistics System mortality rates

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Objective: Over the past 25 years, increased therapeutic use of prescription opioids has led to an epidemic of opioid abuse, diversion, and overdose throughout the USA [1]. Much of the data surrounding deaths due to opioid overdose is provided by the Centers for Disease Control and Prevention (CDC) National Vital Statistics System (NVSS) [2]. However, this data is often delayed and may not be able to discriminate between licit and illicit forms of opioids. Data from poison centers (PCs) are reported in real-time and have more detailed information regarding substances involved. Our objective was to compare opioid exposure and mortality rates between PC and NVSS data.
Methods: Trends over time were evaluated for the Research, Abuse, Diversion and Addiction Related Surveillance (RADARS®) system PC Program exposures and direct deaths and the NVSS multiple cause-of-death mortality files for natural and semisynthetic opioids, synthetic opioids, and methadone from 2003 through 2015. Rates were calculated per population, and Pearson correlation coefficients were calculated comparing PC with NVSS rates.
Results: PC exposure and mortality rates peaked for natural and semisynthetic opioids in 2010 (15.58 and 0.68 per 100,000, respectively), synthetic opioids in 2010 (1.66, 0.01), and methadone in 2007 (1.46, 0.02). NVSS mortality rates peaked for natural and semisynthetic opioids in 2014 (3.81 per 100,000), synthetic opioids in 2014 (1.74), and methadone in 2007 (1.83). PC opioid exposure and mortality rates correlated with NVSS mortality rates for natural and semisynthetic opioids ($r = 0.83$, $r = 0.67$) and methadone ($r = 0.83$, $r = 0.47$). These rates also correlated well for synthetic opioids through 2014 ($r = 0.83$, $r = 0.61$) but diverged from 2012 to 2014 ($r = 0.64$, $r = 0.14$).
Conclusion: Trends in PC opioid exposure and mortality rates track well with trends in NVSS mortality rates, however PC data may be more timely and better able to discriminate between specific types of opioids and specific products. The time frame where the synthetic opioid mortality rates diverged drastically from 2012 through 2014 coincides with the marked increase in illicit fentanyl abuse. NVSS data is unable to differentiate between illicit fentanyl and prescription fentanyl, and likely overestimates the mortality rate associated with prescription synthetic opioids compared to PC data.

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236. Tramadol poisoning in the intensive care unit: clinical presentation and prognostic value of plasma tramadol concentration on admission

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Objective: Tramadol poisonings are increasing significantly due to the increase in prescriptions since dextropropoxyphene was withdrawn from the European market in 2011. Tramadol-related analgesic effects are mediated by its antagonist activity on the norepinephrine and serotonin transporters in addition to the