K5 Death Attributed to Intravenous Oxycodone

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The authors will present the first case of death caused by intravenous oxycodone at the Provincial Toxicology Centre.

Oxycodone is a semisynthetic narcotic analgesic derived by chemical modification from codeine. It produces potent euphoria, analgesic and sedative effects, and has a dependence liability similar to morphine.

A 34-year-old Caucasian male was pronounced dead in hospital. A full autopsy was performed approximately 24 hours after death. Autopsy findings included acute bronchitis and bronchiolotis, and recent puncture sites in left arm, pulmonary edema, mucous plugging of small airways, and cerebral edema. Specimens were collected for toxicological analysis.

Blood (central) and urine specimens were initially subjected to a thorough qualitative analysis. Screening was performed for illicit drugs including morphine and cocaine by radioimmunoassay. Basic drugs were screened for by liquid-liquid extraction followed by GC-NPD and GC-MS electron impact detection. Acidic and neutral drugs were screened for by liquid-liquid extraction followed by HPLC-DAD. Volatiles were assayed by GC-FID. Qualitative analysis identified methadone, cocaine/benzoylecoginine (BE), and oxycodone. The methadone concentration was quantitated by GC-NPD and found to be 0.034 mg/L (0.11 umol/L) in blood. Quantitation of cocaine/BE was performed by GC-MS. Neither cocaine or BE were detected in blood, and no cocaine was detected in urine; however, BE was detected in urine at 0.11 mg/L (0.38 umol/L). This suggests remote cocaine useage. The methadone level was considered to be insufficient as the cause of death.

Oxycodone was assayed in biological specimens as follows: briefly, to 1 mL of specimen standards and controls 100 uL of prazepam solution (internal standard, 1.0 ug/L) and 1 mL of saturated sodium carbonate solution was added, and extracted into 5 mL n-butyl chloride. The extract was concentrated under nitrogen, reconstituted with 100 uL of methanol, and 1 IL was injected into an Agilent model 6890 gas chromatograph coupled to a NP Detector using a 30 m HP-5 capillary column (Agilent). Separation was achieved isothermally at 250°C. The concentration was measured by comparison of peak height ratio of the drug to that of prazepam against a standard curve. Since prazepam is not used therapeutically in Canada and extracts efficiently under the above conditions, it was chosen as the internal standard. Linearity was observed from 0.010 mg/L up to 0.50 mg/L. Samples with concentrations exceeding the linearity were diluted.

Elevated concentrations of oxycodone were found in blood 0.27 mg/L (0.86 mmol/L). The usual adult oral dose is 2.5-5 mg as the hydrochloride salt every 6 hours, although patients with moderately severe pain may take 10-30 mg every 4 hours. Published pharmacokinetic studies involving oxycodone show that plasma concentrations are generally less than 0.100 mg/L. For example, the peak plasma concentrations in 12 patients receiving a 10 mg oral dose averaged 0.030 mg/L. There is little reported on the lethal levels of oxycodone in blood when administered intravenously. For oral oxycodone alone, a minimum lethal level of 5.0 mg/L has been suggested, and fatal concentrations involving oxycodone and at least one other depressant drug have been reported at 0.60 mg/L. Although the concentration of oxycodone in this case was lower, it is well known that for other opiates the minimum lethal level can be considerably lower when administered intravenously than when orally administered. The cause of death in this case was ascribed to oxycodone administered by intravenous route.

Oxycodone, Intravenous, Fatality

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