



G111 Toxicology and Pathology of 149- Methadone-Related Deaths

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After attending this presentation, attendees will understand that careful interpretation of methadone related deaths in the presence of concomitant drug intake and pathological changes is very important.

This presentation will impact the forensic science community by illustrating the difficulty of interpreting postmortem methadone blood levels due to the possible interaction with others drugs acting on the QT- interval or on the cytochrome P450, as well as the presence of pathological changes.

Methadone-related deaths are often difficult to interpret, especially in the presence history of chronic drug use, concomitant intoxications and if pathological changes are observed. Historically, the presence of methadone was often considered to be an incidental finding of the postmortem examination, unrelated to the cause of death. It was recently reported that methadone may prolong the QT interval, resulting in torsade de pointes. Sudden deaths with therapeutic levels of this synthetic opioid have been reported. Moreover, clinicians are increasingly aware of interactions between methadone and others drugs that prolong the QT interval or decrease the elimination rate of methadone.

The goal of this study was to evaluate methadone related deaths by dividing them into three groups according to the peripheral blood level of methadone: lower than 200 µg/L, 200 to 1000 µg/L, and higher than 1000 µg/L. The primary purpose of the study was to determine whether differences exist between the presence of illicit drugs, drugs acting on QT interval and drugs metabolised by cytochrome P450. This study also aimed to determine whether there are differences between the cardiac, hepatic and pulmonary pathology of the three groups.

Materials and Methods: Methadone-related cases were reviewed retrospectively. The age of the victims ranged between 17 and 65 years. Most of the cases were male (109 cases). For all cases the complete autopsy, including histological examination and a full toxicological screening, was performed.

Results: The methadone blood levels were lower than 200 µg/L in 37 cases; between 200 and 1000 µg/L in 89 cases; and higher than 1000 µg/L in 23 cases. In the last group methadone was detected in hair for all victims. Hair analysis was performed in 61 cases: 49 cases tested positive for methadone (80.3%) and 39 cases were positive for cocaine. Higher methadone blood levels were observed in men (p -value 0.052) and did not differ significantly by age.

Only in five cases methadone was alone, in 90 cases other drugs metabolised by cytochrome P450 were found, without significant

differences between the three group (p -value 0.81). Illicit drugs were found in 62 cases (p -value 0.29), drugs acting on QT interval in 79 cases (p -value 0.07) and respiratory depressant drugs, mostly benzodiazepines, in 139 cases (p -value 0.38).

Different pathological changes (cardiac, pulmonary, hepatic) were observed in 97 cases (p -value 0.24). Coronary disease was observed in 60.6% of chronic methadone or cocaine abusers.

Discussion: This study illustrates the difficulty of interpreting postmortem methadone blood levels due to the possible interaction with others drugs acting the QT-interval or on the cytochrome P450, as well as the presence of pathological changes. The various interactions between drugs remain unclear and do not appear to be related to the methadone blood level. Genetic variability may exist in the response of sub-group of individuals to the drug and its metabolism, making them more susceptible to an overdose. More postmortem studies should be performed in order to further understand and prevent fatalities which are mostly often observed during substitutive programmes or during illicit intake.

Methadone, QT Interval, Overdose