G95 Methadone in Methadone-Related Deaths and in Impaired Drivers: Comparative Study of Results of Toxicological Analyses

Marc P. Augsburger, PhD, Bugnon 21, Lausanne 1011, SWITZERLAND; Gregory Schmit, MD, Service de Médecine LégaleBelgium, Cliniques Universitaires Saint-Luc Tour Franklin, Brussels 1200, BELGIUM; Sébastien Prat, MD, Service de Médecine Légale, Hôpital Trousseau, Centre Régional Hospitalier Universitaire de Tours, Tours, MB 37000, FRANCE; Patrice Mangin, MD, PhD, Centre Universitaire, Romand de Medecine Legale, Rue du Bugnon 21, Lausanne CH-1011, SWITZERLAND; and Katarzyna Michaud, MD, Centre Universitaire Romand de, Medecine Legale, Rue du Bugnon 21, Lausanne 1005, SWITZERLAND*

After attending this presentation, attendees will learn about postmortem methadone interptatation, that concomitant drug intake is very frequent in methadone-related deaths, and that the drugs most frequently involved are prescription drugs such as benzodiazepine and neuroleptics, which may prolong the QT interval. Drugs acting on central opioid receptors and cocaine are less frequently observed in postmortem cases than in impaired drivers.

This presentation will impact the forensic science community by increasing understanding and interpretation of methadone-related fatalities and showing that there is a need to perform more studies in order to further understanding and prevent methadone fatalities, especially during substitutive programs. Complete toxicological analyses are essential to understand the role of concomitant prescription drugs intoxication.

The goal of this study was to evaluate methadone-related deaths and to determine whether differences exist between the concomitant drugs found during toxicological analyses between methadone-related deaths and impaired drivers under the influence of methadone.

Materials and Methods: Methadone-related cases were reviewed retrospectively on autopsy reports concerning methadone-related deaths performed at the University Centre of Legal Medicine in Lausanne from 2000 to 2010 and on results of toxicological analyses of impaired drivers under the influence of methadone controlled between 2000 and 2007. For postmortem cases, complete autopsies, including histological examination and full toxicological screenings, were performed. The urine was screened for illicit drugs using immunoassays. Comprehensive drug screenings were performed on peripheral blood and urine by Gas Chromatography/Mass Spectrometry (GC/MS). Drug screenings were also performed on peripheral blood by High-Performance Liquid Chromatography coupled with Diode-Array Detection (HPLC-DAD) and by Headspace-Gas Chromatography-Flame Ionization Detection (HS/GC/DIF) for the detection of volatile substances. The confirmation and quantification of drugs was done by GC/MS, GC/MS/MS, or HPLC/MS/MS. Then a comparative study of toxicological analyses between both groups was performed.

Results: A total of 126 postmortem cases were selected (89 men and 37 women). The age of the victims ranged between 15 and 57 years with the mean age of 33 years. In the group of drivers, there were 148 cases (133 men and 15 women) with the age ranging between 19 and 58 years and the mean age of 34 years.

The median methadone blood level was 395µg/L in the postmortem group and 147µg/L in the drivers' group. Methadone was detected in blood without any other substances in one postmortem case and in five driver cases. Benzodiazepines were the most frequently observed concomitant drugs (78% in the postmortem group and 53% in the drivers' group). The distribution of other concomitant drugs was as follows: drugs acting on central opioid receptors (33% in the postmortem group and 57% in the drivers' group), QT-acting drugs (37% in the postmortem group, and 12% in the drivers' group), cocaine (33% in the postmortem group and 52% in the drivers' group), and ethanol (21% in the postmortem group, and 23% in the drivers' group).

Discussion and Conclusion: The determination of whether or not a death is related to methadone is controversial because therapeutic and toxic blood levels overlap and others drugs are frequently found during toxicological postmortem analysis. This study's results are in accordance with current clinical guidelines suggesting a higher risk of sudden death when methadone is administered with other drugs. This study illustrates that methadone-related deaths could be due to the toxic effects of other drugs acting on the central nervous system (respiratory depression) or due to cardiac arrhythmias. More postmortem studies should be performed in order to further understand and prevent methadone fatalities, especially during substitutive programs.

Methadone, Benzodiazepines, Long QT Drugs

 ** Presenting Author*