



Suspected Methadone toxicity: From hospital to autopsy bed

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Objective: High mortality rates have been reported with methadone in both adults and children due to delayed clinical manifestations including respiratory depression and apnoea. We aimed to determine the pattern of toxicity, possible underlying diseases and treatment challenges in patients referred to our centre with early diagnosis of methadone toxicity who later died.

Methods: Medical files of all methadone-poisoned patients who had been admitted to our centre between March 2011 and March 2016, died during the hospital stay and sent for autopsy to Legal Medicine Organization were retrospectively evaluated. Outcomes were defined as time of cardiac or respiratory arrest post methadone ingestion or post naloxone discontinuation, withdrawal or poisoning manifestations post naloxone administration. Cause of death was categorized into toxicity-related and non-toxicity-related. Those who died due to toxicity were divided into three groups: those who died due to pure methadone toxicity, co-ingestions (including methadone), and other toxicities (other opioids± medication/illicit drugs). All toxicity-related deaths were also divided into deaths directly due to opioid-induced respiratory depression versus deaths due to infection, hypoxic brain damage, etc.

Results: In a total of 94 patients, cause of death was pure methadone toxicity in 57 (60.6%). Other causes of death were ischaemic heart disease in ten, co-ingestions (toxicities including methadone) in eight, brain haemorrhage, multi-organ failure and pneumosepsis (each in four), meningitis/encephalitis in three and head trauma and other toxicities (other than methadone but including an opioid, each in two) patients. In ED, 36 patients (38.3%) received median [IQR] naloxone of 0.4 mg [0.4, 0.95] (range, 0.04 to 5.6 mg) while three developed respiratory depression and needed naloxone after hospitalization. Thirty-one patients received naloxone infusion with an average dose of 0.4 [0.25, 0.6] mg/h (range, 0.1 to 2 mg/h) for 11 [8, 17] hours (range, 2 to 114 hours). Four (4.3%) and 26 (27.7%) showed complete and incomplete response to naloxone administration while eight (8.4%) had not responded to antidote therapy, at all. Arrest time was significantly different between pure methadone toxicity vs. other causes ($p = 0.01$). Patients who had died due to co-ingestions and other toxicities were younger ($p = 0.029$) and took more bolus doses of naloxone ($p = 0.042$).



Conclusion: In methadone users, especially in older ages and those with trivial response to naloxone administration, loss of consciousness should not be strictly attributed to methadone toxicity. In such patients, thorough evaluation for other possible causes of loss of consciousness is mandatory.