

## ORAL PRESENTATIONS

### [ID-O#116] Intramuscular versus intravenous naloxone for the reversal of methadone overdose: A randomized clinical trial

Ali Jangjou<sup>a</sup>, Ali-Asghar Kolahi<sup>b</sup>, Mahbobeh Taheri<sup>c</sup>, Niloofar Deravi<sup>d</sup>, Rebecca McDonald<sup>e</sup>, Nicolas Buckley<sup>f</sup> and Hossein Hassanian Moghaddam<sup>g</sup>

<sup>a</sup>Department of Emergency Medicine, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran; <sup>b</sup>Social Determinants of Health Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran; <sup>c</sup>Department of Community Medicine, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran; <sup>d</sup>School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran; <sup>e</sup>Institute of Clinical Medicine, University of Oslo, Oslo, Norway; <sup>f</sup>Clinical Pharmacology, Sydney Pharmacy School, University of Sydney, Sydney, Australia; <sup>g</sup>NEXT STEP Drug and Alcohol Services, Perth, Australia

**Background:** Overdoses from long-acting opioids require ongoing antagonist administration, but the optimal route is not established

**Objective:** To compare the effectiveness of intramuscular (IM) versus intravenous (IV) naloxone in methadone-overdose patients.

**Methods:** A single-center randomized trial was conducted with patients aged 19-59. After basic life support and an initial IV naloxone bolus, patients received either IM or IV naloxone. In the IV group, about two-thirds of the effective dose was administered hourly. In the IM group, the dose was adjusted every 4 hours based on the calculated hourly requirement: 0.4 mg, 0.8 mg, 1.2 mg, or 1.6 mg, depending on the hourly need (<0.2 mg/h, 0.2- 0.4 mg/h, 0.4-0.6 mg/h, or >0.6 mg/h, respectively). Naloxone dosing adjustments were guided by arterial blood gas analysis and consciousness levels. Response rates and withdrawal symptoms were monitored during hospitalization.

**Results:** Of 160 patients with methadone overdose, 10 were excluded due to withdrawal syndrome post-ED naloxone administration. Groups were comparable in sex, drug use history, pre-hospital naloxone use, and overdose profile. The IM group had a lower median [IQR] methadone overdose compared to the IV group (50 [40, 95] vs. 80 [50, 100] mg). In the ED, full response rates to naloxone were similar between the IM (50.8%) and IV (49.2%) groups ( $p>0.05$ ), with the remainder showing partial response. After the first dose, IM naloxone resulted in a significantly lower median [IQR] pulse rate change (-4 [-10, 0.5] vs. 6 [-0.5, 13] in IV). Oxygen saturation and  $pCO_2$  levels were similar between groups. Withdrawal symptoms, assessed by COWS criteria, were significantly higher in the IV group. The IM group required less naloxone (4.1 [2.4, 6.8] vs. 11.0 [4.4, 20.4] mg) during hospitalization.

**Conclusion:** IM and IV naloxone were equally effective for methadone overdose. However, IM naloxone caused fewer withdrawal symptoms and may be more accessible, making it a potential standard treatment in emergency departments.