



## Opioid toxicity: Why has it become a worldwide public health concern?

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**Background:** Opioid analgesics represent the first cause of drug-induced death in the US since several years. In Europe, Asia, Africa and pacific regions, the exact data regarding opioid abuse and related fatalities are lacking, although partial reports confirm that opioids are responsible for a worldwide health issue.

**Methods:** Literature review.

**Results:** Several factors explain the increase in opioid abuse including the development of multiple molecules and formulations by the pharmaceutical companies, the facilitated opioid prescriptions to fight against acute/chronic pain, the underestimation by physicians of the risk of addiction and dependence in the chronically opioid-treated patients and the spread of new opioid-based psychoactive substances on the recreational scene. All these factors have contributed to the enhanced availability of illicit and licit opioids at homes, while common pathways resulting in dependence have been clearly shown to facilitate the cross-use from one to another opioid. Opioid overdose is responsible for central nervous system depression resulting in an almost pathognomonic triad combining consciousness impairment, miosis and bradypnea, at risk of leading to respiratory arrest and asphyxic death. Onset and duration of toxicity are highly variable, depending on the properties, formulation and route of administration of the involved opioid. The opioid dose is not the unique factor that influences the risk of overdose: gene polymorphisms, drug-drug interactions, additional toxicity mechanisms of the new opioids also contribute to explain the individual vulnerability. Naloxone, a competitive antagonist at the opioid receptors, is the first-line antidote available to reverse life-threatening opioid-related neuro-respiratory toxicity. Maintenance treatments are the cornerstone for the management of opiate dependence. Recently take-home intranasal naloxone programs with education of the populations at risk of opioid overdose were developed in the US and some European countries to allow laypersons who might witness an opioid overdose administering the antidote to the opioid-overdosed person, preventing respiratory arrest onset and giving enough time to the paramedics or to the pre-hospital medical services to transport the intoxicated victim to the hospital. Highly encouraging results of these programs were shown to contribute to the prevention of opioid overdose-related death in the communities at risk.



**Conclusions:** Abuse of opioid analgesics in combination with the recent return of heroin and the frightening spread of new opioid-based psychoactive substances represents a major threat that require better international cooperation, law harmonization, and pharmacological approach using maintenance treatments and take-home naloxone.