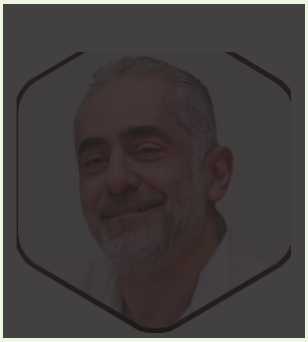
INVITED SPEAKERS



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1. The Fentanyl Overdose Crisis: What Next?

A major crisis of opioid overdose-related fatalities is ongoing in the occidental countries since the end of the 90s. The crisis has progressed in three successive waves, attributed to the neuro-respiratory toxicity of prescription opioid analgesics (1st wave), heroin (2nd wave), and more recently fentanyl and analogues (3rd wave). In 2023, about 120,000 opioid users died in the US, mainly due to fentanyl abuse or misuse. This lecture will analyze the epidemiological findings that may influence the crisis development in the next years. Despite the massive decrease in opioid prescription, deaths related to the recreational use of non-medical opioids have exponentially progressed. Modification of the route of fentanyl abuse/misuse (inhalation and intravenous injection instead of dermal exposure) and co-exposures to stimulant drugs (including cocaine and amphetamine) have highly contributed to the progression of the number of overdose-related fatalities. Interestingly, the number of deaths has far more increased than incidence of opioid use disorder in the American population, in relation to the increased availability of extremely potent synthetic opioid molecules at high risk of dependence and tolerance development. In 2023, the US authorities seized ~78 M fentanyl-lace fake pills and ~12,000 pounds of fentanyl powder, equivalent to ~377 million deadly doses. Similarly, 20 million fake prescription pills were seized in 2023. Today, the danger comes when patients thinking purchasing legitimate prescription medications use pills often containing lethal amounts of illicit drugs. Additional factors might explain that the crisis may not rapidly stop. Use of various new potent synthetic opioids is spreading including the use of 2-benzylbenzimidazoles (e.g., nitazenes), cyclohexylbenzamides (e.g., AH-7921) diphenylethylpiperazines (e.g., MT-45), benzimidazolones (e.g., brorphine), and U-drugs (e.g., U47700). Combination of fentanyl and xylazine, a veterinary a2-adrenergic receptor agonist drug is also spreading under the denomination of “zombie drug”. Xylazine induces sedation and muscle relaxation, accompanied by specific toxicities such as hypotension, bradycardia and ulcerative wounds; however, its exact contribution to the overall neuro-respiratory toxicity remains questioned. In conclusion, opioid overdose epidemic still represents a challenging health concern worldwide and its possible future development remain worrying and threatening.

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2. Pregabalin Misuse in MENA Region Migrants: Dangers of a Neglected Epidemic

Pregabalin, a structural GABA analog, is used to treat neuropathic pain, generalized anxiety disorder and refractory partial epilepsy as an adjunct drug. Despite preclinical studies suggesting a low potential for abuse, signals of misuse/abuse have emerged since its marketing in 2004 following rapidly increased prescriptions, mainly in opioid users in the occidental countries. Life-threatening poisonings with severe or fatal neuro-respiratory depression have been described. Toxicity was attributed to pregabalin combination with an opioid or benzodiazepine. This lecture will focus on pregabalin use disorder as a major but poorly reported issue in the Mena-region and as possibly resulting in a neglected epidemic in the developing countries. In Europe, pregabalin misusers/abusers are mainly 1st-generation young male migrants from the Mena-region. Pregabalin misuse is associated with challenging/ traumatic migration pathways, precarious living conditions, nonstable income, and psychiatric/somatic comorbidities without adequate care. Pregabalin is mainly used to cope with the daily situation, as a self-medication for anxiety-depressive disorders and chronic pain, initiated in home country, and exceptionally used alone. Interestingly, pregabalin was ranked in the 10 top pharmaceuticals involved in the emergency department presentations for recreational drug abuse/ misuse, as shown by Euro-DEN-Plus data. Reports have pointed out its constantly increased use among the adolescents in Europe, generally responsible for minor-to-moderate neurological symptoms on referral (restlessness, confusion, agitation). However, severe cases have been reported with CNS depression, encephalopathy, seizures, heart blocks and withdrawal syndromes. A dose-toxicity relationship exists. Management is supportive with fluids and oxygen but may require mechanical ventilation support. In severely pregabalin-poisoned patients with normal kidney function, EXTRIP workgroup experts suggested against performing extracorporeal treatment in addition to standard care, by contrast to patients with kidney impairment. In an effort to control the epidemic, rescheduling gabapentinoids was accompanied by negligible effects on the prescribing behaviors of the UK GPs whereas pregabalin de-prescribing interventions in Saudi Arabia resulted in a direct drop in pregabalin use with a proportional increase in gabapentin use, supporting all encountered difficulties by the health authorities to control the epidemic. In conclusion, the available literature's data support an ongoing pregabalin misuse/ abuse epidemic in the western countries, reflecting or at least partly in relation to the less reported Mena-region's worrying situation.