Opioid complications

Countering opioid side effects [1].

Opioid analgesics remain the mainstay for managing intractable chronic pain, but their use is limited by detrimental side effects such as analgesic tolerance and hyperalgesia. Calcium-dependent synaptic plasticity is a key determinant in opiates tolerance and hyperalgesia. However, the exact substrates for this calcium-dependent synaptic plasticity in mediating these maladaptive processes are largely unknown. Canonical transient receptor potential 1, 4, and 5 (TRPC1, 4, 5) proteins assemble into heteromultimeric nonselective cation channels with high Ca2+ permeability and influence various neuronal functions. However, whether and how TRPC1/4/5 channels contribute to the development of opiates tolerance and hyperalgesia remains elusive. Here, we show that TRPC1/4/5 channels contribute to the generation of morphine tolerance and hyperalgesia. Chronic morphine exposure leads to the upregulation of TRPC1/4/5 channels in the spinal cord. Spinally expressed TRPC1, TPRC4, and TRPC5 are required for chronic morphine-induced synaptic long-term potentiation (LTP) as well as remodeling of synaptic spines in the dorsal horn, thereby orchestrating functional and structural plasticity during the course of morphine-induced hyperalgesia and tolerance. These effects are attributed to TRPC1/4/5-mediated Ca2+ elevation in the spinal dorsal horn induced by chronic morphine treatment. This study identifies TRPC1/4/5 channels as a promising novel target to prevent unwanted morphine tolerance and hyperalgesia [2].

Intrathecal drug delivery systems (IDDS) utilizing opioids, especially morphine, but also other agents including hydromorphone, fentanyl, tramadol, sufentanil, methadone, baclofen, clonidine, and ziconiotide have been associated with granulation tissue. Non drug delivery devices have also been implicated, including: lumbar shunts, ventricular shunts, and spinal cord stimulators.

Opioid dependence

Opioid dependence

Opioid Use During Pregnancy

Dijkzeul AJCM, Tiemeier H, Volovici V. Opioid Exposure During Pregnancy and Child Cognitive Outcomes-The Importance of Defining the Study Base. JAMA Netw Open. 2022 Jul 1;5(7):e2222431. doi: 10.1001/jamanetworkopen.2022.22431. PMID: 35852807.

1)
Lindsay NM, Scherrer G. Countering opioid side effects. Science. 2019 Sep 20;365(6459):1246-1247. doi: 10.1126/science.aay9345. PubMed PMID: 31604226.
2)
Chu WG, Wang FD, Sun ZC, Ma SB, Wang X, Han WJ, Wang F, Bai ZT, Wu SX, Freichel M, Xie RG, Luo C. TRPC1/4/5 channels contribute to morphine-induced analgesic tolerance and hyperalgesia by

enhancing spinal synaptic potentiation and structural plasticity. FASEB J. 2020 May 2. doi: 10.1096/fj.202000154RR. [Epub ahead of print] PubMed PMID: 32359120.