

ARE PHYSICIANS FULLY AWARE OF THE POTENTIAL TRANSGENERATIONAL AND MULTIGENERATIONAL EFFECTS OF A LARGE OPIOID MISUSE IN THE POPULATION?

To the editor:

In recent years there has been a dramatic increase in medical use and misuse of prescription opioids in many Countries and in particular in the United States. Consequently, epidemiological information have shown a significant rise in opioid-related morbidity and mortality. Although prescription opioids represent a key pharmacological treatment for both opioid addiction and severe pain, clinicians are generally more worried for the opioid acute effects than for the long-term consequences. In particular, while physicians are afraid from overdose morbidity and mortality, they frequently undervalue the potential important transgenerational and multigenerational implications related with a large opioid consumption in the population. Opioid receptors are widely present in the central nervous system cells, but they are also expressed by germline. Particularly, μ -opioid receptor is expressed in sperm cells¹ while μ , δ and κ -opioid receptors are all expressed in oocytes.² The expression of opioids receptors in germline suggest that these receptors exert a role in gamete function, but it is also suggestive of a vulnerability of these cells to the epigenetic effects produced by opioid agonists. Epigenetic changes involving germline could be transmitted to the subsequent generation as transgenerational inheritance. At this regard, human studies have shown that opioids such as methadone and heroin can increase the DNA methylation at the OPRM1 gene promoter in sperm cells and this epigenetic change has been associated with hyperalgesia, tolerance and methadone dose response.^{3,4} On the other hand, opioid can cross the placenta and they can affect fetal and embryonic opioid receptors producing clinical effects including neonatal abstinence syndrome and neurodevelopmental alterations. Animal studies have shown that opioids such as morphine, buprenorphine, methadone, and oxycodone can induce alterations in synaptic plasticity, hippocampal-based learning, attention, motor activity, behavior regulation, and reward control in offspring.⁵

These alterations could be the consequence of a multigenerational phenotypes derived from a direct exposure to the opioids.’ On the whole, despite being considered fundamental medicines for the treatment of opioid addiction and pain, prescription opioids could be responsible for epigenetic consequence in future generations and their large use in the population could promote a rise of some clinical conditions such as drug addiction and neurodevelopmental disorders in next generations. Physicians should be fully aware of the potential transgenerational and multigenerational consequences associated with both prenatal and parental exposure to opioids and they should carefully manage patients treated with opioids evaluating case-by-case the cost /benefit ratio.

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