

Abstract

Introduction: In many studies, an inherently harmful potency of different analgesic agents has been cleared on nervous system. Besides relieving pain, normal functional and integrity of various types of tissues are being affected by chronic use of morphine. Up to now, a lack of comprehensive data exists on mechanistic effect of morphine on CNS with focusing on neural stem cells healthy status and neuro-steroidogenesis.

Methods: The potent adverse effects of morphine (100 μ M) on rat neural stem cells viability, clonogenicity and the proliferation-associated proteins Ki-67 evaluated by MTT assay and flow cytometry in the presence or absence of naloxone (100 μ M) over a time course comprised of 24, 48, 72 h. In addition, the expression of p53, and genes related sex hormone synthesis, namely aromatase and 5-alpha reductase was monitored by real-time PCR.

Results: According to data, we determined an increase in cell survival with a 1.5-fold decrease in Ki-67 and 2 fold in colony formation rate after treatment with morphine. Naloxone blunted the detrimental effects of morphine. Additionally, we notified a 2.5 fold increase in level of p53, 5- α reductase, and aromatase in cells exposed to morphine.

Conclusions: Based on taken results, morphine strongly impaired the healthy status of neural stem cells by the induction of p53 apoptotic-related gene which was coincided concurrently in elevation of aromatase and 5-alpha reductase values. In truth, a linkage of aromatase and 5-alpha reductase genes expression, and modified neurosteroidogenesis along with p53 activity are substantial in morphine-based neural stem cell toxicity.