

## SUN-489: Opioid Epidemic and Related Endocrine Effects: A Systematic Review and Meta-analysis

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**Objective:** The increased use of opioids has resulted in an unprecedented opioid epidemic, with non-negligible numbers of opioid-induced deaths. It is well-known that chronic opioid use affects the activity of the gonadal axis, but the frequency of this and other potential pituitary hormone deficiencies remains unclear. The aim of this systematic review and meta-analysis was to systematically review the effect of exogenous opioids on endocrine function.

**Methods:** Following the PRISMA statement, eight electronic databases were searched in May 2018 for randomized, and observational studies assessing endocrine function in patients using exogenous opioids. A random effects model meta-analysis was performed to obtain weighted proportions of hypogonadism and hypocortisolism with a 95% confidence interval. Due to the heterogeneity in studies, meta-analysis for the effects on other axes, and for subgroups could not be performed, and is systematically reviewed.

**Results:** 52 articles were included with 18.428 patients in total. The patient population consisted mainly of pain patients (n=21 studies), patients on maintenance treatment for opioid addiction (n=9) and healthy volunteers (n=4) with similar opioid effects between these groups. Morphine (n=17) was mostly used, followed by methadone (n=15) and opioid dose defined as morphine equivalent daily dose (MEDD) (n=14) with no difference in effects between groups. Based on 15 studies containing 3.250 patients (% male: 99.5) on chronic opioids, the prevalence of hypogonadism was 65% (95% CI: 57% to 73%, I<sup>2</sup>=91.16%). Based on 5 studies with a total of 207 patients (% male: 57.5), the prevalence of hypocortisolism, based on non-dynamic testing, was 19% (95% CI: 10%, 29%, I<sup>2</sup>=74.21). Results of the systematic review showed an increasing trend for serum prolactin concentrations, and no clear effects on the somatotrophic (n=5) and thyrotropic axes (n=7). Six studies reported that testosterone replacement in opioid induced hypogonadism increased testosterone levels, but clinical effects were not reported.

**Conclusion:** While the evidence on other endocrine axes remains insufficient, hypogonadism occurs in more than half of the male chronic opioid users, and hypocortisolism in approximately a quarter fifth of all patients. Periodical evaluation of endocrine function, especially of the activity of the gonadal and adrenal axes, is mandatory in these patients. More studies are needed on the effects of chronic opioid use on the female gonadal axis and the other endocrine axes, also focusing on experienced symptoms and symptom management.

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