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Review Article

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Abnormal Glycemic Control, Obesity, and Increased Infection Risk in Patients on Chronic Opioid Therapy

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Abstract

Since 2007, the rate of opioids prescribing has steadily increased among physicians more likely to manage acute and chronic pain. Most health care workers are well aware of prescription opioid-related risks of addiction and overdose; however, the recent studies have shown other potential risks such as: abnormal glycemic control, obesity, and increased risk of infections. In this review, we discuss the latest available evidence examining the relationship of prescription opioid use with increased obesity, abnormal glycemic control, and risk of infections.

Introduction & Background

Several preclinical studies have highlighted the associated between chronic opioid exposure and increased sugar intake. While trying to investigate the pathways associated with increased sugar intake, these studies indicated the possible direct affect of opioids at the hypothalamus, paraventricular nucleus, and nucleus accumbens resulting in development of sweet preference [1-5]. These findings gave rise to clinical studies in order to establish the relationship between abnormal glycemic control, obesity and opioid therapy [6-9].

Similarly, decades of preclinical research have found that some opioids have immunosuppressive properties, such as reduced natural killer cell cytotoxicity and impairment of neutrophil chemo taxis [10,11]. These findings led to the three epidemiological studies, which examined the relationship between opioid use and risk of serious infection [12-14].

Review

Abnormal glycemic control, obesity and chronic opioid therapy

One of the latest study assessing the changes in body mass index (BMI) of patients on methadone maintenance therapy was performed by Peles et al. in 2016, consisting of 114 patients. The study concluded that BMI of the patients increased from 22.5 ± 3.8 to 24.4 ± 4.3 ($P < 0.0005$), independently of the methadone dosage. The study also concluded that patients with higher BMI had less knowledge about healthy diet and had higher sweet-foods preference [6].

In a retrospective chart review conducted by Fenn et al. in 2015 for 96 patients enrolled in an outpatient methadone clinic for greater than six months, also showed results consistent with the above-mentioned study. Mean BMI of all patients increased from 27.2 ± 6.8 to 30.1 ± 7.7 kg/m2, in approximately twenty months [7].

Similarly, to assess the preference for sweet-foods in the patients on methadone maintenance treatment, Nolan et al. in 2002, administered a questionnaires to 14 patients and 14 controls with similar demographic characteristics. This study showed that patients on opioid therapy reported higher consumption of sweets, higher eagerness to consume sweet foods, and a wish to consume quantities larger than that desired by controls [8].

From the above-mentioned studies and rest of the literature, it is fair to conclude that heightened taste preference for sweet foods, a slowing of gastric motility, delayed absorption of glucose, and a delayed insulin response all have potential to play a role in development of opioid-induced change in glycemic control [15-17]. However, due to limitations of all these clinical studies, currently there are no specific guidelines regarding this potential risk of opioid-induced change in glycemic control.

As shown by the above-mentioned studies that relationship between opioids and abnormal glycemic control cannot be ignored; however, it is important to notice that most of the patients on methadone maintenance treatment are below the poverty line, which limits their accessibility to healthy food options. This limited accessibility to healthy food is also a possible contributor to abnormal glycemic control, insulin resistance, and obesity. Further studies characterizing this possible relationship specifically in those methadone maintenance treatment patients who have healthy eating habits.

Increased risk of infections and chronic opioid therapy

In the most recent 2018 case-control study by Wiese et al. conducted in a Tennessee Medicaid population, 1,233 patients with laboratory-confirmed invasive pneumococcal disease (IPD) were matched to 24,399 control participants by diagnosis date, age, and country of residence. The purpose of the study was to assess the association between prescribed opioid use and risk of IPD. Opioid use was

measured based on pharmacy prescription records. Invasive pneumococcal disease was defined by the isolation of Streptococcus pneumoniae from a normally sterile site. After accounting for known IPD risk factors (confounders), participants with IPD had greater odds than controls of being current opioid users (adjusted odds ratio [aOR] 1.62, 95% CI 1.36-1.92). Additionally, association between opioid use and IPD was strongest with long-acting opioid use (aOR 1.87, 95% CI 1.24-2.82), with high-potency opioids (aOR 1.72, 95% CI 1.32-2.25), and with higher opioid doses. This is a landmark study in terms of establishing opioid use as an independent risk factor for IPD [12].

In another self-controlled case series analysis conducted by Wiese et al. in 2016, consisted of rheumatoid arthritis patients in Tennessee Medicaid population. Within-person comparison for risk of hospitalization for serious infection during opioid use versus non-opioid use was assessed. After accounting for confounders, the risk of serious infection was higher during the current opioids use compared to nonuse periods (incidence rate ratio [IRR] 1.39, 95% CI 1.19-1.62). Additionally, the risk was highest during periods of long-acting opioid use (IRR 2.01, 95% CI 1.52-2.66), in new users (IRR 2.38, 95% CI 1.65-3.42), and with the use of opioids deemed immunosuppressive (IRR 1.72, 95% CI 1.33-2.23) [13].

The first study epidemiological study evaluating the association between pneumonia and opioid use by Dublin et al. was conducted in 2011, consisting of 1,039 immuno competent adults aged 65 to 94 with community-acquired pneumonia were matched to 2,022 control participants. Results showed that current opioid use was associated with a 38 percent greater risk for community-acquired pneumonia compared with nonuse (adjusted odds ratio [aOR] 1.38, 95% CI 1.08-1.76). Furthermore, similar to the other two above-mentioned studies, the risk was highest for long-acting opioids (aOR 3.43, 95% CI 1.44-8.21) [14].

All of the above mentioned studies suggest that prescription opioids are associated with an increased risk of serious infection. It is also important to note that all of the above mentioned studies showed higher risk with long-acting opioids. Furthermore, the results of these three studies are consistent with the preclinical studies that demonstrate the opioid-related immunosuppressive effects.

Conclusions

At present, it is reasonable for clinicians to be cautious while prescribing opioid therapy to immuno suppressed and medically fragile population. However, further studies are needed to determine whether the risk varies with different types of opioids or treatment regimen, different patient characteristics, or different types of organisms causing the infection.

Similarly, further studies are needed to characterize this potential for opioid-induced change in glycemic control in patients with pain, patients with healthy eating habits, and those with already existing diabetes. Meanwhile, clinicians should still keep this potential risk in mind while prescribing opioids.

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