Association Between Opioid Use and Risk of Erectile Dysfunction: A Systematic Review and Meta-Analysis

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ABSTRACT

Background: Opioid analgesics have been widely used to relieve chronic pain conditions; however, a connection between opioid analgesic administration and increased susceptibility to erectile dysfunction (ED) has been hypothesized.

Aim: To evaluate whether opioid use was a risk factor for ED in a systematic review and meta-analysis.

Methods: The PubMed, Cochrane Library, and Embase databases were searched to identify eligible studies concerning opioid use and risk of ED from inception to April 2017. The association between opioid use and risk of ED was summarized using the relative risk with 95% CI. Sensitivity analyses were conducted to assess potential bias. The Begg and Egger tests were used for publication bias analysis. The GRADE evidence profile tool was used to assess the quality of the evidence.

Outcomes: The overall combined risk estimates for the effect of opioid use on ED were calculated using a random-effects model.

Results: This meta-analysis included 8,829 men (mean age = 41.6 years) from 10 studies, 2,456 of whom received opioid management (duration of intervention = 4 months to 9.5 years). Pooled results demonstrated that the use of opioids was significantly associated with an increased risk of ED (relative risk = 1.96, 95% CI = 1.66–2.32, P < .001). Estimates of the total effects were generally consistent in the sensitivity analysis. No evidence of publication bias was observed. The overall quality of evidence was rated as low.

Clinical Implications: We found that men with opioid use had a significantly increased prevalence of ED, which suggests that patients and clinicians should be aware of the potential role played by opioid administration in the development of ED.

Strengths and Limitations: This is the first meta-analysis performed to describe the relation between opioid use and ED risk based on all available epidemiologic studies. However, the direction of causality between opioid use and risk of ED should be interpreted with caution because most included studies used a cross-sectional design.

Conclusion: Evidence from the included observational studies indicated that men with opioid use had a significantly increased risk of ED. Further randomized controlled trials are still needed to confirm this relation. Zhao S, Deng T, Luo L, et al. Association Between Opioid Use and Risk of Erectile Dysfunction: A Systematic Review and Meta-Analysis. J Sex Med 2017;XX:XXX-XXX.

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Key Words: Opioid; Erectile Dysfunction; Systematic Review; Meta-Analysis

INTRODUCTION

Chronic pain represents a major public health problem worldwide. Prevalence estimates have indicated that chronic pain affects up to 100 million adults in the United States and affects more than 80 million adults in European countries. Another study reported that the age-standardized prevalence of chronic pain conditions was 41% in developing countries. Opioid analgesics, which are derived from the medicinal poppy plant Papaver somniferum, have been widely used for centuries to relieve chronic pain conditions. During the past two decades, the number of prescriptions using opioid

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analgesics for the management of chronic pain increased from 75.5 to 209.5 million in the United States. Although effective, opioid analgesics have been reported to have some common side effects such as dizziness, sedation, constipation, pruritus, nausea, addiction, respiratory depression, urinary retention, and confusion. More importantly, opioids have gradually been recognized to have other less common deleterious adverse events, especially the potential for misuse and abuse, such as hyperalgesia, hypogonadism, and sexual dysfunctions such as erectile dysfunction (ED).

ED, as a public health problem, is an age-related problem affecting a significant proportion of men. Epidemiologic studies have suggested that approximately 10% to 20% of men in the general population have experienced ED, with an overall incidence of 30% and 18.4% in the European Union and the United States, respectively. ED is strongly associated with negative effects on the sexual relationships and quality of life of patients and their partners. Some risk factors contributing to ED have been confirmed by many studies in recent years, such as diabetes mellitus, hypertension, cardiovascular disease, obesity, dyslipidemia, hypogonadism, and lifestyle factors. In addition, the association between medication usage and risk of ED is increasingly recognized by the public. Some previous studies have reported a close connection between opioid analgesic administration and increased susceptibility to ED. Although results were not always consistent, a trend toward a higher incidence of ED in patients using opioids was found (average ED prevalence = 21–52%).

Despite several studies that have explored the association between opioid use and risk of ED, reliable results have been inconsistent and a consensus of opinions has not emerged. To our knowledge, no specific conclusive review or meta-analysis of the association between opioid use and risk of ED has been conducted to date. Therefore, we performed a meta-analysis of the available studies to assess the risk of ED in opioid users.

METHODS

This systematic review and meta-analysis were conducted in accordance to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The PRISMA checklist is presented in eTable 1.

PICOS Question

Based on the patient, intervention, comparison, outcome, and study design (PICOS), the question that guided this review was, does chronic opioid use increase the risk of ED?

Search Strategy and Data Sources

A literature search was conducted using Medline (PubMed), EMBASE, and the Cochrane Library. The timeframe spanned from the inception of these databases to April 2017. We used subject headings and text keywords for the search. The search was restricted to the English language and human participants. The complete search procedure used a combination of MeSH terms and free text words. The search strategy used for Medline, including the MeSH terms and text words, was ((("Analgesics, Opioid"[Mesh]) OR "Opioid"))) AND ((("Erectile Dysfunction"[Mesh]) OR "Sexual Dysfunction, Physiological"[Mesh]) OR “Sexual Dysfunctions, Psychological”[Mesh] OR sexual dysfunction) OR sexual function) OR impotence). We also reviewed the bibliographies of relevant articles to identify additional studies. No restrictions were placed on the publication date of the articles. The literature search, study selection, quality assessment of eligible studies, and data extraction were performed by two authors (S.K.Z. and T.D.) independently. Disagreements were resolved by consensus or consultation with a third author (Z.G.Z.).

Measurement of ED

We included studies in which ED was measured using any of the existing and validated instruments. These included questionnaires, physical examination, and clinical assessment of erectile function in the eligible studies, which consisted of (i) the five-item International Index of Erectile Dysfunction (IIEF-5) questionnaire; (ii) the standard 15-item International Index of Erectile Function (IIEF-15) questionnaire; (iii) the IIEF; and (iv) pertinent history and physical examination.

Study Selection

We included all available epidemiologic evidence on the association between opioid use and risk of ED in men. Subjects in this study were limited to the broad-spectrum population diagnosed with opioid use and ED. The PICOS evidence base consisted of the following combinations: (i) participants: men with ED, impotence, or sexual dysfunction; (ii) interventions: opioid use; (iii) comparisons: compared with the general population; (iv) outcomes: diagnosis of ED and erectile disorders; and (v) study design: all study designs were accepted. Also included were studies on the pertinent subjects that provided relative risk (RR) or hazard ratio estimates (or odds ratios in case-control studies) with 95% CIs or sufficient data to allow the calculation of these effect measurements. The exclusion criteria included the following: (i) the control data were not reported (from a separate control group or the unaffected side); (ii) review or meta-analysis articles; (iii) duplicated or updated data; (iv) meeting abstracts, comments, editorials, letters, case reports, or congress reports; and (v) animal experiments. For multiple publications based on the same study sample, only the most recently published results were included.

Data Extraction and Quality Assessment

Data were extracted using the predetermined selection criteria. In addition, a cross-reference search of eligible articles was conducted to identify studies not found in the computerized search. The following data were extracted from all eligible studies: the first author’s name, year of publication, study regions, the case and control sample sizes, age, study design, methods of ED