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Review Article

Opioid use in gynecologic oncology in the age of the opioid epidemic: Part II – Balancing safety & accessibility

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HIGHLIGHTS

- Nationally, opioid misuse is causing significant morbidity and mortality.
- Historically the problem in cancer pain has been undertreatment, not overtreatment.
- Validated screening tools exist for opioid misuse risk.
- Patients should be counseled about safe opioid storage and disposal.
- We must advocate to have opioid regulations recognize the uniqueness of cancer pain.

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ABSTRACT

As the only oncologists that provide both medical and surgical care, gynecologic oncologists encounter an exceptionally broad range of indications for prescribing opioids in clinical situations ranging from management of acute post-operative pain to chronic cancer-related pain to end-of-life care. While opioids are essential to the practice of gynecologic oncology, they can also have significant side effects and can be misused. Due to the explosive growth of opioid prescriptions and opioid-related overdoses and deaths during the first decade of the 21st century, there has been a recent concerted public health effort to prevent and treat opioid misuse through both legislation and education [1]. The first article in this two part series focused on appropriate use of opioids across clinical settings. This article addresses both the clinical and regulatory aspects of balancing opioid safety and accessibility for patients with gynecologic cancer.

Contents

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1. Introduction

Cancer pain is distinct from non-malignant pain in that opioids remain appropriate first line therapy [2]. The contribution that opioids prescribed to cancer patients has made to the opioid crisis remains unknown. If we are to balance opioid safety and accessibility for our patients at the individual and population level, we must be familiar with the scope of the national problem of opioid misuse, efforts to combat the problem and the potential impact of those efforts on gynecologic oncology patients and providers. Only then will we be able to make informed clinical, educational and advocacy decisions for ourselves and for our patients.

2. Opioid misuse: scope of the problem

2.1. Definitions

The term opioid includes any compound that activates the opioid receptors in the brain to produce a morphine-like effect. The term opiate refers to naturally occurring opioids found in the opium poppy plant, such as morphine and codeine. The term narcotic has varied definitions, both medical and legal. Medically it can refer to any drug that dulls the senses, relieves pain and can induce sleep. Legally it refers to drugs that cannot be legally possessed, sold or transported except for medicinal uses for which a prescription is required; it is sometimes used to refer to any illicit drug. Because of the ambiguity of the term narcotic and its illegal connotations, in this paper we will use the term opioid and we recommend that term for conversations with patients as well.

Opioids can be categorized as synthetic or non-synthetic (naturally-occurring). Synthetic opioids include hydromorphone, oxycodone and fentanyl and non-synthetic opioids include morphine and codeine. Opioids can also be categorized based on production as pharmaceutical or illicit. Pharmaceutical opioids are legally produced and dispensed with a prescription whereas illicit opioids are produced and distributed illegally. For example, fentanyl is an opioid that is available in pharmaceutical form and produced illicitly, and heroin is an opioid that is purely illicitly produced.

Definitions of terms commonly used in discussions of opioid misuse are included in Table 1. The terms abuse and misuse are often used interchangeably to denote inappropriate use of a chemical substance; opioid misuse is considered a broader and less pejorative term and will be used for the remainder of this paper. The term pseudoaddiction refers to a constellation of behaviors that could be construed as medication seeking or concerning for misuse. There is some debate about the validity of pseudoaddiction as a clinical construct and whether its use has contributed to overprescription of opioids [3]. The Diagnostic and Statistical Manual of Mental Disorders (DSM) has also abandoned use of the term "substance abuse," and has begun referring to "substance use disorders" that are graded depending on level of severity (Table 2) [4].

2.2. Opioid misuse in the United States

From 1999 to 2014, >165,000 deaths in the United States were attributed to opioid-related overdoses [9]. The opioids involved in those overdoses have been synthetic and non-synthetic and pharmaceutical and illicit, as described above. Likely due to the greater awareness of opioid misuse and diversion within the medical establishment, there has been a gradual decrease in the number of opioid prescriptions written nationally since 2011 and the opioid overdose death rate appeared to plateau from 2009 to 2013 [1,10]. Unfortunately, 2014 saw a sharp increase in the number of opioid related deaths [9]. While this most recent bump may be primarily related to illicitly produced opioids, pharmaceutically manufactured, provider-prescribed opioids do contribute to the problems of misuse, diversion and opioid-related deaths [11]. The question of the etiology of this crisis is complex and multifactorial, with contributors possibly including liberalization of laws governing prescribing, pain management standards focusing on the right to pain relief, as well as aggressive marketing by the pharmaceutical industry [12,13].

Particularly relevant to gynecologic oncologists, there is emerging evidence that the prescription of opioids following acute pain episodes, such as surgery, can function as an initiator to chronic opioid use. One survey of chronic (>90 days) opioid users found that 27% started opioids

Table 1
Opioid term glossary.

Addiction	Repeated use of a psychoactive substance or substances, to the extent that the user (referred to as an addict) is periodically or chronically intoxicated, shows a compulsion to take the preferred substance (or substances), has great difficulty in voluntarily ceasing or modifying substance use, and exhibits determination to obtain psychoactive substances by almost any means [5].
Abuse	Persistent or sporadic excessive drug use inconsistent with or unrelated to acceptable medical practice; **use of term is discouraged given ambiguity** [5].
Misuse	Use of a substance for a purpose not consistent with legal or medical guidelines [5].
Dependence	An altered physiological state that develops to compensate for persistent drug exposure and that gives rise to a withdrawal syndrome upon cessation of drug exposure [6].
Tolerance	A decrease in response to a drug dose that occurs with continued use. Increased doses of alcohol or other drugs are required to achieve the effects originally produced by lower doses [5].
Diversion	Transfer of a controlled substance from a lawful to an unlawful channel of distribution or use [7]. (For example, a patient's family member using or selling the patient's prescribed opioids would be diversion.)
Pseudoaddiction	Term used to describe constellation of behaviors that may be construed as pain medication-seeking or suggestive of misuse that can result from undertreated pain [8]

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