



Pain Management in the Opioid-Dependent Pregnant Woman

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ABSTRACT

Opioid dependence is an epidemic in the United States, and the percentage of pregnant women who are opioid dependent has increased dramatically in the last decade. Pain management, already a concern for intrapartum and postpartum care, is complicated in the context of opioid dependence. This clinical review surveys the literature on pain management in opioid-dependent pregnant women to summarize current consensus and evidence to guide clinical practice. Points of consensus for pain management in opioid-dependent pregnant women include continual opioid maintenance therapy throughout the pregnancy and the postpartum period; adequate management of acute pain; the contraindication of opioid agonist-antagonists for pain management; and the need for interdisciplinary teams using a multimodal approach to provide optimal care to opioid-dependent pregnant women.

Key Words: opioid dependence, pain management, pregnancy

Opioid use disorders (OUDs), involving both prescription opioids and heroin, are epidemic in the United States.^{1,2} The prevalence of opioid use among pregnant women is increasing concurrently.^{2,3} Krans and Patrick² note that, from 1992 to 2012, the percentage of pregnant women seeking treatment of addiction related to prescription opioid

abuse has risen from 2% to 28%. A study by Maeda et al,⁴ using the Nationwide Inpatient Sample, found a 127% increase in pregnant women who were opioid dependent from 1998 to 2011. The opioid use epidemic has significant implications for how pain is assessed and managed in pregnancy.

Whether stemming from a licit or illicit source, opioid dependence is the frequent result of long-term opioid use. Opioid maintenance therapy (OMT) with buprenorphine or methadone, as opposed to medically managed withdrawal, is the recommended treatment option for women with opioid dependence who become pregnant.^{2,5} While a number of excellent reviews exist regarding general care of the pregnant woman receiving OMT, the discussion of pain management in these articles is limited.^{6–10} The purpose of this review is both to identify the unique challenges in providing adequate pain management to opioid-dependent pregnant women and to identify consensus regarding pain management for these women during pregnancy, labor, and the immediate postpartum period. This article focuses on the care of women who are receiving OMT and does not address issues around active substance abuse in pregnancy.

LITERATURE SEARCH

The Cumulative Index to Nursing and Allied Health Literature (CINAHL), PubMed, EMBASE, Scopus, Web of Science, and PsycINFO were searched using the phrase “pain management in opioid dependent pregnant women”; the search was restricted to English language-only articles, and no date parameters were applied. Using this phrase in the different databases returned 620 results, most of which were in PubMed. After reviewing titles, and eliminating duplicates, 60 articles were kept. On the basis of the abstracts, a further 12 articles were eliminated, resulting in 48 articles that were read. A few additional articles were found through reviewing reference lists. Ultimately, 37 articles, including

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literature reviews, clinical guidelines, and original research (eg, a retrospective case-control study and a qualitative study), were analyzed for this clinical review. Pertinent research with nonpregnant patients was included in the review. Little original research has been conducted on pain management in opioid-dependent pregnant women. A clinical review was conducted; this type of review allows for the inclusion of qualitative studies and review articles, in addition to a range of quantitative research. A systematic review, in contrast, includes only certain kinds of quantitative studies (eg, randomized controlled trials) and may include a meta-analysis in which data from the studies are pooled together.

The organization of the article follows the 2 main themes that emerged from the literature review: the unique challenges to adequately treat pain in pregnant women receiving OMT; and the clinical management of pain in this population. The second theme was divided by the periods of pregnancy (antepartum, intrapartum, and postpartum).

UNIQUE CHALLENGES IN THE PAIN MANAGEMENT OF OPIOID-MAINTAINED PREGNANT WOMEN

Opioid drug tolerance refers to the long-term use of opioids resulting in an increased dosage requirement to achieve the original effect of the drug. Tolerance influences the euphoric, analgesic, respiratory and central nervous system effects of the drug. Because of tolerance, increased doses of opioids may be required to adequately control pain in patients receiving OMT.

Cross-tolerance refers to tolerance for one drug leading to tolerance for another. Eyler¹¹ mentions 2 studies that found no pain relief in nonpregnant patients receiving methadone maintenance therapy (MMT) despite morphine dosing greater than 5 times that of opioid-naïve patients'. The opioid-dependent patients' tolerance for methadone created a cross-tolerance to morphine.¹¹

The ability of providers to meet the opioid-dependent patient's higher opioid dose requirements is often limited by a concern for dose-dependent respiratory and central nervous system effects, such as respiratory depression or decreased consciousness. There is some evidence that opioid-maintained pregnant women may suffer less significant dose-related respiratory and central nervous system effects than opioid-naïve counterparts.¹² The extent of the impact tolerance might have on respiratory and central nervous system depression is difficult to quantify; more research is needed to understand its effects completely.

Hyperalgesia, a pathologically increased sensitivity to pain, is a hallmark of long-term opioid use. Both

Wachholtz et al¹³ and Compton et al¹⁴ investigated the pain experience of nonpregnant opioid-dependent patients. Each of these studies^{13,14} found statistically significant hyperalgesia in opioid-dependent patients compared with opioid-naïve controls. As the control group in the study conducted by Compton et al¹⁴ is small enough ($n = 21$), comparisons between groups need to be made with caution. The experimental arms in the Compton et al¹⁴ study involved heroin-dependent individuals being inducted onto buprenorphine maintenance therapy (BMT) or methadone maintenance therapy (MMT). The study by Wachholtz et al¹³ had 3 experimental arms for participants receiving buprenorphine or methadone or with a history of OMT, respectively. Hyperalgesia was noted in every stage of opioid dependence compared with opioid-naïve participants; no significant difference in hyperalgesia was noted between the BMT or MMT groups.^{13,14} The increased sensitivity and decreased tolerance to pain were noted in participants with a history of OMT, although the tolerance in this group was better than in those being actively maintained, suggesting that the changes wrought by opioid dependence on pain perception persist past cessation of opioid use and may be permanent.¹³

Special consideration for BMT

The high affinity of buprenorphine for μ -receptors (one of the receptors to which opioids bind) allows for minimal displacement of the drug from the receptor by other opioids.¹⁵ In the treatment of addiction, this high affinity is protective against the risk of misuse and overdose.¹⁵ In treating pain, however, the strong bond between buprenorphine and the μ -receptor may lead to inadequate analgesia despite increased dosing of opioids.¹⁵ As a result, cessation of buprenorphine is recommended prior to procedures requiring more than 2 days of acute pain management.^{6,16} Expert opinion regarding managing acute pain in opioid-dependent pregnant women, however, recommends that buprenorphine not be discontinued because of the difficulty restarting maintenance therapy.^{8,9,12} There is some evidence that acute pain in women receiving BMT may be managed adequately in pregnancy with short-acting opioids and, in the postpartum period, with short-acting opioids and nonsteroidal anti-inflammatory drugs (NSAIDs).¹⁵ Fentanyl, which has a higher affinity for μ -receptors than buprenorphine, is another option for pain management in a patient with inadequate analgesia due to the presence of buprenorphine.¹⁷

Stigma and provider misconceptions

Preconceived beliefs and ideas of pregnant women with OUDs have been shown to negatively impact the clinical care of pain.¹⁸ The American Society for Pain

Management released a nursing position statement on pain management in patients with substance use disorders.¹⁶ The society states "...every patient with pain, including those with substance use disorders, has the right to be treated with dignity, respect, and high quality pain assessment and management."^{16(p2)} Women who are opioid dependent frequently have histories of abuse, intimate partner violence, and mental health disorders; they have not been treated with respect or dignity.^{7,16,19} Stigma and misconceptions, common in caring for patients who are opioid dependent, create barriers between providers and opioid-dependent women. Some of the misconceptions around managing pain in this population include (a) OMT provides analgesia; (b) prescribing opioids for acute pain may result in relapse; and (c) opioid-dependent patients reporting acute pain are usually drug seeking.^{12,20} These misconceptions contribute to the undertreatment of chronic and acute pain in opioid-dependent patients. Undertreatment of pain significantly increases the risk of relapse.¹³ The risk of relapse in pregnancy is of the utmost concern, as it poses significant health risks to the mother and the fetus.

CLINICAL MANAGEMENT OF PAIN IN PREGNANT WOMEN RECEIVING OMT

Antepartum

Antepartum pain management in opioid-dependent pregnant women is complicated by a lack of research and guidelines.^{12,16,17,21} The result of this is that most of the recommendations for pain management in opioid-dependent pregnant women are based on expert opinion and a wide array of clinical practices. The discussion of acute pain in opioid-dependent pregnant women is frequently limited to the intrapartum and postpartum periods, but the general tenets are applicable to the antepartum period. This section addresses 5 key aspects of antepartum pain management: pain prevention, common complaints of pregnancy, acute pain, chronic pain, and the pain management plan.

Pain prevention

Pain management for pregnant women receiving OMT begins with prevention. Psychosocial well-being, sleep, and tobacco cessation are core components of a healthy pregnancy that influence the pain experience and pain management of opioid-dependent women.

Mental health disorders, especially depression, anxiety, and posttraumatic stress, are frequently found among women who are opioid dependent.^{20,22,23} Some estimates place the prevalence of mental health conditions among opioid-dependent women at 56% to

73%.²⁰ Mental health disorders may negatively impact the opioid-dependent patient's experience of pain.²⁰ Implementing effective interventions to manage mental health disorders in pregnancy has the potential to improve the pain experience for opioid-dependent women. Nonpharmacologic interventions such as cognitive-behavioral therapy and mindfulness-based stress reduction (MBSR) are recommended as safe and effective first-line interventions for mental health disorders in pregnancy.²⁴ One small randomized-controlled trial investigated MSBR in nonpregnant patients being treated for chronic pain with a history of OUD.²⁵ The authors found that the intervention arm, that is, those who participated in mindfulness-oriented recovery enhancement (a version of MBSR), reported decreased pain intensity, which was sustained at the 3-month follow-up, compared with the control group.²⁵

Sleep is also a critical component of well-being, one that is negatively affected by pregnancy and opioid dependence. Sleep quality is impaired at every stage of opioid use (active use, maintenance therapy, and a history of use with no current medication).²⁶ Poor sleep quality is associated with increased sensitivity to pain and is a risk factor for relapse, both of which may further complicate pain management in an opioid-dependent woman.²⁶ This review did not find any studies related to sleep in opioid-dependent pregnant women.

The majority of opioid-dependent women are nicotine dependent. Nicotine dependence is associated with increased sensitivity to pain.^{10,20} Abrupt tobacco cessation, caused by hospital admission, is associated with a need for higher doses of medication to treat pain.^{20,27} In addition, a cross-tolerance exists between nicotine and morphine; as a result, nicotine users may require higher doses of morphine in the absence of other drug dependence or OMT.²⁷ Nicotine dependence may further complicate pain management in an opioid-dependent pregnant woman. This review did not find any research that explicitly studied the relationship between smoking and pain in pregnancy.

Common complaints of pregnancy

Pregnancy tends to bring with it common complaints that increase women's discomfort. Only one article addressed opioid-related constipation in pregnancy.²⁸ Pregnancy is already a state that tends toward constipation, and this is amplified by the addition of opioids. Li et al²⁸ make the point that traditional treatment of constipation—diet, behavioral modifications, and pharmaceuticals—may not suffice for pregnant women who are opioid dependent and they discuss the use of peripherally acting μ -opioid receptor antagonists

(PAMORAs), such as naloxegol, to treat constipation in this population. At this time, there are no studies addressing the safety and efficacy of PAMORAs among pregnant women. Furthermore, no mention was made in the Li et al²⁸ article as to the effect such a medication might have on someone who is opioid maintained (as opposed to someone suffering constipation as a side effect of a shorter course of opioids).

Nausea is another common complaint in pregnancy. Only one study addressed nausea, and it was in the context of looking at the potential abuse of promethazine in nonpregnant population on methadone maintenance in the San Francisco area.²⁹ Promethazine potentiates opioids, and there is some evidence to suggest that it may be misused in conjunction with opioids.²⁹ Lynch et al²⁹ found that of the 9% of the study population that tested positive for promethazine, only 50% of these had a prescription for the medication. While no study of this kind has been conducted among pregnant women who are opioid dependent, this might be information to consider when treating nausea in this population.

Musculoskeletal complaints are common in pregnancy; however, no articles addressed these complaints in the context of opioid-dependent women who have heightened pain sensitivity and lower pain thresholds. Shah et al³⁰ advocate for a multimodal and multidisciplinary approach to pain management in pregnancy but do not specifically address the needs of women receiving OMT. Commonly recommended nonpharmacologic interventions for musculoskeletal complaints in pregnancy are appropriate for opioid-dependent pregnant women (eg, education, exercise, physical therapy, acupuncture, hydrotherapy, osteopathic manipulation, and massage). In the case of severe musculoskeletal complaints that do not respond to conservative treatment, consultation is warranted.³⁰

Acute pain

Continuation of OMT, both methadone and buprenorphine, is recommended during the management of acute pain in opioid-dependent pregnant women.^{8,9,12} Opioid maintenance therapy medication does not provide analgesia for acute pain. Oliver et al¹⁶ offer recommendations for acute pain management in patients receiving OMT; these recommendations include maximizing nonpharmacologic interventions and nonopioid analgesics. Acute pain that does not respond to the aforementioned interventions may be treated with a limited course of short-acting opioid agonists, such as those noted in Table 1.¹⁶

Higher doses of short-acting opioids may be required because of hyperalgesia, opioid tolerance, and the resulting cross-tolerance.^{9,17} Buprenorphine maintenance

Table 1. Common opioids for pain relief and drugs to avoid in opioid dependent women

Opioids for pain relief: Short-acting opioid agonists
Morphine
Fentanyl
Meperidine
Codeine/acetaminophen
Hydrocodone
Oxycodone
Drugs to avoid: Opioid agonist/antagonists
Butorphanol
Nalbuphine

therapy may pose additional difficulties in acute pain management, as mentioned previously.^{16,17} In treating pain in opioid-dependent pregnant women, it is critical to remember not to use opioid agonist-antagonists, as these may induce opioid withdrawal.

Chronic pain

Evidence-based guidelines and recommendations for managing chronic pain in opioid-dependent pregnant women are not available at this time.^{16,17,21,31} Chronic pain in pregnancy is frequently addressed poorly or left untreated.^{21,32} Neither the review of chronic pain management in pregnancy by Souzdałnitski and Snegovskikh¹⁷ nor the one by Pritham and McKay²¹ addresses chronic pain in women whose pregnancy is complicated by opioid dependence. Pregnancy itself may aggravate some chronic pain conditions, such as low back pain. Ultimately, a multimodal and multidisciplinary approach may be best for adequately managing chronic pain in pregnancy.^{21,33}

The pain management plan

Pain plans have been promoted for pregnant and nonpregnant patients receiving OMT.^{8,12} A pain plan, as seen in Table 2, is created by the patient and the provider (or team) to preemptively address how pain will be managed. Prenatal visits are an ideal time for the woman and the provider to create such a plan for the course of the pregnancy, including labor and postpartum pain management. Upon admission to the hospital, the patient and the provider may review the plan to inform and guide clinical care.

Intrapartum

The lack of a standardized approach to acute pain management in labor has resulted in a wide array of clinical practices and policies.² The treatment of intrapartum pain in women receiving OMT is further complicated by patients' altered pain perception and

Table 2. Opioid dependence in pregnancy pain plan^a*Antepartum*

Continue OMT

Create a pain plan with the patient

Pain prevention strategies

Address mental healthcare needs

Evaluate sleep hygiene and develop plan to improve sleep quality

Support, resources, and progress on smoking cessation

Pain management strategies

Do not use routine OMT dose to treat pain in pregnancy

Maximize nonpharmacologic and nonopioid pain relief options

A short course of opioid agonist medication is acceptable to treat acute pain

If pain is not controlled with short course of opioids a referral to a pain management specialist may be required.

Chronic pain conditions in pregnancy require multidisciplinary approach

Intrapartum and postpartum pain management

Review pain plan with patient

Offer inpatient nicotine replacement therapy

Continue receiving OMT

Verify patient's OMT upon admission for delivery

Establish the patient's desires for pain relief in labor

Do not use patient's routine opioid maintenance dosing to treat peripartum pain

Consider anesthesia consult to address patient's unique pain concerns

Ensure adequate appropriate postpartum pain management

Coordinate continuation of outpatient OMT

Establish all multidisciplinary follow-up appointments prior to discharge

Abbreviation: OMT, opioid maintenance therapy.

^aFrom references 8–10, 12, 16, 20, 22–27, 34, 35.

providers' concerns for the safety of the mother and the fetus. The American Congress of Obstetricians and Gynecologists⁵ summarizes current consensus on intrapartum pain management, including continuing OMT during labor, providing adequate analgesia, and not using agonist-antagonist opioids. There is limited research in opioid-dependent pregnant women to guide practice in the intrapartum period.^{11,31} Only 4 studies—all retrospective and relatively small—examine pain management in opioid-dependent women in labor.^{27,36–38}

Labor pain management for the opioid-maintained woman

Studies by Meyer et al^{37,38} found that women receiving OMT reported adequate control of intrapartum pain with epidural anesthesia. Furthermore, Meyer et al^{37,38} found that there were no differences in reported in-

trapartum pain or in the use of intravenous narcotics or epidurals between the BMT, MMT, or opioid-naïve groups. Höflich et al²⁷ initially found, in retrospective case-control study, that epidural analgesia was used more in the OMT group than in the opioid-naïve group, but this difference disappeared when smoking status was included as a variable. Cassidy and Cyna³⁶ conducted a medical record review and found that, of 67 women with OUD who received anesthesia services, 20 required supplemental anesthesia after epidural placement. Meyer et al,³⁸ in a 2007 study, found that women receiving MMT required more supplemental epidural anesthesia than those in the opioid-naïve control group; the follow-up study in 2010³⁷ lacked sufficient power to make the comparison between the BMT and control groups.

The 2010 Meyer et al³⁷ study and a review by Goodman³⁹ specifically looked at pain management in women receiving BMT. Despite discussion by Jones et al¹⁵ and Souzdanitski and Snegovskikh¹⁷ regarding buprenorphine's "ceiling effect," Meyer et al³⁷ found that adequate pain control in women receiving BMT was achieved with short-acting opioids and epidurals. Some authors have suggested split dosing of BMT during the hospital stay to provide some analgesia, decrease additive opioid requirements, and decrease risk of respiratory and central nervous system depression.^{7,11} This approach has not been studied in the treatment of peripartum pain. At this time, lacking further evidence, intrapartum pain management occurs alongside the continuation of BMT. Difficulties in intrapartum pain management for the woman receiving BMT warrant an anesthesia, pain service, or substance abuse consult to address the issue.

Postpartum

During the postpartum period, pain management for the woman receiving opioids involves adequate analgesia, continuing OMT, and coordinating discharge services. A number of studies suggest that pain management for these women deteriorates after birth.^{34,36–38} Cassidy and Cyna,³⁶ in a retrospective medical record review conducted in Australia, found that 74% of opioid-dependent women undergoing cesarean delivery had inadequate postoperative pain control. The findings of Meyer et al^{37,38} and Jones et al³⁵ align with those of Cassidy and Cyna³⁶; they found that women receiving OMT experience increased pain postpartum compared with opioid-naïve women. Furthermore, Jones et al³⁵ found that maternal pain decreased appropriately over the immediate days postpartum, indicating that the pain reported by opioid-dependent women was not drug-seeking behavior but an indication of worsening pain management. Höflich et al²⁷

were not able to refer to pain scores, but the authors noted differences in how pain was managed in opioid-naïve versus opioid-dependent women postpartum, including significantly more opioids dispensed to the opioid-naïve group post-cesarean delivery. The data suggest a reticence on the part of providers to dispense opioids to women receiving OMT.²⁷ In summary, continued vigilance is needed in assessing and adequately treating postpartum pain for women who are opioid dependent.

In considering how best to manage postpartum pain for opioid-dependent women, 2 reviews noted that increased frequency and higher doses of pain medications may be required because of hyperalgesia and tolerance.^{9,15} Jones et al³⁵ found that postpartum pain in buprenorphine-maintained women was adequately treated with opioids and NSAIDs. Alto and O'Connor⁶ recommend scheduled dosing as opposed to "as needed" in order to better manage pain; in addition, this may allay women's fears of inadequate pain treatment. While a number of options for managing postpartum pain are discussed in the literature, the majority of authors recommend short-acting opioids, intravenous acetaminophen, and NSAIDs, titrating appropriately to oral medications.^{6,7,9,11,35,37,38} Pain management after a cesarean delivery may present additional difficulties; some studies found an increased need for short-acting opioids postoperatively.³⁵⁻³⁸ OMT continues during the postpartum period according to the woman's regular schedule and does not treat the woman's postpartum pain. Nicotine replacement and other adjuvant methods (eg, heating pads, ice packs, sitz baths, and ambulation) may be offered to improve the woman's comfort.⁴⁰

Hospital discharge, including continuity of OMT, discharge pain medications, and follow-up appointments, is a critical part of a pain plan. Coordination among the healthcare team is required to ensure that the woman's OMT will not be disrupted upon leaving the hospital. To discharge any patient receiving OMT without provision for that maintenance is unethical. Jones et al³⁴ mention that adequate discharge pain coverage for opioid-dependent women is typically equivocal to non-opioid-dependent patients. Specific to opioid-dependent women who have had a cesarean delivery, Gopman⁷ recommends prescribing oral opioids tapering by the end of the first week, with an early follow-up appointment. According to Park et al⁹ and Goodman et al,⁴⁰ women are at a high risk of relapse in the postpartum period. There is no evidence that the short-term prescription of opioid analgesia to manage postpartum pain in women receiving OMT promotes relapse.³⁵ In fact, there is evidence that undertreatment of pain is a risk factor for relapse.¹³

DISCUSSION

Despite the need for further research, there is consensus on certain points in the literature.^{18,21,33,41} Women who are opioid dependent may experience pain differently than their opioid-naïve peers do; their pain still needs to be treated adequately.^{7,11,17,21,27,31,35,36,41-43} Pain tolerance, and what is considered an acceptable amount of pain (or adequate analgesia), is unique to each individual. Optimal pain management involves a personalized approach developed collaboratively by the healthcare team and the patient. The research on pain management in opioid-dependent pregnant women is minimal, and there is conflicting evidence about analgesia requirements in this population.^{27,35-38} Despite the conflicting evidence, a woman's pain must be appropriately assessed and adequately treated.

Opioid maintenance therapy continues through the antepartum, intrapartum, and postpartum periods and does not address acute pain.^{5,6,27,31,33,35,41} Maintenance therapy addresses the patient's opioid dependence; any pain the patient experiences while receiving OMT needs to be assessed and treated. Numerous barriers exist to adequate treatment of pain in opioid-dependent patients, including misinformation and misconceptions about pain and opioid dependence.^{12,16} Participation in continuing education, whether via conferences, journal clubs, or in-services, is one way for clinicians to strive to improve and refine the care offered to opioid-dependent patients.

Opioid agonist-antagonists are contraindicated in women receiving OMT.^{5,7,17,31} This contraindication is due to the potential of opioid agonist-antagonists to precipitate withdrawal in opioid-dependent patients. Communication among members of the healthcare team regarding this contraindication is crucial for appropriate patient care.

Interdisciplinary teams using a multimodal approach are recommended for providing optimal care to opioid-dependent pregnant women, especially in the context of chronic pain.^{21,30,33} As this article was being prepared, the Substance Abuse and Mental Health Services Administration³ published an article calling for stakeholders and organizations to work together to better serve opioid-dependent women. It notes that the best care strategies are comprehensive, focusing on the needs of women beyond treatment of substance abuse. Interdisciplinary teams are not always available to clinicians serving opioid-dependent pregnant women. In such cases, working to establish such a team, developing relationships with colleagues in other disciplines, and referring patients appropriately might all be viable options.

The most significant limitation to this clinical review is the lack of original research on pain management in

opioid-dependent pregnant women. Only one²⁷ of the 5 studies^{27,35–38} that investigated pain management in opioid-dependent pregnant women was published in the last 5 years. These studies are the basis of numerous literature reviews and clinical guidelines.^{5–7,11,31,43} It is also possible that, despite careful searching of a number of databases, important research was omitted from this review. More research is needed to inform the development of evidence-based guidelines. Prospective cohort studies, as well as further case-control studies, are needed to look at pain in opioid-dependent pregnant women and its management, especially during the intrapartum and postpartum periods. Qualitative studies with women who are opioid dependent are needed to create a deeper, more nuanced understanding of this vulnerable population in order to improve care quality.

CONCLUSION

Oliver et al¹⁶ offer recommendations for providers caring for patients who are opioid dependent, including being aware of current literature in the field, modeling best practices, and advocating for patients. Ultimately, it is the art of nursing and medicine, the accordancy of dignity, respect, and compassion to patients, that must be combined with science in order to provide the best possible care.

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