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Research Article

Opioid-Free Perioperative Acute Pain Management in Non-Spinal Orthopedic Procedures

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Abstract

Currently, the United States is in the throes of an opioid epidemic. Opioid use disorder (OUD) accounts for significant national, state, and local resource allocation in an attempt to reduce the number of deaths related to opioid overdose. Elective surgeries, such as cosmetic surgery, orthopedic surgery, and dentistry, can expose a patient to opioids, leading to OUD. Orthopedic surgeries are one of the highest volume specialties seeing annually greater than 15 million patients annually. Eliminating the initial or subsequent exposure to opioids from as many contributing sources as possible should significantly alleviate the current opioid epidemic in the United States. However, despite of efforts at the local, state, regional, and federal levels, opioid use disorder and opioid-related overdoses and deaths continue to rise. This research article builds upon the foundational article, "Eliminating Opioid Dependency by Knowing the APTA (Anatomy, Physiology, Treatment, and Assessment) of Pain", by Flores and Kerna (2020) and published by *EC orthopedic.* The following paper describes the methodology, findings, and conclusions of a retrospective review of records of prior surgeries with opioid-augmented pain management compared to more recent surgeries with opioid-free pain management in non-spinal orthopedic surgeries in fifteen voluntary participants (thirteen law enforcement officers and two civilians). The results of this study indicate that opioids are not necessary when using a comprehensive integrative approach for opioid-free perioperative acute pain management of non-spinal orthopedic surgical procedures. Utilizing opioid-free perioperative acute pain management in non-spinal orthopedic procedures is a vital factor in achieving UOD-reduction and curtailing and eliminating the opioid epidemic.

Keywords: *Epidemic; Law Enforcement Officer; Opioids; Opioid-Free; Opioid Use Disorder; Pain Management; Peri-Surgical*

Abbreviations

ACOEM: American College of Occupational and Environmental Medicine; ACL: Anterior Cruciate Ligament; ASC: Ambulatory Surgery Center; CDC: Centers for Disease Control and Prevention; CEP: Comparative Effectiveness Research; CIAOF: Comprehensive Integrative Approach for Opioid-Free; CNS: Central Nervous System; ED: Emergency Department; LEO: Law Enforcement Officer; LMA: Laryngeal Mask Airway; MTUS: Medical Treatment Utilization Schedule; MME: Morphine Milligram Equivalent; MMA: Multimodal Anesthesia; NSAID: Nonsteroidal Anti-inflammatory Drug; ODG: Official Disability Guidelines; OFP: Opioid-Free Protocol; OUD: Opioid Use Disorder; PCA: Patient-Controlled Anesthesia; PONV: Postoperative Nausea and Vomiting; QoL: Quality Of Life; RDT: Random Drug Testing; SWAT: Special Weapons and Tactics; TKA: Total Knee Arthroplasty; VAS: Visual Analog Scale

Introduction

On March 18, 2016 in response to the rising death rate attributed to opioid overdose, the United States Centers for Disease Control and Prevention (CDC) released the comprehensive CDC "Guideline for Prescribing Opioids for Chronic Pain". The CDC determined that from 1999 to 2014 opioid overdose and opioid use disorders (OUDs) accounted for at least 165,000 deaths in the United States [1]. During the

same period, researchers were able to statistically correlate a rise in opioid sales and deaths among adults aged 55–64 and therefore, were able to make certain assumptions based on the empirical data [2]. The CDC guideline provided a peer-reviewed framework for acute and chronic pain treatment protocols for primary care physicians. The chronic pain guidelines were designed to drastically reduce the use of prescription opioids and associated deaths, and were based on a review of the best available evidence [3]. The overall intent of the guideline was to ensure that clinicians and patients consider safer and more effective treatment, improve patient outcomes (such as reduced pain and improved function), and reduce the number of persons who develop opioid use disorder, overdose, or experience other adverse events related to these drugs [4].

Nevertheless, to date, overdoses and subsequent deaths continue to rise despite implementing full-spectrum programs that include the following: building state, local, and tribal capacity; supporting providers, health systems, and payers; partnering with public safety; empowering consumers to make safe choices; and conducting surveillance and research [1].

In 1997 and subsequently revised in 2009, the American College of Occupational and Environmental Medicine (ACOEM) guidelines defined chronic pain as pain that lasts greater than three months beyond the time of routine tissue healing for occupational injuries [5,6]. The CDC also recognized this definition and suggested that primary care clinicians use the full range of therapeutic options by providing them clinical guideline resources that outlined a framework of when and how to prescribe opioids—and non-opioid and non-pharmacologic options that may also be effective with less risk—to collectively reduce the amount of opioids being prescribed across the spectrum of care. The authors indicated that the CDC guideline did not include active cancer, hospice care, and end of life treatment protocols for these highly-specific conditions. Palliative care was defined as care for patients 18 years of age or older with chronic pain who are receiving treatment consistent with the Institute of Medicine that provides management of their pain and symptoms to support their quality of life (QoL).

The CDC guideline, therefore, encompasses chronic pain across all health care platforms in the United States. For example, in the Workmen's Compensation system, whichever treatment guidelines the individual state chooses to implement, all states are required to adhere to the mandated CDC "Guideline for Prescribing Opioids for Chronic Pain" regardless of individual state laws. This mandate implies that the guideline is applicable across all healthcare platforms regardless of prior contractual agreements at the state, local, or federal levels.

The CDC guideline offered a compelling solution based on multidisciplinary medical evidence that was logical, rational, and sensible in a collective effort to decrease the daily morphine milligram equivalent (MME) within a safe margin to mitigate exposure and decrease the attributed deaths [7]. However, the determination to decrease the MMEs was not without significant repercussions, namely cost-drivers to the payers, resulting in a national increase of 29.7% to emergency departments (EDs) for opioid overdoses—a total of 142,557 ED visits [8]. The CDC guideline relied heavily on the individual healthcare providers working within various healthcare platforms and specialties to continue to provide treatment with significantly reduced MMEs/day. As physicians rely on their residency training and years of implementation—to remove or reduce opioids as the mainstay of their treatment paradigms limited the ability of many physicians to manage chronic pain, and as a result, inevitably led to a cascade of behaviors resulting in more overdoses and deaths [9].

In 2016, published data compiled by the United States Public Health Department indicated that 1.4 million deaths annually had been attributed to opioids [10]. In 2017, the death rate increased to 1.5 million annual deaths, which indicated that efforts to reduce the epidemic were not sufficient, and deaths continued to climb [11]. CDC's funding to promote a public health approach to the opioid crisis increased from $0 in 2014 to $475 million in 2019, with a majority of funding going to the states for their prevention efforts [12]. The CDC program focused on five areas to prevent opioid overdoses and related harms: 1) build state, local, and tribal capacity, 2) support providers, health systems and payers, 3) partner with public safety, 4) empower consumers to make safe choices and 5) conduct surveillance and research [12].

The opioid epidemic continues to worsen despite the efforts by multiple government departments at the federal and state levels since the implementation of the 2016 CDC guideline [13]. To "buy time", on April 23, 2019, through the Department of Health and Human Services, the Surgeon General, Jerome M. Adams, M.D, M.P.H., released the "Surgeon General's Advisory on Naloxone and Opioid Overdose" that made Naloxone (an opioid antagonist that temporarily reverses a slowed or stoppage of breathing due to the effects of an opioid overdose) available at low to no cost, and beyond civil and criminal liabilities for healthcare professionals, as well as Good Samaritan laws to protect people who might also administer the lifesaving Naloxone [14]. The Surgeon General identified and asserted that expanding awareness, education, availability, and targeted distribution of this medication would serve as an integral part of the immediate public health response to reduce overdose deaths. However, the effort is a temporary solution for a majority of at-risk individuals who may be beyond the initial and subsequent rescue doses, and due to their behaviors, ultimately succumb to an overdose-death. Soon, the low- or no-cost subsidy will prove extremely costly to payers and government programs. Thus, the proposed solution is but one part of a collective effort that targets prevention, treatment, overdose-reversal strategies, and policies to sustain these programs.

Thus far, the initial solution of limiting and reducing MMEs has not resulted in individual program or joint program reduced overdose-related opioid deaths, and has subsequently caused a rapid proliferation of illicitly-manufactured Fentanyl and other highly potent opioids as unexpected outcomes. The National Center for Statistics 2017/CDC identified and quantified data between 1999 and 2016 regarding the number of deaths from overdose due to prescription and illicit opioids, and found that the number doubled from 21,089 in 2010 to 42,249 in 2016 [15]. Fentanyl and other highly-potent and illicit drugs are sold alone or as super-potent heroin or mixed with heroin to increase potency [16]. The illicit drugs are being pressed into counterfeit tablet forms to mimic the drug they are imitating to promote sales to naïve individuals who believe they are buying the same drug their doctor no longer is prescribing them [16]. Because these illicitly-manufactured drugs are obtained without the direction of a licensed physician, the users are unknowingly mixing their prescription drugs with illicitly-obtained drugs, and are unaware of the dangerous chemical inter-reactions.

This illicit buying-behavior results in persistent and unpredictable exposure that is extremely dangerous as it can result in overdose and death [17]. For example, the coadministration of opiates and benzodiazepines can have synergistic central nervous system (CNS) and respiratory depressant effects. Subsequently, the naïve individual, who has been subject to rapid tapering by his physician, resorts to buying on the street as they believe they are purchasing the same medications; however, they end up overdosing due to the harmful ingredients of the illicit drugs [18].

To date, implemented treatment and identification strategies that have incorporated MME reduction, doctor and patient education, detox programs both rapid and innovative, abuse-deterrent formulations of opioid medications, and federal funding have not averted the opioid epidemic. Instead, they have statistically demonstrated substantial increases in the incidence of overdoses and deaths [19]. A study cited by the CDC noted that, between 2015 and 2017, program effectiveness by providers (as the number of opioids prescribed in the U.S.) has decreased by over 20% with reductions noted in 74% of the U.S. counties, which indicates that the opioid crisis continues to result in an increase in overdose death. A decrease in the legal availability of pharmaceutical-grade drugs increases the risk of exposure to overdose by obtaining opioids through illicit means [20,21].

The next logical step to reduce OUD is to limit and reduce initial exposure to the illicit and street drug variants. In 2010, the CDC published a "Fact Sheet for National Ambulatory Medical Care Survey" that noted an estimated 63 million patient visits to non-federally employed, office-based physicians specializing in orthopedic surgery; greater than 50% of the overall patients were 25–64 years old. Patients 45–64 years of age were the highest group of orthopedic patient visits [22].

Hydrocodone with acetaminophen (Norco), naproxen, and ibuprofen were the top three medications provided to these patients [22,23]. Given a surgical population that is medically exposed to opiates (as a regular part of surgical anesthesia and subsequent postop-

erative pain management), there will be a percentage of this population that is at-risk for addiction, diversion, and opioid misuse by the patient and members of the patient's household or social group.

Hospital and ambulatory surgery centers (ASCs) often rely on the most cost-effective and predictable means of general anesthesia sedation for all elective surgical procedures, assuming the patient is healthy and not allergic to the medications; in compromised or allergenic patients, other more costly medications are utilized.

Typically for surgical procedures in both the hospital setting and ASC, the anesthesiologists or nurse anesthetists tend to utilize—as trained—fentanyl or sufentanil (up to 7–8 milliliters). If there are overnight stays in the hospital, postoperative pain management can consist of patient-controlled analgesia (PCA): morphine or hydromorphone released in a predetermined bolus for pain control that is time-limited between doses. After discharge from the hospital or ASC, and depending on the type of surgery, the patient is typically sent home with instructions for ambulation, pain control in the form of prescription medications (typically consisting of opioids, anti-inflammatories, antiemetics, muscle relaxants, and NSAIDs) and instructions for a follow-up visit (about ten days postoperatively), and physical therapy. During this postsurgical period, the patient might experience some degree of nausea, constipation, dizziness, increased pain, confusion, depression, euphoria, headache, withdrawal symptoms, and an inability to sleep due to the side effects of the conventional general anesthesia and prescribed pain medications. The degree of intensity of these side effects is related to the number of opioids the patient was exposed to before the perioperative period and perioperatively.

This treatment protocol—from the initial injury to surgical intervention to postoperative physical therapy and pain management—is considered the conventional, appropriate, and cost-effective protocol for patients and payers. Thus, due to exposure to opioids, the at-risk population will continue to contribute to the overall opioid use disorder epidemic.

Selecting an appropriate study population for opioid-free perioperative acute pain management in non-spinal orthopedic procedures

Cities and municipalities dedicate significant resources of time and money to put a police cadet through the academy training program. The appointed law enforcement officers (LEOs) become more valuable to the cities and counties they represent as they mature and gain valuable experience in the performance of their duties that often involve the apprehension of criminal suspects on a daily basis, assessing and reacting to a spectrum of stressful and potentially lethal situations, and protecting civilians as well as their own lives when confronted with the dynamic scenarios of law enforcement. LEOs regularly incur physical injuries due to their exposure to dangerous and harmful situations and job duties, which occur at a higher frequency than most non-LEO jobs.

Most LEOs desire a full career, pensioned retirement, public service, and are highly motivated to return to work after an injury. Therefore, LEOs provide an exceptional study population for opioid-free perioperative acute pain management in non-spinal orthopedic procedures.

Any proposed treatment for injured LEOS was pre-authorized through the California Workmen's Compensation utilization review process. Permission was granted to perform opioid-free perioperative non-spinal orthopedic surgical procedures, under the provisions of multimodal analgesia (MMA). Thus, this study is unique in that no opioids were used at any stage of the subject patients' multidisciplinary care. (Although some manner of non-opiate treatment, including prehab physiotherapy and non-opioid postoperative protocols, have been noted in evidence-based, peer-reviewed treatment guidelines for California Worker's Compensation, they have never been jointly studied, and utilized opioids at some stage of treatment.) All subject patients were willing participants and signed the appropriate consents.

The opioid-free protocol (OFP) is similar to MMA but without the opioids. Patient exposure to opioids perioperatively sets the stage for OUD in previously opioid-exposed or initially opioid-exposed patients. This OFP was co-designed by Drs. John V. Flores, Neil Ghodadra, and Grant Williams of the United States, and has been used to treat perioperative pain successfully without opioids since 2016, eliminating patient exposure to opioids and decreasing the incidence of OUD.

Methodology

A retrospective review of records was utilized to obtain visual analog scale (VAS) scores from the selected patients' prior surgeries that met the research criteria for comparative analysis. Updated VAS scores were obtained through orthopedic surgeon-patient interviews in the ordinary course of examination (that matched the prior VAS timelines, including how the patients felt at the time of their injuries, at postoperative time 0, and postoperative day-10).

Additional data were collected by a patient care coordinator (PCC) who was present at the orthopedic evaluations. The PCC also interviewed the subject patients according to a formatted questionnaire that included previous preoperative and postoperative VAS scores. Subject patients were asked to report VAS at additional specific times: time 0; 10 minutes postoperatively; 20 minutes postoperatively; and whether or not they had postoperative nausea and vomiting (PONV). Patients were discharged, and the recovery time noted. They were followed-up every day by phone to obtain VAS and PONV at days-1–4, with day-5 and day-10 as in-office postoperative visits.

Population and sample size

Fifteen surgically-experienced patients (nine men and six women) were selected from a pool of fifty prospective subjects according to the following criteria: between the ages of 25–56 and limited to having had prior experience of at least one non-spinal orthopedic surgical procedure to the upper and or lower extremities within a two years period (and treated with traditional perioperative pain management). Thirteen of the 15 subjects were LEOs (as this population has one of the highest exposure rates for work-related injuries, and are deemed responsible and reliable in their VAS scoring). Two (of the fifteen subjects) were not LEOs but did satisfy the selection criteria. Thus, their participation served in not limiting the subject population to LEOs and provided a more representative population. Of the two subjects that were not LEOs, one was male, and the other was female.

All subject patients were experienced in standard perioperative opioid and MMA pain management. All of the subjects were willing and compliant participants and understood they must not miss any treatment appointments or fail to provide their postoperative medications for pill counts.

Research design

A comparative effectiveness research (CER) model was utilized to compare the subject patients' previous VAS pain test scores (VASPs) to their current VAS test pain scores (VASCs). The pain level from previous surgery with opiate intervention was compared to current surgery without opiate intervention.

However, as noted by Flores and Kerna (2020), pain is highly subjective and unreliable [24] in evaluating and comparing inter-subject patient findings over an expanding period. Subject reporting of VAS becomes less reliable and inconsistent over time; obtaining patient records also proves more difficult over time.

Procedures

All subjects understood and were counseled extensively in the program specifics, including 3–6 weeks of prehab passive physical therapy using Interferential current neuromuscular stimulation (to stimulate hypertrophy in the surrounding operative muscle groups passively) according to the American College of Occupational and Environmental Medicine, California Medical Treatment Utilization Schedule (ACOEM/MTUS) guidelines and the Official Disability Guidelines (ODG) for preemptive physical therapy (known as prehab) up to the day before surgery. All patients were counseled throughout prehab, and two days before surgery were started on the following preoperative opioid-free medications: gabapentin (600mg bid), Celebrex (200mg bid), and acetaminophen (1000mg tid). Immediately before surgery, all patients received ultrasound-guided nerve block, as follows:

- The upper extremity shoulder patients received an ultrasound-guided interscalene nerve block using a 20–28 cc 50/50 mixture of 0.50% ropivacaine and 1.25% lidocaine that also included 4mg of preservative-free decadron to prolong the sensory block.
- The lower extremity patients that were to have knee surgery received an ultrasound-guided nerve block at the sciatic (popliteal) and femoral nerves using a 40 ml mixture of 10cc of 0.25% ropivacaine and 30cc of 1.5% lidocaine that included 4mg of preservative-free decadron to prolong the sensory block. (This group did not include anterior cruciate ligament (ACL) reconstruction with Achilles tendon allograft or total knee arthroplasty (TKA).
- The lower extremity patients that were to have ACL reconstruction with Achilles tendon allograft received ultrasound-guided nerve block at the sciatic (popliteal) and femoral nerves using a 40ml mixture of 10cc of 0.25% ropivacaine and 30cc of 1.5% xylocaine that included 4mg of preservative-free decadron to prolong the sensory block.
- The lower extremity patients that were to have a TKA received ultrasound-guided nerve block at the sciatic (popliteal) and femoral nerves using a 40ml mixture of 10cc of 1.3% (13.3 mg/mL) Exparel and 30cc of 0.25% ropivacaine.

During all procedures, all patients received opioid-free anesthesia, consisting of a mild, general laryngeal mask airway (LMA)-delivered anesthetic of 0.8 MAC Desflurane, 30mg of ketorolac IV, and 4mg Zofran IV.

Upon discharge, all patients received written instructions that included a continuation of gabapentin 600 mg bid, Celebrex 200mg bid, and acetaminophen 1000mg tid to control pain for up to five days postoperatively. Also, all patients were appropriately prescribed Norco (5/325 mg x 10 tabs) as security for emergency breakthrough-pain should the block prematurely wear off, or the protocol described fail to control any severe pain.

All patients understood that they would be receiving daily follow-up phone calls, and were required to return to the office at day-5 post-op for evaluation, debridement of the wound, pill count, to surrender any unused Norco, stop using gabapentin and Celebrex, continue using acetaminophen 1000 mg tid and receive a new prescription for Diclofenac. All patients understood that they were to return to office on day-10 post-op for suture or staple removal and to begin physical therapy.

Lastly, all patient participants consented to random urine drug testing (RDT) to rule out the subject's use of narcotics, illicit medications, or medications outside of the study. Most LEOs are accustomed to RDT.

Methods of data analysis

Independent samples t-test was used from VASP (previous surgery with opiates) compared to VASC (current surgery without opiates) to assess if the comprehensive approach for integrative opioid-free perioperative acute pain management in non-spinal orthopedic surgical procedures is efficacious in controlling pain without opiates. The arithmetic mean was derived from the data. The P-value was determined, which rejected the null hypothesis and supported the hypothesis that opioids are not necessary when using a comprehensive integrative approach for opioid-free perioperative acute pain management of non-spinal orthopedic surgical procedures.

Research results: VASP versus VASC

VASC consisted of the average reported experiences of all patients, which were substantially lower when compared to the subjects VASP at the three data points: pre-op, post-op, and day-10 post-op (Figure 1). At day-10, the VASC mean score was 1.5/10, whereas, the VASP mean score was 5.5/10.

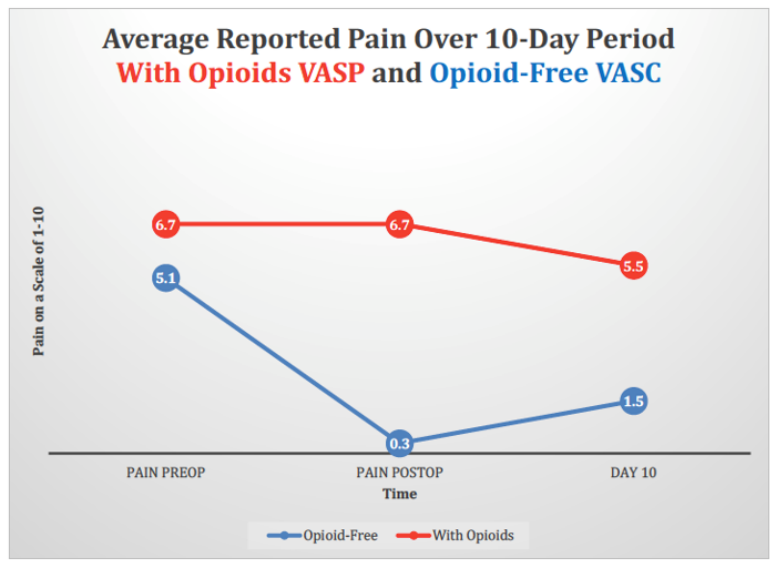

Figure 1: *Average reported pain over a ten days period; VASP compared to VASC.*

The average reported pain for all VASC patients at eight postoperative data points is shown in Figure 2.

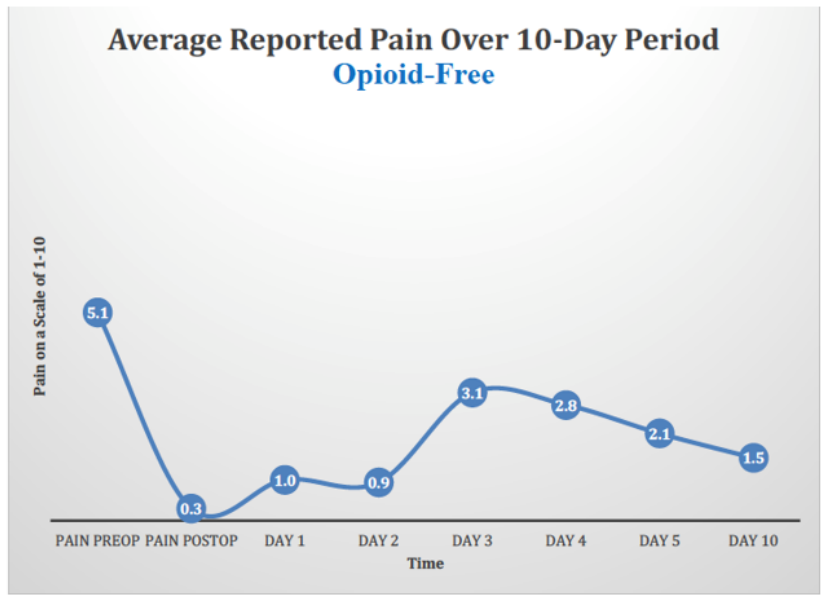

Figure 2: *Average reported pain over a ten days period.*

Research results for regarding PONV

None of the fifteen VASC patients that were administered an OFP at the ASC experienced any degree of PONV, although they had previously experienced PONV at VASP with traditional opioid-augmented pain management (Figure 3). Results indicated that the utilization of the OFP eliminated PONV in all patients. Opioid-augmented treatment resulted in patients' disrupted sleep, limited range of motion (ROM), painful arc, constipation and PONV (Figure 3).

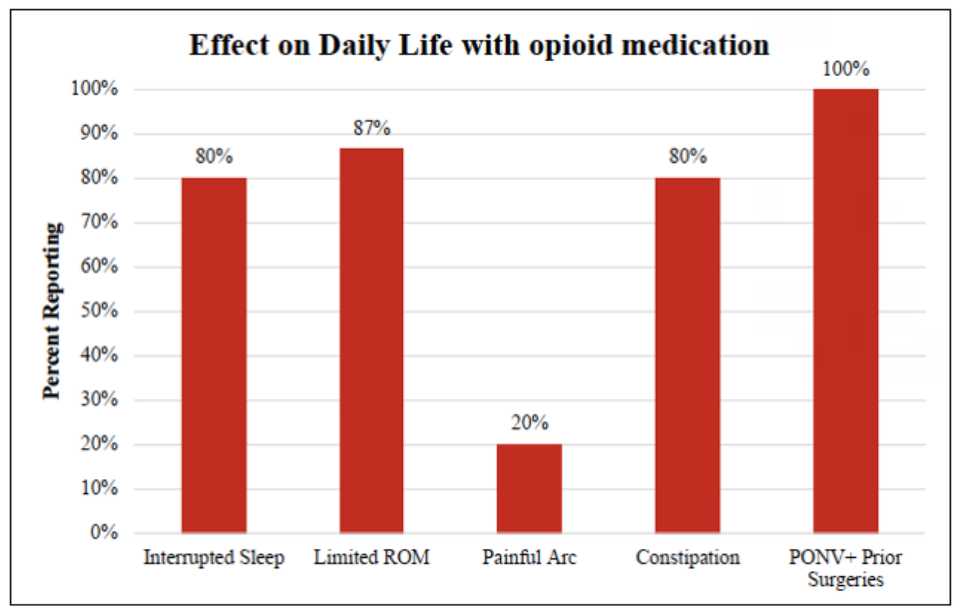

Figure 3: *The effects of opioid-augmented treatment in acute non-spinal postsurgical pain management.*

Discussion

The research indicates that comprehensive integrative opioid-free perioperative acute pain management for non-spinal orthopedic surgical procedures is superior (by comparing VAS scores for VASP versus VASC) and is also superior in PONV (non-opioid treatment versus opioid-augmented treatment in this surgical population).

There were fifteen participating patients, all of whom had all previously received traditional pain management for surgical intervention; they noted their experience using VASP, which was directly compared to their current integrated opioid-free surgical intervention VASC. Mean pain scores comparing traditional (opioid) scores to integrative (opioid-free) scores were evaluated at day-10 post-op. Mean pain scores were 5.5 with opioid VASP and 1.5 opioid-free VASC. The standard deviation of VASP scores was 1.2, while the standard deviation for VASC scores was 0.9. The integrative non-opioid (opioid-free) scores demonstrated a P-value of .00001 (Table 1).

	Opioid	Opioid-free
Mean pain score	5.5	1.5
Standard Deviation	1.2	9

Table 1: *Day-10 post-op opioid-augmented and opioid-free mean pain score versus standard deviation.*

The disposition of the research hypotheses is as follows:

- The null hypothesis (H0) was rejected.
- Accepted hypothesis (H1): Opioids are not necessary when using a comprehensive integrative approach for opioid-free perioperative acute pain management of non-spinal orthopedic surgical procedures.
- Rejected null hypothesis (H0): Comprehensive integrative approach for opioid-free perioperative acute pain management in non-spinal orthopedic surgical procedures is not effective in pain control.

Whether the patient had the surgical procedure in a hospital or an ASC with opioid-augmented protocol, the pain scores and PONV were significantly higher when compared to the integrative opioid-free perioperative acute pain management protocol at an ASC. Pain scores and PONV were significantly higher for ASC when utilizing the standard of care opioid-augmented protocol (Figure 4).

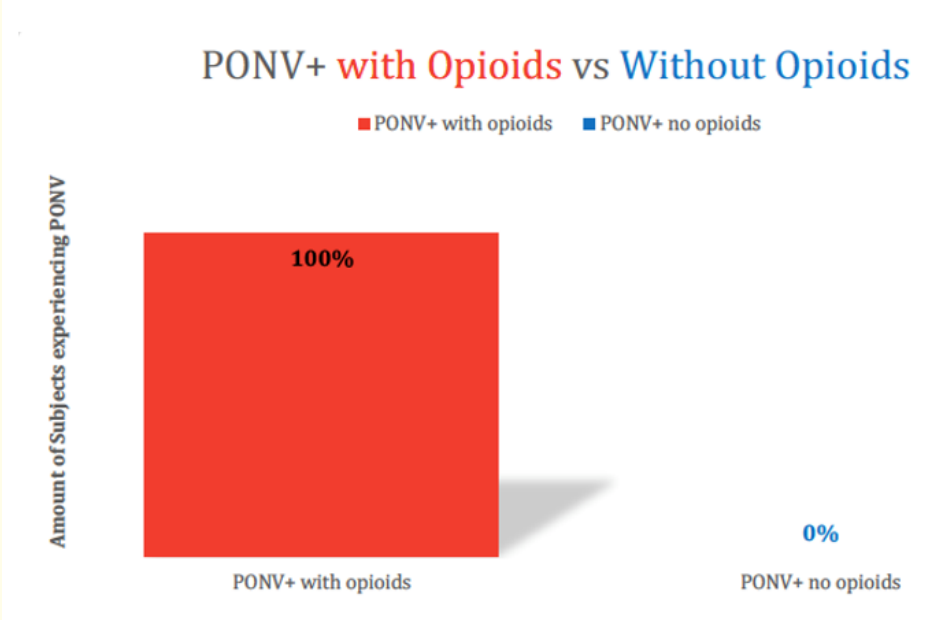

Figure 4: *A comparison of PONV with opioid-augmented treatment versus opioid-free treatment.*

When comparing in-patient hospital protocol to out-patient ASC protocol, hospitals have at least a 1–2 day overnight stay for TKAs (thus, the postoperative pain is managed over a 1–2 day period; whereas, ASCs have a maximum 23 ½ hour hold (thus, they release the patient sooner than a hospital, resulting in the patient leaving an ASC in more pain compared to hospital discharge). Subsequently, ASCs

typically send the postsurgical patient home with more medication, so they do not wind up at an emergency department or emergency room for further emergency pain control (Figure 5).

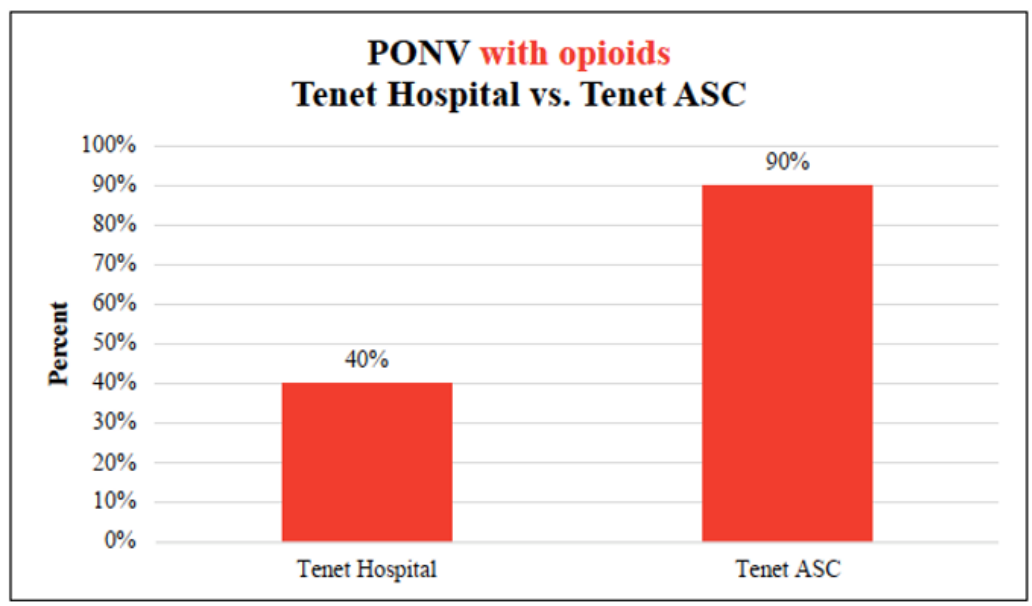

Figure 5: *A comparison of PONV in hospitals using opioid-augmented treatment versus ASCs using opioid-augmented treatment. Note: The term "tenet" used herein refers to medical facilities that adhere to the conventional practice of opioid-augmented pain management to the exclusion of non-opioid protocols.*

Summary

As patients and payers seek more cost-effective means for surgery, especially orthopedic surgery, ASCs are seen as a more cost-effective solution compared to in-patient hospital surgery. However, given the high number of patients having elective orthopedic surgery at ASCs and the high amount of take-home opioids being prescribed, a significant number of patients are being placed at-risk unnecessarily for developing OUD.

Although comprehensive integrative non-opioid protocols might appear initially more expensive, there is an overall cost-savings to the payer as well as the patient's ability to return to gainful employment sooner. These and other factors could reduce global OUD-costs and lessen the burden of payers for detox, emergency room visits, additional surgeries, state disability, and unemployment.

These benefits of an OFP in non-spinal orthopedic surgery are crucial for higher-risk-for-injury jobs, such as law enforcement. LEOs are more likely to have multiple orthopedic surgical procedures over their careers, costing the cities, municipalities, counties, and federal government more funds to cover surgery, surgical-related costs, and possible UOD treatment.

The protocol for comprehensive integrative non-opioid surgical procedures only works for this group (LEOs) because the payers (insurance carriers and cities) see value in the OFP (or MMA) and can authorize the comprehensive integrative non-opioid procedures as requested, with due deliberation.

These experimental findings regarding the comprehensive integrative approach for opioid-free perioperative acute pain management indicate that by applying this protocol to other specialties, it might be possible to provide the same pain relief for other non-orthopedic surgical procedures. By working towards more effective opioid-free pain management methods, it is possible to reduce the overall costs associated with OUD and systematically reduce the national opioid epidemic. Although many factors are contributing to the opioid epidemic, healthcare providers can at least reduce a large percentage of the problem by implementing methods that are readily available but are often incorrectly applied. Non-opioid pain management protocols are not taught in medical school, residency, or subsequent fellowship training.

Unexpected research findings:

- None of the 15 patients that were provided with an opioid-free perioperative acute pain management protocol at the ASC experienced any degree of PONV.
- None of the 15 patients reported any degree of postoperative constipation with comprehensive integrative opioid-free treatment.
- None of the 15 patients that previously reported disrupted sleep with previous opioid-augmented surgical procedures reported any degree of sleep disruption with the administration of the opioid-free perioperative acute pain management protocol.
- All 15 patients that were provided an opioid-free perioperative acute pain management protocol demonstrated complete closure of sutures and staples at the day-10 post-op with no signs of infection.
- All of the 15 patients that received an opioid-free perioperative acute pain management protocol began physiotherapy on day-10 post-op and continued to report 1-3/10 VAS pain at three weeks post-op despite various levels of participation in physical therapy that was dependent on the type, degree, and area of the surgical procedure (upper or lower extremity).
- When comparing the side effect of constipation between surgical hospitals using opioid-augmentation versus ASCs using opioid-augmentation, the reported national average for constipation was 40% for the hospitals compared to 70% for the ASCs, indicating a significantly higher opioid use-rate in ASCs compared to surgical hospitals.

People cope with pain in various ways. The business of medicine must continually strive to be more efficient and cost-effective. When patients present to doctors' offices with complaints of pain, pain medications are a viable means of controlling pain for the majority of the population who either do not have the time or money for conservative treatment, and instead prefer a "quick fix". As patients' conditions change from acute to chronic, the need for additional pain medication increases, in order for them to be able to participate in normal activities of daily living and work [25]. Thus, the stage is set for OUD, the opioid epidemic, and a steep rise in opioid-related deaths.

Many of the CDC's programs, recommendations, and directives regarding opioid prescribing, OUD, and the opioid epidemic—although well-meaning—have had unexpected deleterious effects, turning opioid use into an opioid epidemic within two years from the CDC's initial response to the opioid crisis.

Opioid-dependent, chronic pain patients seek illicit medication to control their pain, often leading to overdose and death; naively, these patients are purchasing narcotics that are up to fifty times more potent than the prescription medicines they were previously taking. To increase sales, illegal drug manufacturers have been pressing counterfeit tablets that are mixed with heroin or fentanyl to mimic the opioid narcotic effect. These types of illicit medications are decidedly responsible for the increase in the death rate associated with overdose.

The CDC, through state and local partners, formed outreach and educational programs in the areas most affected by the crisis. The

immediate response by the U. S. Surgeon general was to reduce the opioid-related death rate that continues to climb, despite numerous programs for interventions at the state and local level. The Surgeon General also approved various laws to provide Naltrexone, an opioid antidote, to save lives. The laws implement government subsidies that allow the at-risk population, family, and first responders to purchase Naltrexone at significantly discounted rates [25,26]. As a short-term solution, the laws provided resources to be used to stop the deaths by overdose. As a long-term solution, considering the costs associated with multiple visits to urgent care centers and hospitals as a result of the lifesaving Naltrexone as well as patients seeking and using illicit drugs, the benefits have yet to be realized.

There are several risk factors to opioid dependency, including genetic susceptibility, chronic pain, psychological conditions, and gender; however, regarding the large surgical population where opioid prescription in some form is common, surgical patients remain the largest at-risk group.

Some experts opine that Naltrexone will significantly raise the at-risk opioid-addicted population and become a burden on emergency care facilities as OUD-individuals will continue to overdose only to be rescued by emergency care personnel and Naltrexone [27,28]. By preventing the use of opioids in the first place, the opioid problem can be mitigated.

There are many components to the opioid epidemic, however, by immediately focusing on doctors and reevaluating and updating how pain is managed for elective non-spinal orthopedic surgeries, a significant portion of the soon to be at-risk surgical population can avoid being at-risk by the administration of integrative treatment methods and protocols.

Initial opioid exposure typically begins in the treatment of skeletal-neuromuscular disorders. Most patients will take over-the-counter NSAIDs for 1–3 days in an attempt to relieve the pain. People might repeat this procedure numerous times during their lifetimes [29]. When a patient suffers an insidious injury or sudden accident that does not resolve and worsens, they present to their primary care provider who will initially recommend prescription NSAIDs and perhaps some sort of physical therapy. If the pain persists, the patient will demand that their doctor provide further relief; the doctor then prescribes stronger medications (including opioids) on subsequent visits [27-29]. Thus, begins the cascade of symptoms and prescription that can lead to an opioid use disorder.

Elective surgeries, such as cosmetic surgery, orthopedic surgery, and dentistry, can expose a patient to opioids, leading to OUD. Orthopedic surgeries are one of the highest volume specialties, seeing annually greater than 15 million patients [29].

Chronic pain patients are the most at-risk patients for OUD in the United States. The CDC recently announced, per the September 14, 2018 "Morbidity and Mortality Report for 2016", that an estimated 20.4% (50.0 million) of U.S. adults had chronic pain and 8.0% of U.S. adults (19.6 million) had high-impact chronic pain, with a higher prevalence of both chronic pain and high-impact chronic pain reported among women, older adults, previously but not currently employed, adults living in or near poverty, and rural residents. Also, the age-adjusted prevalence of chronic pain and high-impact chronic pain were significantly lower among adults with at least a bachelor's degree compared with all other education levels [30].

This research indicates that opioid-free perioperative acute pain management in non-spinal orthopedic surgical procedures is a viable and cost-effective solution, not only in non-spinal orthopedic surgery but also possibly in other specialties, and especially in pain management for chronic patients who would most benefit from a multispecialty integrative approach.

Opioids are, initially, a cost-effective means to treat pain immediately in a large population; however, they also contribute to the current opioid crisis and associated costs to fund various OUD-treatment or -prevention programs. Initially, payers might not favor MMA or opioid-free pain management that uses non-opiate medications due to the expense of providing alternate medications and additional procedures. However, in California, when payers consider the costs associated with a LEO's time off from work, reserve's management, permanent disability ratings, and future medical care as well as the risk of opioid use disorders, they typically realize that any additional

upfront costs for integrative opioid-free perioperative acute pain management are funds well allocated and will dramatically reduce the overall case costs in the long-term.

Conclusion

The United States is in the throes of an opioid epidemic due to OUD and manufactured illicit drugs. The demand for illicit opioids by the OUD population continues to grow as do the illicit suppliers to meet the demand of the chronic pain patients who seek other means of medication. The addictive nature of opiates makes them very difficult to stop using and inevitably leads to a cascade of behaviors to seek additional illicit narcotics at the irreversible cost of damaging personal relationships with loved ones, family members, friends, and employers. The exposure to illicit drugs has caused a surge in death rates, as overdose is more likely due to counterfeit products that are being sold as brand-name medicines. With continued purchases by the opioid-naive, the risk of overdose and death increases. Law enforcement is working together at the state, local, and federal levels to monitor trends and outbreaks of overdose deaths, to raid those highly affected areas, and stop the manufacture, distribution, and sale of dangerous narcotics, such as illicitly manufactured Fentanyl and other highly-potent opioids that are inexpensive to make.

The Surgeon General made Naloxone readily available to the general public by approving additional government subsidies to purchase the opioid overdose antidote at significantly reduced prices and implemented laws to protect those who administer the medication, intending to save the lives of those with opioid use disorder.

The CDC supports health promotion, prevention, and preparedness activities in the United States to improve public health. The CDC recognized overdose deaths involving prescription opioids have increased by about five times since 1999 and has defined opioid abuse, opioid dependence, and opioid addiction as "opioid use disorder" (OUD). OUD is a problematic pattern of opioid use that causes significant impairment or distress and is responsible for the rise in overdose-related deaths in the United States. A campaign to prevent OUD has been enacted to help reduce exposure to opioids and prevent OUD: prescription drug monitoring programs, state prescription drug laws, formulary management, authorization and utilization review strategies in insurance programs, tracking opioid prescriptions, physician and patient education, quality improvement programs in health care systems to increase implementation of recommended prescribing practices, enhanced awareness, and shared resources regarding the risks of prescription opioids and the cost of overdose to patients and families.

Of the total annual surgeries provided in hospitals and ASCs, elective orthopedic procedures represent one of the largest volume specialties to provide surgery and, therefore, act as a large contributor to opioid exposure in opioid-augmented perisurgical pain management. This study evaluating the comprehensive integrative approach for opioid-free perioperative acute pain management in non-spinal orthopedic surgical procedures was performed at a Joint Commission fully-accredited ambulatory surgery center that included the following:3–6 weeks of prehab physiotherapy, education, preoperative opioid-free PO medications, ultrasound-guided blocks, opioid-free anesthesia, postoperative opioid-free PO medications, daily follow-up phone calls, and required return to the office at day-5 and day-10 post-op for evaluation.

By way of VAS, all patients in the study reported markedly decreased pain levels and no PONV. All patients compared their overall experience with prior opioid-augmented surgery to recent opioid-free protocols and stated that they would recommend the integrative opioid-free approach to family and friends. All patients began physical therapy on day-10 post-op with no need for pain medication.

Opioid-free perisurgical pain management for non-spinal orthopedic surgery (a subtype of MMA) is not a new protocol; it has been utilized across the U.S. for some time in some manner.

Some published research has noted conflicting findings regarding the use of MMA compared to anesthesia, indicating that there was no difference in the VAS scores. However, it was discovered that, at some point in those studies, opioids had been introduced, yielding some degree of exposure to opioids and resulting in PONV, increased pain, and a significant risk of developing OUD. It appears that opioids play an important role in managing pain for specific surgeries, such as thoracotomies and mastectomies; however, they are not necessary for controlling pain in non-spinal orthopedic surgical procedures. Thus, eliminating or reducing unnecessary exposure to opioids during non-spinal orthopedic surgical procedures should help alleviate the overall risk for opioid use disorder in the United States and other countries that use an opioid-augmented protocol as the standard treatment.

Opioid use disorder accounts for significant national, state, and local resource allocation in an attempt to reduce the number of deaths related to opioid overdose. By eliminating the initial or subsequent exposure to opioids from as many contributing factors as possible should significantly contribute to alleviating the current opioid epidemic in the United States. Utilizing opioid-free perioperative acute pain management in non-spinal orthopedic procedures seems to be a vital factor in achieving this UOD-reduction goal.

Conflict of Interest Statement

The authors declare that this paper was written in the absence of any commercial or financial relationship that could be construed as a potential conflict of interest. The first author acknowledges proprietary interests in several surgical centers that specialize in opioid-free perioperative pain management in Los Angeles, California, USA.

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Volume 11 Issue 6 June 2020