Opioid Use and Incidence of Surgical Site Infection after Repair of Ventral and Incisional Hernia - A Prospective Clinical Study in a Tertiary Care Hospital in Tirupati

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ABSTRACT

BACKGROUND
Preoperative opioid use is one of the predisposing factors for complications after most of the surgical procedures. This study intends to evaluate the effect of preoperative opiates on the outcomes following repair of ventral hernia.

METHODS
We conducted a prospective study of patients who underwent consecutive ventral hernia repair for over one year with institutional review board approval. Data were obtained regarding the usage of opioids during the preoperative period, intraoperative period, and postoperative period. Follow-up of the cases was done during the postoperative period. Data were obtained regarding the postoperative complications, duration of hospital stay, and the analyzed results.

RESULTS
A striking thirty percent of the total sixty patients have satisfied the criteria for the usage of opioids preoperatively. Preoperative history and operative details were found to be almost similar between the two categories of patients (no preoperative opioid use versus preoperative opioid use). The median hospital stay duration trended toward increased patients with opioid usage versus non-opioid users (P = 0.06). The bowel function’s return to the normal was delayed in opioid users compared with non-opioid users (P = 0.018). The risk of superficial surgical site infection was increased among patients who used opioids preoperatively than the patients without preoperative opioid usage (55.5 % vs. 9.5 %; P < 0.001) and remained the same after multivariable logistic regression.

CONCLUSIONS
Among patients who underwent repair of ventral hernia, those with preoperative opioid usage experienced an increased risk of superficial surgical site infection than patients without preoperative opioid usage.

KEYWORDS
Opioid, Ventral Hernia Repair, Surgical Site Infection
Acute postoperative pain is an undeniable consequence following surgery. It is somewhat anticipated if there is (typically) massive tissue injury, inflammation, and stress response resulting from surgery. However, it is well known that the "anxious patient, who is fearful of moving or breathing," i.e., the patient who is suffering from severe postoperative pain, is considered to be at increased risk of postoperative complications and adverse outcomes. Patients in whom severe postoperative pain compromises respiratory act, when combined with coughing, lack of chest physiotherapy, and early mobilization are more likely to acquire postoperative respiratory infections and thromboembolic events. Pain is a significant stressor both from the physiological and psychological point of view. Postoperative pain relief should be optimized so that certain postoperative infections can be prevented.

The hypothalamus-pituitary-adrenal (H.P.A.) axis to perceived stress and the central nervous system response towards the pain involves a complex network of signaling molecules which is brought by catecholamines, endorphins and cortisol. The stress response towards a surgical procedure is the result of stimulation of the hypothalamic corticotrophin-releasing hormone (CRH) and considerably increased levels of cortisol and adrenocorticotropic hormone (ACTH). On the other hand, surgical stress also enhances the secretion of other metabolically active hormones, mainly catecholamines and glucagon, prolactin, growth hormone, and β-endorphin.1

This enhancement in the postsurgical stress response leads to high cortisol levels and can result in Immunosuppression.2 In the surgery setting, the immune function might have further implications, as animal studies prove that surgery-induced stress is associated with impaired activity of natural killer (N.K.) lymphocyte activity, impairing the body’s immune function.2

Even with the various advances in surgery, anaesthesia, and preoperative care, long standing surgical procedures are still complicated with undesirable sequelae like pain, infective, cardiopulmonary, thromboembolic complications, cerebral dysfunction, gastrointestinal paralysis, fatigue, postoperative complications, nausea and prolonged recovery. Such morbidity can be explained in relation to the type of preoperative analgesia used, anesthetic technique, surgical skill, and the kind of postoperative analgesia used. However, still complications may occur regardless of skill and type of anaesthesia used. No single method or drug regimen has been shown to eliminate postoperative morbidity and mortality to date. One of the standard features considered by all surgical patients is the organ functional, known as the surgical stress response. These functional responses are thought to be mediated through trauma-induced endocrine changes, metabolic and activation of various biological cascade systems (complement, cytokines, arachidonic acid metabolites, nitric oxide, free oxygen radicals, etc.). Even though these responses have evolved with time to offer an advantage for survival, they also contribute to the erosion of body cell mass and physiological reserve capacity if amplified and prolonged.

During and after a surgical injury, the body responds with various profound changes in almost all significant systems like metabolic, neural, and endocrine systems and alterations in the organ function.1 These changes are characterized by decreased secretion or effects of anabolic hormones, a change in the coagulatory – fibrinolytic systems favoring coagulation and thrombosis, pain, increased secretion of catabolic hormones, hypermetabolism, and improved cardiac work as a result of autonomic system activation, impaired pulmonary function, gastrointestinal side effects with nausea and ileus, and loss of Immunosuppression and muscle tissue. Although the surgical stress response may represent a universally conserved cellular defense mechanism, the stress-induced changes in postoperative organ function can also be implicated in developing system-specific postoperative complications. Based on this, the concept of "stress-free anesthesia and surgery" to minimize the trauma-induced physiological responses with subsequent morbidity reduction has been proposed. In an elective surgery, the primary mechanism in stress responses isafferent neural stimuli from around the surgical area. Also, various humoral substances such as arachidonic acid cascade metabolites, nitric oxide, cytokines, endotoxins and other biological cascades were involved. Both pathophysiological responses to surgery and perioperative risk factors need to be recognized and avoided as far as possible or treated to control alterations in the preoperative physiology and reduce morbidity. Factors responsible for outcome should be promptly intervened in time.

Preoperative Assessment and treatment of the concomitant pathologies that increase the overall morbidity needs to be carried and optimization of organ function, improving nutrition, and other factors that increases infective rate delays the recovery. Complications need to be addressed in time so that morbidity can be reduced—malnutrition and Alcohol consumption increase overall morbidity postoperatively. Preoperative alcohol consumption augments the intra-operative surgical stress by increasing the demands at the organ level. This leads to catabolism, Immunosuppression, and organ dysfunction in surgical procedures and anesthetic procedures like Minimally invasive surgery, pain relief, neural block, and pharmacological interventions. Blood transfusion helps in decreasing the postoperative pain and complications associated with it. Avoid unnecessary use of blood as heat loss increases surgical stress responses during the rewarming phase. Reduce heat loss or use external heating to alleviate hypothermia - related complications.

Postoperative pain impairs organ function and delays patient mobilization as well as overall recovery rate. Practical, dynamic pain relief with multimodal effective pain therapy and Immunosuppression is essential to increase the recovery rate. Specific measures like immunomodulation, avoiding unnecessary blood transfusion are proven to be beneficial. Nausea / ileus associated with the usage of opioids delays recovery and early oral nutrition and increases catabolism. Therefore, pain relief using neural block and
NSAIDs, reduce the usage of opioid, pharmacological intervention (serotonin antagonists, etc.). Hypoxaemia increases the risk of cerebral, cardiac, and wound complications (infection / healing). Oxygen administration, stress reduction, mobilization, avoid sleep disturbances are beneficial as sleep disturbances may increase fatigue and postoperative hypoxaemia. Interventions to enhance stress reduction, pain relief, reduce the use of opioids, reduce noise and night time interventions can decrease the Catabolism / muscle loss responsible for increasing all-over morbidity and fatigue and delays the recovery. Stress reduction, pain relief, active rehabilitation, early enteral nutrition, electrical muscle stimulation, and growth factors promote early healing. Immobilization increases the incidence of thromboembolic and pulmonary complications. Other factors like increase fatigue, hypoxemia, and loss of muscle Pain relief, delayed rehabilitation, Drains / nasogastric tubes / traditions hinder recovery and may add to the infectious complications. Therefore, by avoiding unnecessary usage and by employing standard perioperative care, postoperative morbidity can be reduced. Surgical stress response is related to the severity of the surgical injury, and correspondingly lower morbidity rates were observed after minor surgical procedures, including minimally invasive surgery. The critical question in our understanding of postoperative morbidity’s pathogenesis is related to the pathophysiological role of the various components contributing the surgical stress response, and modification of such reactions may improve surgical outcome.

Therefore, the development of novel drugs and multimodal analgesia approaches in the past few decades that would dramatically improve the postoperative pain management quality can help reduce the undesired hormonal and inflammatory consequences associated with surgical stress. Even though there are various anesthetic techniques, both invasive and non-invasive modalities available, like epidural analgesia and large doses of opiates, to attenuate this undesirable stress response by decreasing the intensity of pain, there is a limitation in their usage like these can be employed particularly during the preoperative period and continuing them during the postoperative period being still debatable at the cost of their associated adverse effects is still questionable.

Therefore, it is better to know the side effects of long-term analgesics for pain relief during the peri and postoperative period. Various drugs have been invented that would rapidly exhibit their impact with minimal side effects like remifentanil, which undergoes rapid metabolism and could manage this undesirable response. Studies are being conducted for the drugs that can be utilized with minimal side effects and produce immediate pain relief, improving the patient outcome with minimal stress response and lessened postoperative complications.

Objectives
To study the effect of opioids on postoperative morbidity in patients operated for ventral abdominal hernia and the operated patients’ various outcomes.

METHODS
This hospital-based study was conducted over a period of one year from 1st April 2019 to 31st March 2020 in the Department of General Surgery of S.V.R.R.G.G.H. hospital in Tirupathi. The eligible 60 subjects fulfilling the inclusion and exclusion criteria were divided into two groups, those on opioid analgesics and those on non-opioid analgesics and were studied. The results were analysed. Patients electively operated for ventral abdominal hernia were included and Patients who underwent emergency surgical repair for ventral abdominal hernia were excluded.

The study population was asked about using opioids for any chronic illnesses like osteoarthritis, previous orthopedic surgical procedures, psychiatric disorders, chronic painful conditions, chronic cough, and cardiopulmonary diseases. The study population was segregated based on whether they were on any opioid usage preoperatively or not. Then the opioid use was stratified based on the total dose of milligram equivalents. Data were obtained regarding the usage of opioids during the preoperative period, intraoperative period, and postoperative period. In the present study, patients were not treated with opioids during the intraoperative and postoperative periods. All the study population was followed during their postoperative period for 30 days. The outcome was assessed based on the duration of hospital stay, surgical site infections, and other surgery-related complications. The results were studied.

Statistical Analysis
Data were entered in Microsoft Excel, and analysis was done using S.P.S.S. version 17. Categorical data were expressed in proportions and Continuous variables in means and standard deviations. chi-square and Fischers exact test were applied wherever necessary. P-value of less than or equal to 0.05 was considered statistically significant.

RESULTS

| Age Group (Years) | No. of Patients | Percentage |
|-------------------|----------------|------------|
| < 30              | 6              | 10 %       |
| 30 - 40           | 16             | 26.6 %     |
| 40 - 50           | 24             | 40 %       |
| 50 - 60           | 8              | 13.3 %     |
| 60 - 70           | 2              | 3.3 %      |
| > 70              | 4              | 6.6 %      |

Table 1. Distribution Based on Age

In our study group, most of the patients operated for ventral hernia fell under the age group of 40 - 50 years with a maximum percentage of 40 %.

| Types of Analgesia Used Preoperatively | No. of Patients | Mean Age Group |
|---------------------------------------|----------------|----------------|
| Opioid analgesia                      | 18             | 50             |
| Nonopioid analgesia                   | 42             | 59.5           |

Table 2. Mean Age Distribution of Groups
In our study, among both the groups, patients' mean age distribution was the same: around 50 years.

| Types of Analgesia Used Preoperatively | Max Duration of Hospital Stay | Mean Duration of Hospital Stay |
|--------------------------------------|------------------------------|------------------------------|
| Nonopioid analgesia                  | 24                          | 20                           |
| Opioid analgesia                     | 24                          | 20                           |

**Table 3. Distribution Based on the Duration of Hospital Stay**

In our study, the maximum duration of hospital stays in patients using opioid analgesia was more – 24 days than those who used non-opioid analgesia, which was 16 days. The mean duration of hospital stay was also more in patients on opioid usage.

| Complications          | No. of Patients | Opioid Analgesia | Nonopioid Analgesia |
|------------------------|-----------------|------------------|---------------------|
| Pleural effusion       | 24              | 2                |
| Pneumonia              | 8               | 4                |
| Paralytic ileus        | 4               | 1                |

**Table 4. Distribution Based on Postoperative Complications Other Than S.S.I.**

Among the patients studied, postoperative complications like pleural effusion, pneumonia, and paralytic ileus were more with opioid usage than non-opioid usage.

| Complication               | No. of Patients | Opioid Analgesia | Nonopioid Analgesia | Total |
|----------------------------|-----------------|------------------|---------------------|-------|
| Surgical site infection    | 10 (4.2/0.01)   | 4 (9.6/3.43)     |                     | 14    |
| No surgical site infection | 8 (13.8/2.44)   | 38 (32.2/1.04)   |                     | 46    |
| Total                      | 18              | 42               |                     | 60    |

**Table 5. Distribution Based on the Incidence of Surgical Site Infection**

In our study, S.S.I. incidence was significantly lower in patients using non-opioid analgesia than those who used opioid analgesia. The chi-square statistic was 14.9246. The P-value was 0.000112, which was significant at P < 0.05.

**DISCUSSION**

In our present study, most of the patients operated for ventral hernia fell under the age group of 40 - 50 years with a maximum of 40 %; among both groups, the patients' mean age distribution was the same, which was around 50 years. The maximum duration of hospital stays in our study in patients using opioid analgesia was 24 days than those who used non-opioid analgesia, which was 16 days. The mean duration of hospital stay was also more in patients on opioid usage. Among the patients studied, postoperative complications like pleural effusion, pneumonia, and paralytic ileus were more with opioid usage than non-opioid usage. In our present study, S.S.I. incidence was significantly lower in patients using non-opioid analgesia than those who used opioid analgesia. The chi-square statistic was 14.9246. The P-value was 0.000112, which was significant at P <0.05.

Opioids are the commonly used drugs in the management of acute postoperative pain. Patient education concerning post-surgery pain management is essential to address prescription opioid abuse. Doctors have widely led patients to believe that postoperative pain control is to eliminate all pain; in reality, the goal should be modulation of pain to a level that does not overly interfere with daily functions and sleep. Patients can manage all kinds of daily pains without getting addicted to narcotics, so they should be taught that some postoperative pain will not require anesthetics.

This might be convincing as many patients have routinely received pain prescriptions after a surgical procedure and were preoccupied that the drug was necessary. Surgeons should also discuss how and when to use prescription analgesics best when discussing post-procedure pain management with the patients.

The patient may be fine by just consuming the prescription drug at bedtime in some scenarios, using non-prescription drugs during the day. One may limit how many prescription doses the patient requires by augmenting a prescription drug with a non-prescription. Surgeons should explain to the patient why they are doing so and consider limiting the number of doses prescribed. Patients can request their pharmacy to get the remainder later on if needed and to partially fill a prescription. Opioids were delivered systemically either through pro re nata (as needed) dosing or scheduled or using an analgesia device controlled by the patient based on the type of surgery. Alternatively, the regimen used in postoperative opioids may include neuraxial delivery using an epidural catheter as a part of the patient-controlled epidural analgesia (P.C.E.A.) technique.

Mainly, opioids like short-acting morphine, hydromorphone, oxycodone (in countries where the parenteral formulation is available), and occasionally fentanyl tramadol (is a serotonin-norepinephrine reuptake inhibitor and a weak opioid agonist and) were being employed for acute postoperative pain relief.

Opioids are effective in treating acute postoperative pain; but not without significant side effects. Among the reported side effects and most commonly observed in this setting are vomiting, pruritus, nausea, sedation, and constipation. Respiratory depression is the more severe one which is potentially life-threatening. It is the most feared side effect with usage of opioid medications. Control of respiration and tidal volume by the brain stem is usually through the afferent input of CO2 (through chemosensors in the brainstem) and arterial O2 partial pressure (carried through chemosensors in carotid and aortic bodies). Opioids, through m-opioid receptor-mediated depression of excitability of brainstem chemosensory neurons, depress the ventilatory response to increased CO2, thus depressing respiration.3

Opioids also exhibit their effects on the endocrine system in the following ways:4 Opioids affect the hypothalamic-pituitary-gonadal (H.P.G.) axis.5 Opioids affect the H.P.A. axis, leading to various long-term complications like decreased attention, decreased libido, fatigue, erectile dysfunction, osteoporosis in men, amenorrhea, and impaired adrenal androgen production6 in women. Current data from outpatient surgical settings and in patient indicate that between 30 % and 50 % of postoperative patients have experienced moderate to severe pain continuously.
To supplement general anesthetic agents, opioids are actually used during surgery. Adverse effects are significant and include respiratory depression, ileus, nausea and vomiting, and hyperalgesia in spite of their advantages following acute opioid administrations. In addition to the well-described short-term side-effects, the potential for preoperative opioid exposure influencing the long-term outcomes has also been demonstrated. Preoperative opioid use is associated with postoperative complications and increased healthcare resource utilization as stated in a recent study of abdominopelvic surgeries found. The public concern regarding the use of opioids preoperatively and above factors have resulted in the use of opioid-sparing anesthetic techniques as alternative approaches to achieving analgesia and balanced anesthesia with reduced reliance on opioids. In both the in vitro studies and animal models, opioids were shown to have immunosuppressive effects, modifying both the adaptive and innate immune systems. 

Opioids were implicated in the development of various infections, including human immunodeficiency virus (H.I.V.), hepatitis C virus (HCV), and opportunistic bacterial infections.

Apart from the increased interest in research in opioids, few studies conducted in the arthroplasty literature have studied subsequent development of infection following preoperative opioid consumption. Concerning surgical site infections, Menendez et al. in their study, found that preoperative opioid utilization was associated with a higher rate of patient morbidity, which includes an increased risk of surgical site infections. For P.J.I., Cancienne et al. in a national database review, found that preoperative narcotic use was associated with increased risk of P.J.I. within one year. Similarly, Bell et al. reported in a study that preoperative opioid usage was independently associated with an increased risk of Periprosthetic joint infection (PPI) within two years. Furthermore, preoperative opioid use has been implicated as a risk factor for early revision surgery.

However, neither of the two database surveys in the literature performed further sub-analyses on the type of revision. Hence, the relationship between preoperative opioids and septic revisions remains still debatable.

**CONCLUSIONS**

Among patients who underwent repair of ventral hernia, those with preoperative opioid usage experienced an increased risk of superficial surgical site infection than in patients without preoperative opioid usage. More studies are needed to further understand the relationship between opioid use and surgical site infection after repairing the ventral hernia.

**Limitations**

There is still limited evidence to support the role of opioids as a risk factor for S.S.I. development. Given the scope of the danger posed by these medications, there is a need for further studies to develop more concrete recommendations for potential risk factor modification.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.

Financial or other competing interests: None.

Disclosure forms provided by the authors are available with the full text of this article at jebmh.com.

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