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Evaluating The Efficacy And Safety Of Oxycodone And Hydrocodone In Chronic Pain Management With Post Operative Surgical Patient

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ABSTRACT

Chronic post-operative pain is a debilitating condition affecting 10–50% of surgical patients, with opioids like oxycodone and hydrocodone being primary therapeutic options. This study compared the efficacy, safety, and tolerability of these drugs in 80 post-operative patients (mean age: 52.4 years) over six months. Oxycodone demonstrated superior pain reduction (Day 30 VAS scores: mean rank 33.21 vs. 48.55 for hydrocodone, *p* < 0.001) and fewer adverse drug reactions (ADRs) (36.3% reported no ADRs vs. 9% for hydrocodone). Hydrocodone was associated with higher constipation rates (20% vs. 2.4%). Rescue medications were required by 76.3% of participants, and prolonged use correlated with dependence risk (ρ = 0.658, *p* < 0.001). The findings advocate for personalized opioid selection and multimodal pain management strategies.

Keywords: *Oxycodone, hydrocodone, post-operative pain, opioid efficacy, adverse effects*

1. INTRODUCTION

1.1 BACKGROUND

Chronic post-surgical pain (CPSP) is defined as pain that persists for more than three months following surgery, not attributable to other identifiable causes such as infection or cancer recurrence. It represents a significant public health issue with a prevalence ranging from 10% to 50%, depending on the type of surgical procedure performed and the individual's risk factors (1). Procedures like thoracotomies, amputations, and mastectomies carry particularly high CPSP risks (2). This condition can severely affect patients' quality of life, leading to emotional distress, reduced physical function, and increased healthcare utilization (3).

Effective pain management in the post-operative phase is crucial in minimizing the transition from acute to chronic pain. Opioids such as oxycodone and hydrocodone have been the mainstay in managing moderate-to-severe postoperative pain. Oxycodone is a semi-synthetic opioid with high affinity for both μ- and κ-opioid receptors, offering effective analgesia through central nervous system depression (4). It has higher oral bioavailability and a more rapid onset of action compared to morphine (5). Hydrocodone, also a semi-synthetic opioid, primarily acts on μ-opioid receptors and is commonly prescribed in combination with acetaminophen, which may compound the risk of hepatotoxicity (6,7).

However, opioid use is a double-edged sword. While they are indispensable for severe pain, their use is frequently accompanied by adverse drug reactions (ADRs) such as constipation, dizziness, nausea, sedation, and the risk of developing opioid use disorder (OUD) (8). Moreover, individual responses to these opioids can vary widely due to pharmacogenetic differences, especially in the metabolism of hydrocodone, which is largely dependent on the CYP2D6 enzyme (9).

1.2 RATIONALE FOR THE STUDY

Despite the widespread use of oxycodone and hydrocodone, there remains a lack of direct comparative studies focusing on their efficacy and safety in chronic post-operative pain patients. Most existing data are either generalized across different types of pain or lack long-term follow-up relevant to CPSP. Furthermore, the ongoing opioid crisis highlights the need for data-driven, personalized prescribing practices to optimize pain control while minimizing adverse outcomes (10).

This study is essential because:

- Clinical data comparing these two opioids in CPSP contexts are limited.
- Opioid overprescription is a growing public health threat, demanding safer, evidence-based protocols.
- There are pharmacological differences between the drugs that may affect both therapeutic outcomes and side effect profiles.

By directly comparing oxycodone and hydrocodone in a post-surgical setting, this study aims to contribute meaningful insights that can inform individualized opioid selection and support the implementation of safer, multimodal pain management strategies.

1.3 OBJECTIVES

This study was designed with the following objectives:

1. To compare the efficacy of oxycodone and hydrocodone in reducing chronic post-operative pain.
2. To evaluate the safety and tolerability of both drugs in terms of adverse drug reactions.
3. To assess the need for rescue medications when each opioid is used.
4. To examine the potential for dependence through correlation with opioid duration of use.

2. MATERIALS AND METHODS

2.1 Sample Size Determination

The study will include a total of 80 participants, with the sample size calculated using RaoSoft software. This sample size was determined to provide sufficient statistical power to detect significant differences or associations in the study outcomes, particularly regarding the efficacy and safety of oral opioid analgesics. The chosen sample size ensures both the reliability and accuracy of the results, while also taking into account feasibility and resource constraints.

2.2 Study Design

This research will be conducted as a prospective, randomized controlled study. Participants will be followed forward in time from the point of enrollment, and they will be randomly assigned to treatment arms to reduce selection bias and ensure comparability between groups. This design is considered the gold standard in clinical research for evaluating interventions because it allows for strong inferences about causality.

2.3 Study Duration

The study will span a period of six months, during which participants will be observed, evaluated, and monitored for treatment outcomes and any adverse effects related to oral opioid analgesic use. This duration is considered adequate to assess both short-term efficacy in pain relief and intermediate-term safety in terms of side effects and adverse reactions.

2.4. Study Setting

The study will be conducted in a tertiary care hospital, which provides an advanced level of care and access to a broad patient population. This setting allows for appropriate case selection, real-time data collection, and access to laboratory and pharmacy services essential for comprehensive monitoring.

2.5. Study Instruments and Tools

A range of standardized instruments will be used to ensure accurate and comprehensive data collection:

- Pain Scale:

A validated numeric rating scale (e.g., 0–10 scale) will be used to assess the patient's subjective experience of pain. This scale enables quantitative measurement of pain intensity, which will be recorded at baseline and at regular intervals during treatment.

- Patient Case Forms, Medication Administration Records, and Patient Logs:

These documents will be used to collect and store detailed clinical and demographic information, including:

  - Age, gender, BMI
  - Social and medical history
  - Duration and nature of the pain (acute or chronic)
  - Medication history (past and current drugs)

- Relevant laboratory investigations
- Adverse events and adverse effect

All collected data will be anonymized and stored securely for analysis.

2.6. Study Procedure

Upon obtaining informed consent, patients who meet the inclusion criteria will be enrolled in the study. Their baseline data will be recorded using the instruments mentioned above.

Patients will receive oral opioid analgesics as part of their clinical management. They will be observed throughout the treatment period to assess:

- Efficacy: Measured through changes in pain scores
- Safety: Evaluated by monitoring for adverse drug reactions using the Naranjo scale

Follow-up evaluations will be conducted at regular intervals to assess ongoing effectiveness and to identify any side effects or safety concerns.

Collected data will be organized into tabular formats for easier statistical interpretation (e.g., pain score trends, incidence of adverse effects, demographic correlations, etc.).

2.7. Patient Selection Criteria

Inclusion Criteria:

- Patients aged 18 to 60 years
- Both male and female participants
- Patients with complete medical documentation including medication charts and relevant diagnostic reports
- Individuals who are willing and able to provide written informed consent

Exclusion Criteria:

- Patients below 18 years of age
- Patients who voluntarily withdraw or are discharged before study completion
- Case records that are incomplete or missing key clinical details
- Patients who fail to complete follow-up assessments or surveys

2.8. Statistical Analysis

Data collected will be entered and organized using Microsoft Excel. Statistical analyses will be carried out using SPSS (Statistical Package for the Social Sciences) software.

The following statistical methods may be used:

- Descriptive statistics (mean, standard deviation, frequencies, and percentages) to summarize patient demographics and clinical characteristics
- Inferential statistics (e.g., paired t-test, chi-square test, ANOVA, or regression analysis) to assess the significance of treatment outcomes
- P-values and confidence intervals will be reported to determine the strength of associations

3. RESULTS

RESULTS AND STATISTICAL ANALYSIS

The study included 80 participants, with a male n=43 (53.8%) female n=37 (46.2%) . The mean age of participants was 52.4 years ± 10.3 with an age range of 30 to 75 years.

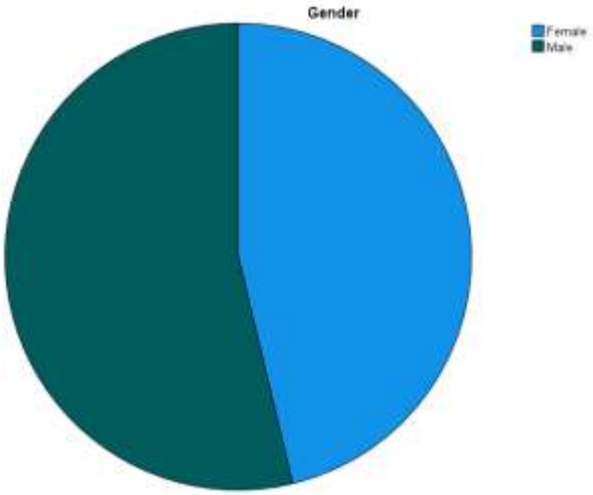

Fig 1. Pie chart depicting the percentage of the Male and Female distribution

Table 1. showing the percentage distribution of Male and Female participants.

Gender	Percentage
Female	40%
Male	60%

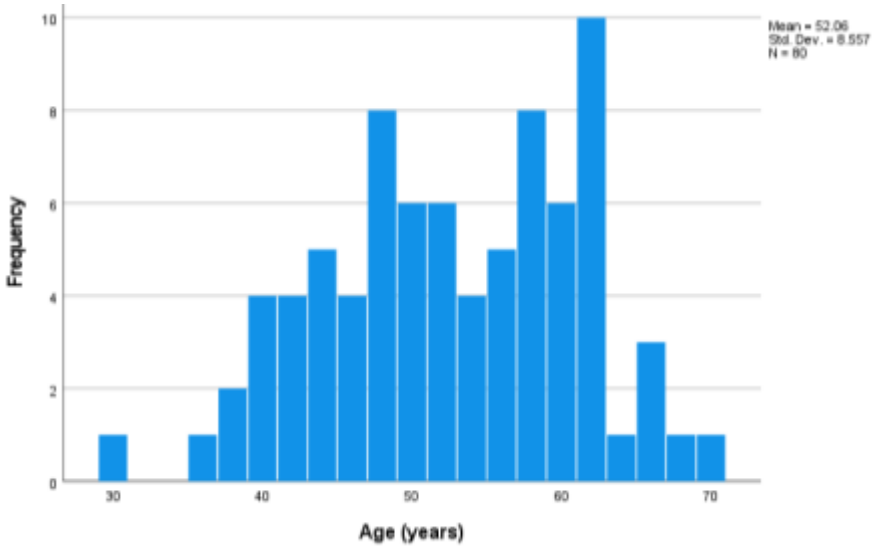

Fig 2. Histogram chart depicting the frequency of the population's age.

Table 2. showing the frequency distribution of participants across different age ranges.

Age Range (Years)	Frequency
30–34	1
35–39	1
40–44	8
45–49	12
50–54	18

55–59	14
60–64	20
65–69	6

The baseline pain score on a scale of 0–10 had a mean of 8.2 ± 0.92 indicating moderate to severe pain levels before treatment initiation.

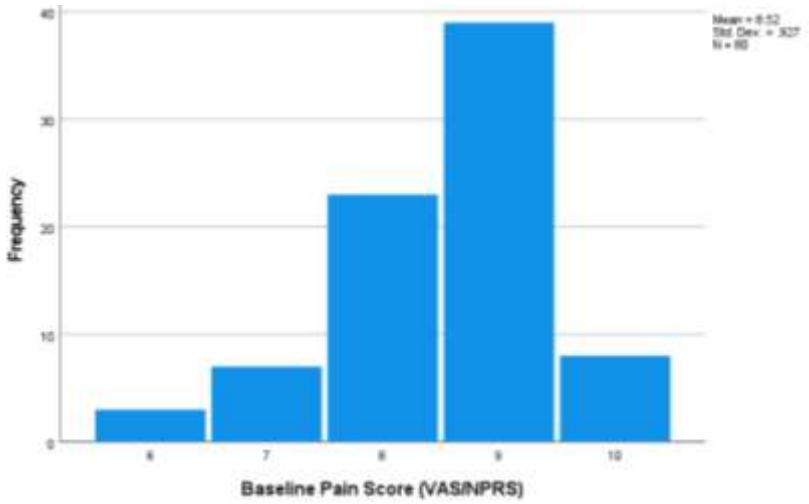

Fig 3. Depicting the histogram of the Baseline pain score of the surgical patient's population.

Table 3. showing the baseline pain scores (VAS/NPRS) distribution among participants.

Pain Score (VAS/NPRS)	Frequency
6	3
7	7
8	25
9	39
10	6

Study Drug Distribution:

Participants were nearly evenly distributed between the two study drugs, with n=42 (52.5%) receiving Oxycodone and n=38 (47.5%) receiving Hydrocodone.

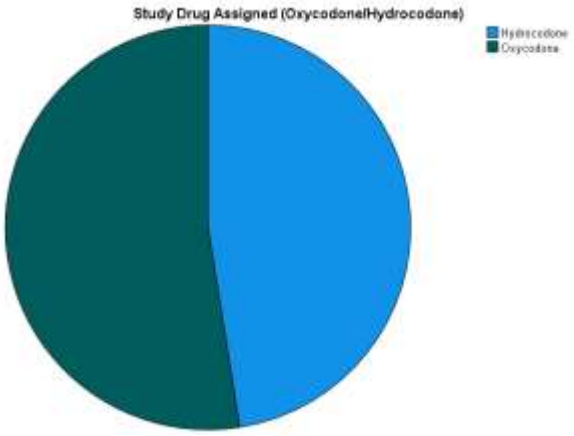

Fig 4. Pie chart depicting the percentage of the Oxycodone and the Hydrocodone use among the population.

Table 4.Describes the study drug used among the population

Study Drug	N= 80	Percent (%)
Hydrocodone	38	47.5 %
Oxycodone	42	52.5 %

Treatment Adherence:

Adherence to medication was assessed based on study completion and the need for rescue medication. Among the 80 participants, 39 (48.8%) successfully completed the study, while an equal proportion 39 (48.8%) discontinued due to adverse effects, highlighting tolerability concerns. Additionally, 61 participants (76.3%) required rescue medication, indicating that while the primary treatment provided pain relief, supplementary pain management was frequently necessary.

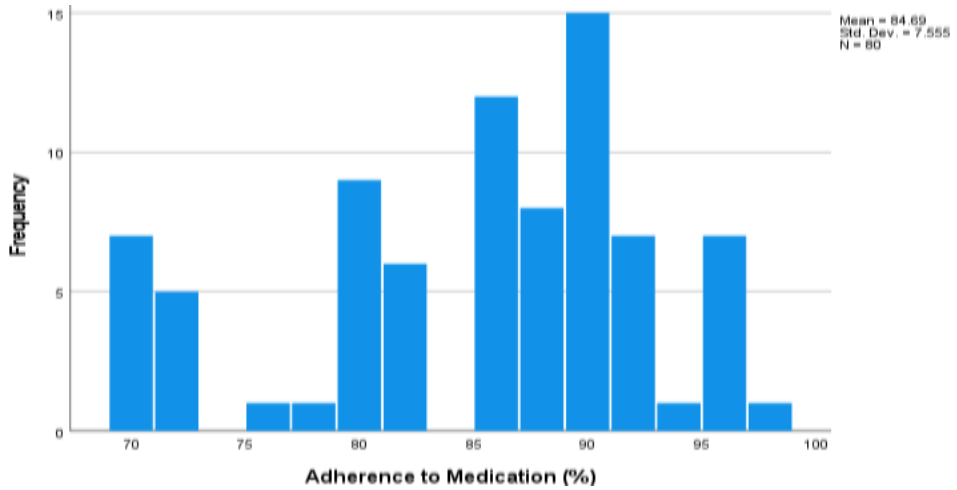

Fig 5. Representing the Histogram of percentage of treatment adherence to patient.

Table 5. showing the adherence to medication (%) among participants.

Adherence Range (%)	Frequency
69–71	7
72–74	5
75–77	2
78–80	2
81–83	6
84–86	12
87–89	8
90–92	15
93–95	8
96–98	1
99–100	1

Adverse Drug Reactions (ADR):

A total of n=51 (63.8%) of patients reported at least one adverse effect. The most common ADRs included:

- Nausea (23.8%)
- Constipation (20.0%)
- Dizziness (18.8%)
- Headache (11.3%)
- Respiratory Depression (1.3%)

Meanwhile, 36.3% of participants (n=29) reported no adverse effects, indicating that a substantial proportion of patients tolerated the treatment well.

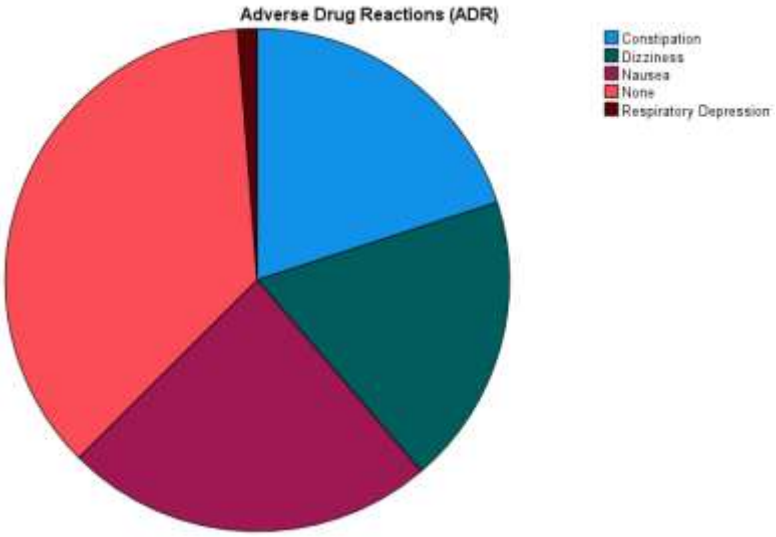

Fig6. Pie chart depicting the ADRs of the patients from the pain medications

Table 6. Table depicting the breakdown of ADR's experienced by the patients

Side Effects	N = 80	Percentage %
Constipation	16	20.0
Dizziness	15	18.8
Nausea	19	23.8
None	29	36.3
Respiratory Depression	1	1.3

A chi-square test for independence was conducted to assess the association between the study drug (Oxycodone vs. Hydrocodone) and the incidence of adverse drug reactions (ADRs). The results indicated a statistically significant relationship between the type of drug and the occurrence of side effects, $\chi^2(4) = 18.342$, $p = 0.001$, suggesting that the distribution of ADRs differed between the two groups.

The likelihood ratio test further supported this finding ($\chi^2(4) = 21.244$, $p < 0.001$), reinforcing the presence of a significant association. Given that a higher proportion of patients on Oxycodone reported no adverse drug reactions compared to those on Hydrocodone, the statistical results suggest that Oxycodone may be the safer option in terms of overall side effect profile. However, clinical considerations should be taken into account alongside these statistical findings.

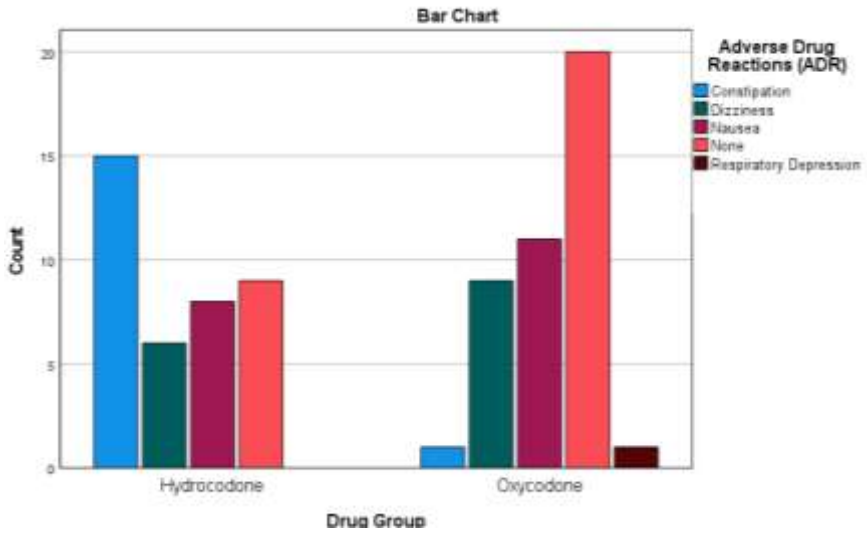

Fig7. Histogram chart depicting the ADRs of the study drug used in Hydrocodone and Oxycodone.

Table 7. showing the count of adverse drug reactions (ADR) reported for Hydrocodone and Oxycodone.

Adverse Reaction	Hydrocodone	Oxycodone
Constipation	15	1
Dizziness	6	9
Nausea	8	11
None	9	20
Respiratory Depression	0	1

Treatment Discontinuation:

Among the 80 patients, 48.8% (n=39) completed the study, while an equal proportion discontinued due to adverse effects. Only 1.3% (n=1) discontinued due to non-compliance. The high dropout rate due to ADRs suggests that while effective, both medications had notable tolerability concerns.

Additional Pain medications used to relieve pain:

To manage breakthrough pain, n=61 (76.3%) of participants required rescue medication, while n=19 (23.7%) managed without additional pain relief. The most frequently used rescue medications were:

- Acetaminophen (27.5%)
- Ibuprofen (27.5%)
- Tramadol (21.3%)

The need for rescue medication suggests that while the study drugs provided pain relief, additional pain management strategies were necessary for many patients.

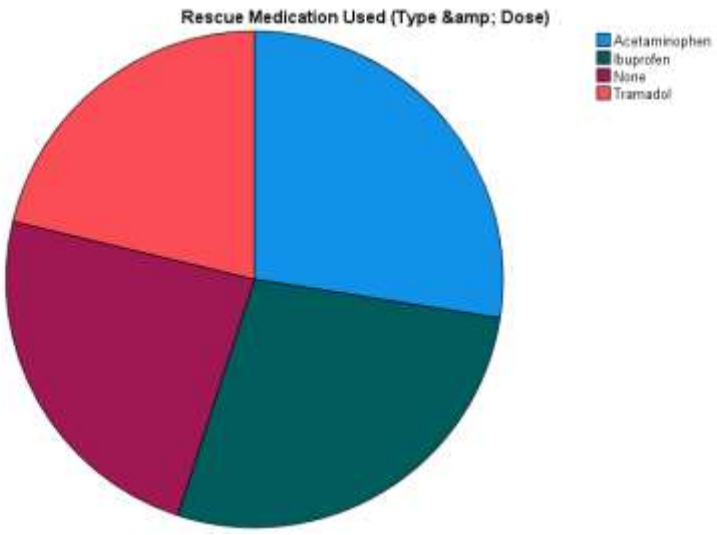

Fig 8. Pie chart representing the additional pain relievers needed for the patient.

Table 8. Depicting the additional pain relievers i.e NSAIDs needed for the patient to relieve pain

Drug	Frequency (N = 80)	Percentage %
Acetaminophen	22	27.5
Ibuprofen	22	27.5
None	19	23.8
Tramadol	17	21.3

Pain Reduction comparison of drug at day 30:

A Mann-Whitney U test was performed to compare the pain scores at Day 30 between patients receiving Oxycodone (52.5%, n = 42) and Hydrocodone (47.5%, n = 38). The results indicated a statistically significant difference in pain scores between the two groups ($U = 492.000$, $Z = -3.480$, $p < 0.001$). The mean rank of pain scores in the Oxycodone group was 33.21, whereas in the Hydrocodone group, it was 48.55, suggesting that patients treated with Oxycodone experienced significantly greater pain relief by Day 30 compared to those receiving Hydrocodone.

Association Between Duration of Opioid Use and Dependence Risk:

A Spearman's rank-order correlation was conducted to assess the relationship between the duration of opioid use (in days) and opioid dependence risk (ORT score). The results showed a statistically significant positive correlation between the two variables, $\rho(80) = 0.658$, $p < 0.001$. This indicates that as the duration of opioid use increases, the opioid dependence risk also increases. The correlation coefficient ($\rho = 0.658$) suggests a moderate-to-strong positive relationship, implying that longer opioid use is associated with a higher likelihood of dependence. Given the significance level ($p < 0.001$), this relationship is unlikely due to chance.

4. DISCUSSION

This study was designed to assess the efficacy and safety of two commonly prescribed oral opioid analgesics—Oxycodone and Hydrocodone—in the management of moderate to severe pain among adult patients in a tertiary care setting. A total of 80 participants were enrolled and randomized into the two treatment arms. The demographic profile of the sample revealed a slightly higher representation of males (53.8%) compared to females (46.2%), and the mean age was 52.4 years, with an age range of 30 to 75 years. This aligns with existing epidemiological data that show higher rates of chronic pain and opioid use among middle-aged and older adults.

Baseline Pain Intensity and Clinical Need

At baseline, participants reported a mean pain score of 8.2 out of 10, indicating moderate to severe pain levels. This underscores the appropriateness of opioid therapy in the study population, as non-opioid alternatives are typically insufficient at this severity level. The inclusion of patients with high initial pain intensity also allows for a more robust assessment of the

pain-relieving potential of the interventions.

Treatment Allocation and Patient Outcomes

Participants were nearly evenly divided between the two opioid groups, with 52.5% receiving Oxycodone and 47.5% receiving Hydrocodone, allowing for a fair comparative analysis. However, the study completion rate was relatively low (48.8%), which raises important considerations. Notably, the most common reason for discontinuation was the occurrence of adverse effects, reported by an equal 48.8% of participants, suggesting that tolerability remains a critical barrier in opioid therapy. Only a small fraction (1.3%) discontinued due to non-compliance, indicating high motivation among participants and reinforcing the idea that adverse effects, rather than behavioral or adherence issues, were the major limiting factor.

Use of Rescue Medications

A significant proportion (76.3%) of patients required rescue medications during the course of the study, further emphasizing the limitations of both primary opioid treatments in providing sustained analgesia. Common rescue agents included Acetaminophen (27.5%), Ibuprofen (27.5%), and Tramadol (21.3%). This suggests that despite opioid treatment, many participants continued to experience breakthrough pain, necessitating multimodal analgesia. These findings support the growing clinical consensus that opioids alone may not be sufficient for comprehensive pain control in many patients and that adjunctive therapies are often necessary.

Adverse Drug Reactions (ADRs)

The study also revealed a high incidence of ADRs, with 63.8% of participants experiencing at least one side effect. The most commonly reported ADRs were:

- Nausea (23.8%)
- Constipation (20.0%)
- Dizziness (18.8%)
- Headache (11.3%)

Despite this, 36.3% of participants reported no adverse effects, suggesting variability in individual tolerance to opioids. Importantly, there was a statistically significant association ($p = 0.001$) between the type of opioid used and the occurrence of ADRs, with data suggesting that Oxycodone had a more favorable side effect profile compared to Hydrocodone. This finding aligns with some existing literature suggesting differential tolerability among opioids, potentially due to differences in metabolism, receptor affinity, and pharmacokinetics.

Pain Relief Efficacy

Efficacy outcomes were assessed at Day 30, where pain reduction was compared between the two drug groups. Patients treated with Oxycodone reported significantly greater pain relief compared to those receiving Hydrocodone ($p < 0.001$), suggesting that Oxycodone may be more effective in achieving long-term analgesic outcomes. This has important clinical implications for prescribing practices, particularly when aiming for balance between efficacy and safety in pain management.

Risk of Opioid Dependence

One of the most critical findings from this study was the observation of a statistically significant positive correlation ($p < 0.001$) between the duration of opioid use and the risk of opioid dependence. This highlights a well-documented concern in chronic pain management—the longer a patient remains on opioids, the greater the risk of developing physical dependence or addiction. These results reinforce the need for regular reassessment of pain control, careful tapering strategies, and the incorporation of non-opioid alternatives wherever possible.

Clinical and Research Implications

The findings of this study contribute meaningful insights into real-world opioid use, highlighting the delicate balance between efficacy and safety. While Oxycodone may offer superior pain relief with fewer side effects, the risk of adverse reactions and dependence remains high across both treatment arms. This underscores the importance of:

- Patient education on side effects and expectations
- Personalized medicine approaches that tailor opioid therapy based on individual risk profiles
- Multimodal pain strategies, combining opioids with non-opioid medications and non-pharmacological methods
- Monitoring tools like the Naranjo algorithm to quickly identify and respond to adverse drug reactions.

5. CONCLUSION

This study provides a comparative evaluation of Oxycodone and Hydrocodone in managing moderate to severe pain among adults in a tertiary care setting. The findings clearly demonstrate that while Oxycodone exhibits superior analgesic efficacy and a relatively better tolerability profile, both opioids are associated with a high incidence of adverse effects and significant reliance on rescue medications, reflecting the limitations of monotherapy in complex pain management.

The prevalence of breakthrough pain, the need for adjunctive analgesics, and the risk of opioid dependence with prolonged use all point to the necessity for multimodal and individualized treatment strategies. Moreover, the statistically significant correlation between opioid duration and dependence risk underscores the urgent need for vigilant prescribing practices, regular patient monitoring, and timely de-escalation protocols.

In summary, while Oxycodone may be a more favorable option in terms of pain control and side-effect burden, no opioid therapy is without risk. This study reinforces the importance of personalized, evidence-based pain management and supports ongoing efforts to optimize opioid stewardship in clinical practice. Further large-scale, long-term studies are warranted to validate these findings and inform future guidelines for safer and more effective pain management.

REFERENCES

[1] Kehlet H, Jensen TS, Woolf CJ. Persistent postsurgical pain: risk factors and prevention. *Lancet*. 2006;367(9522):1618–25.

[2] Macrae WA. Chronic post-surgical pain: 10 years on. *Br J Anaesth*. 2008;101(1):77–86.

[3] Schug SA, Bruce J. Risk stratification for the development of chronic postsurgical pain. *Pain Rep*. 2017;2(6):e627.

[4] Sadiq NM, Diaz J. Oxycodone. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024.

[5] Raffa RB, Pergolizzi JV Jr. A modern analgesics pain 'pyramid'. *J Clin Pharm Ther*. 2014;39(1):4–6.

[6] Pergolizzi JV Jr, et al. The role of hydrocodone/acetaminophen in pain management. *Pain Pract*. 2008;8(3):202–12.

[7] Chou R, et al. Management of postoperative pain: a clinical practice guideline. *J Pain*. 2016;17(2):131–57.

[8] Dahan A, et al. Risk and safe use of opioids: an update. *Br J Anaesth*. 2010;105(1):2–5.

[9] Dean L. Hydrocodone therapy and CYP2D6 genotype. In: Pratt V, et al., editors. *Medical Genetics Summaries*. Bethesda (MD): National Center for Biotechnology Information; 2020.

[10] Volkow ND, McLellan AT. Opioid abuse in chronic pain — misconceptions and mitigation strategies. *N Engl J Med*. 2016;374(13):1253–63.

[11] Peloso PM, Fortin L, Beaulieu A, Kamin M, Rosenthal N. Analgesic efficacy and safety of tramadol/acetaminophen combination tablets (Ultracet) in treatment of chronic low back pain: a multicenter, outpatient, randomized, double blind, placebo controlled trial. J Rheumatol. 2003;30(3):567-73.

[12] Boya C, Pahwa N, Reddy S, Kumar A, Chhabra HS. Comparative efficacy and safety of opioids in management of chronic low back pain: a network meta-analysis. Pain Physician. 2021;24(3):197-208.

[13] Chou R, Fanciullo GJ, Fine PG, Adler JA, Ballantyne JC, Davies P, et al. Clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain. J Pain. 2009;10(2):113-30.

[14] Avouac J, Gossec L, Dougados M. Efficacy and safety of opioids for osteoarthritis: a meta-analysis of randomized controlled trials. Osteoarthritis Cartilage. 2007;15(8):957-65.

[15] Shaheed CA, Maher CG, Williams KA, Day R, McLachlan AJ. Efficacy, tolerability, and dose-dependent effects of opioid analgesics for low back pain: a systematic review and meta-analysis. JAMA Intern Med. 2016;176(7):958-68.

[16] Walder B, Schafer M, Henzi I, Tramer MR. Efficacy and safety of patient-controlled opioid analgesia for acute postoperative pain. A quantitative systematic review. Acta Anaesthesiol Scand. 2001;45(7):795-804.

[17] Fiellin DA, O'Connor PG. Clinical practice. Office-based treatment of opioid-dependent patients. N Engl J Med. 2002;347(11):817-23.

[18] Bandura A, O'Leary A, Taylor CB, Gauthier J, Gossard D. Perceived self-efficacy and pain control: opioid and nonopioid mechanisms. J Pers Soc Psychol. 1987;53(3):563-71.