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Comparing the Efficacy of Pentazocine and Tramadol in Post-Operative Surgical Cases and Assessment of ADR- A Comprehensive Review

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Abstract: Postoperative pain management is a critical aspect of patient care, with various analgesic options available to optimize recovery while minimizing adverse effects. This review compares pentazocine and tramadol, two commonly used analgesics, in terms of their pharmacological profiles, mechanisms of action, efficacy, safety, and side effects. Tramadol, a serotonin norepinephrine reuptake inhibitor (SNRI) and a centrally acting opioid has shown effective pain relief with a lower risk of respiratory depression and dependency. Pentazocine, a mixed opioid agonist-antagonist, provides analgesia with a ceiling effect, reducing the risk of overdose but potentially causing dysphoria and hallucinogenic effects at higher doses. Studies indicate that tramadol may offer superior pain relief in the immediate postoperative period compared to pentazocine, particularly due to its dual mechanism of action and fewer cardiorespiratory side effects. However, pentazocine may provide better hemodynamic stability and remains a viable option in certain patient populations. Both drugs have distinct adverse effect profiles, with tramadol linked to serotonin syndrome and seizures, and pentazocine associated with drowsiness, respiratory depression, and dependency risks. The choice between tramadol and pentazocine should be based on individual patient factors, pain severity, and risk-benefit considerations. While tramadol is generally preferred due to its tolerability and balanced analgesic effect, pentazocine remains relevant in select cases. Further research and personalized pain management approaches are necessary to improve patient outcomes.

Keywords: *Postoperative Pain, Tramadol, Pentazocine Analgesics Efficacy, Safety, Side Effects, Opioid, Pain Relief, Dependency.*

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I. INTRODUCTION

Regardless of the reason, pain is a key worry for patients in the postoperative phase and must be relieved right away. The International Association for the Study of Pain claims that pain is an undesirable psychological and physiological manifestation linked to or characterised in terms of existing or possible harm to tissues. Severe difficulty, panic, autonomy, alterations, reflexive activity, and incurring are all components of pain. [(1)] Unmanaged postoperative pain can result in a variety of harmful acute and long-term repercussions. Decreasing nociceptive signals sent to the central nervous system and optimising perioperative pain management, attenuating perioperative pathophysiology during operation, may lessen negative effects and promote regeneration immediately after surgery and after being released from the hospital.[(2)] Most of this operational pathophysiology has been exacerbated by unmanageable postoperative pain, which might further raise individual mortality and hospitalization. Both regional (neuraxial and peripheral) and systemic (opioid and nonopioid). analgesic approaches are among the many alternatives that exist for treating postoperative pain. [(3)] The physician can optimise the postoperative analgesic regimen by taking the individual's needs into account and conducting a personalised evaluation of the advantages and disadvantages of each treatment method for every individual sufferer.[(4)]Thus, systemic opioids are used as painkillers in the majority of labour rooms. They are widely accessible, affordable, and easy to use. Despite having inadequate security records, pethidine has emerged as the least widely used opioid for pregnancy analgesia globally since its debut in 1939. [(5)] Vomiting, nausea, sedation, breathing difficulties, and delayed emptying of the stomach are among the negative impacts experienced by mothers. Pethidine has also been linked to behavioural and eating issues in newborns up to six weeks postpartum, as well as severe respiratory depression. [(6)] Due to all of pethidine's negative side effects, researchers are looking for systemic analgesics that are just as effective but safer. Although other opioids have been explored, pentazocine and tramadol are the two most readily accessible in our country at present. When evaluating the effectiveness of pentazocine with tramadol in treating postoperative pain, the design is essential. [(7)]

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II. OVERVIEW OF PENTAZOCINE AND TRAMADOL IN PAIN MANAGEMENT

Tramadol and pentazocine are a class of analgesics intended to alleviate pain, even though they differ in their properties, modes of action, and sequences of side effects.[8] While pentazocine is a synthetic opioid with mixed agonist and antagonist qualities, Tramadol is a regionally acting opioid agonist and serotonin-norepinephrine reuptake inhibitor (SNRI). [6]A cyclohexanol compound with a respectable strong analgesic action is tramadol. [9] Without a doubt, medications linked to opiate alkaloids are the initial line therapy for following surgery, cancer-induced, and harrowing conditions. [10] It is crucial to note, nevertheless, that tramadol satisfies the requirements for an optimal analgesic with few adverse effects since it has an opiate-like activity without the risk of dependency or breathing problems. [11] A synthetic version of codeine, tramadol, interacts with mu-opiate receptors and prevents the absorption of serotonin and norepinephrine. [12] According to studies, tramadol is a useful analgesic that doesn't delay stomach emptying or cause breathing problems that different opioids frequently cause in mothers and newborns. [6] Initially prescribed as an oral and parenteral medication for moderate-to-severe pain management, pentazocine is a synthetic opioid analgesic that exhibits both agonist and antagonist action at opioid receptors. These days, it's generally sold in tablets that come with naloxone or paracetamol. [13] Usage of pentazocine for mild-to-moderate pain has decreased since it was initially authorised in the US in 1967. It is thought to restrict its misuse potential since it produces conventional opioid analgesic effects at low doses but dysphoria at larger dosages due to its complete agonist response at the κ opioid channel and mild inhibitory or moderate agonist response at the μ-type opiate receptors.[14]

III. USING PENTAZOCINE TO TREAT PAIN

In the past, pentazocine, a synthetic opioid, was used parenterally and orally to treat moderate-to-severe pain. [15] At opium receptors, it has both agonist and antagonistic effects. [15][10] In modern times, pentazocine is frequently combined with acetaminophen or naloxone and is available as tablets. [16] It is commonly used to lessen mild to extreme pain before the operation or in combination with a general anaesthetic. [17] Pentazocine has an end effect, meaning that increasing the dosage doesn't alleviate the pain. [18]

IV. USING TRAMADOL TO TREAT PAIN

Tramadol is an artificial opioid pain medication that acts centrally and is used to treat moderate to severe pain. [19][20] By interacting with pain receptors in the brain and central nervous system, it inhibits signals that cause pain. [11] For moderate-to-severe pain, tramadol is often employed either alone or in combination with nonopioid pain relievers. (21). The action of tramadol is faster than that of pentazocine. [23] Its primary application is in the management of mild to severe chronic pain as well as acute pain. [24].

V. THE EFFECTIVENESS OF PENTAZOCINE AND TRAMADOL AS ANALGESICS

Tramadol has demonstrated similar effectiveness to codeine following tooth extraction and to propoxyphene or pentazocine in the management of postoperative pain. [25] Research suggests that in the hours after delivery; tramadol may be more effective than pentazocine at reducing pain. [26][27] One research study, for example, found that tramadol was much more effective than pentazocine during the first hour and continuing over the following five hours, with tramadol being preferred in the end.[26] On the other hand, some studies show that during a six-hour observation period, both therapies offer comparable analgesia. [28] Although pentazocine is linked to a higher rate of sleepiness, some research indicates that it particularly reduces labour pain more effectively than tramadol. [29]

VI. PENTAZOCINE ADVERSE DRUG REACTIONS

Pentazocine side effects include breathing problems, nausea, vomiting, itching, and oversedation. [30] The following adverse effects (AEs) are commonly reported: tachycardia, sleepiness/sedation/drowsiness, and fast breathing. [31] A few times, some people have negative responses to pentazocine, including nausea and vomiting. [32] A rapid or irregular pulse, blistering or peeling skin, and dark, tarry stools are uncommon but serious side effects. [33] Investigations have evaluated adverse events associated with the illegal pentazocine usage in paediatric surgical candidates to determine prospective risk factors. [34][35]

VII. TRAMADOL ADVERSE DRUG REACTIONS

The following is an inventory of some of the typical tramadol adverse effects: Constipation, vomiting or nausea, feeling drowsy or exhausted, headache, Light-headedness, stomach pain, and Itching. [36] Headaches, a sense of being "spaced out," poor energy, and perspiration are further adverse effects that have been recorded. [37] Additionally, it might result in potentially fatal respiratory issues, especially during the first 24 to 72 hours of treatment or when the dosage is altered. [38] When you are bothered by any of these adverse effects, inform your doctor.

VIII. COMPARISON OF SAFETY PROFILES

Despite being generally considered a lower-risk opioid option for treating moderate to severe pain because of its high tolerability, tramadol has risks, including serotonin syndrome and seizures, particularly when used in conjunction with other serotonergic medications. [39] Pentazocine might provide better haemodynamic stability than tramadol; one study had dizziness as the most frequent side effect in the tramadol-paracetamol group and drowsiness in the pentazocine group; the difference between the two groups' occurrences was statistically significant. [40] Two trials employing tramadol and pentazocine were among the five opioids employed in the included RCTs, according to a systematic review. [41]

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IX. GENERAL DOSAGE INFORMATION

A. Pentazocine

For adults, the usual dosage is 30 mg given intravenously, subcutaneously, or intramuscularly three to four times a day. [42] As a replacement, an entire tablet containing 50 mg of pentazocine and 0.5 mg of naloxone should be taken orally every three to four hours as needed. [43]

➢ *Daily Maximum Dosage:*

No more than 360 mg each day. Do not take more than 12 pills of pentazocine/naloxone per day. [44]

➢ *Administration:*

Given by SubQ, IV, or instant messaging. It is advised that injection locations be rotated. [45]

B. Tramadol

Adults often take 50–100 mg of tramadol orally every 4-6 hours as needed to relieve pain. Some people may begin with 25 mg once daily and work their way up as needed. [46] The maximum dosage per day is 400 mg. The upper limit is 300 mg for people who are 75 years of age or older. [47]

➢ *Management:*

Usually taken orally. 50–100 mg administered intravenously or intramuscularly every 4-6 hours may be utilised in situations of extreme discomfort. [48]

X. CRUCIAL ADMINISTRATIVE GUIDELINES

➢ *Pentazocine*

- *Injection Site Care:*

When administered intramuscularly (IM) or subcutaneously (SubQ), rotate the injection sites to minimise tissue damage and discomfort. [49]

- *Storage Conditions:*

Maintain a controlled room temperature to avoid extreme heat and dampness. [49]

- *Misuse Potential:*

Because of the risks of misuse and dependency, it should only be taken when no other options are available. [13]

➢ *Tramadol*

- Tramadol dose Aspects:

Adjust the dose based on the requirements of each individual and the specific clinical situation. [50]

- Extended-Release Option:

Extended-release formulations, usually used once daily, may benefit patients requiring long-term pain management. [50]

- Serotonin Aspects:

Because of the potential for serotonin-related problems, use care while using tramadol with drugs that affect serotonin levels. [12]

XI. CRUCIAL PARAMETERS FOR MONITORING

➢ *Breathing Issues:*

Pay particular attention to any indications of respiratory depression while starting treatment or adjusting dosages. [51]

➢ *Risks of Dependency and abuse:*

Considering the possibility of habit formation, examine risk factors unique to each patient before prescribing, and do regular evaluations to look for indications of abuse. [51]

➢ *Potential Drug Interactions:*

Take caution when using alcohol, serotonergic medications, and chemicals that depress the central nervous system (particularly if you take tramadol). [52]

➢ *Pentazocine and Tramadol*

Table 1 Summary table of Pentazocine and Tramadol

S.no	Feature	Pentazocine	Tramadol
1.	Usual Adult Dose	30 mg IM/IV/Subcutaneous q3-4hr or 1 tablet (50mg/0.5mg) orally q3-4hr	50-100 mg orally q4-6hr, may start at 25mg daily
2.	Maximum Daily Dose	360 mg or 12 tablets (pentazocine/naloxone)	400mg (300 mg if >75 years)
3.	Administration Route	IM, IV, Subcutaneous, oral (with naloxone)	oral, IV, IM (for severe pain)
4.	Dosing Frequency	q3-4hr	q4-6hr
5.	Renal Impairment	Reduce dose based on Creatinine clearance	Max 100 mg q12hr if Creatinine clearance <30 ml/min
6.	Hepatic Impairment	Use with caution	Not recommended in severe impairment
7.	Key consideration	Abuse potential, respiratory depression.	Serotonin syndrome risk, individualized dosing.

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XII. PHARMACOKINETIC PROFILE OF TRAMADOL

The adult participants who receive one or more oral 100 mg doses of tramadol assimilate it quickly. Tramadol's mean relative bioavailability was around 68%, although it rose to over 90% when administered intramuscularly and in several doses. [53] There were no therapeutically significant changes in the bioavailability of food consumed. Tramadol's maximum plasma concentration (Cmax) was 308 µg/L after 1.6 hours after a single oral dosage of 1 mg and 193 µg/L at 0.75 hours after a single intramuscular injection in healthy adult participants. [54] Following a single oral 100 mg dosage, the M1 metabolite's Cmax was 55 µg/L and was attained in around three hours. With an apparent volume of distribution of around 260 L following parenteral injection, tramadol exhibits a strong tissue affinity.[55] About 10 to 30 percent of an oral dosage of tramadol is eliminated unmetabolized in individuals in good health due to the drug's significant first-pass metabolism in the liver. The kidneys are responsible for 90% of the excretion of tramadol and its byproducts. [56]Tramadol's terminal elimination half-life (t½β) was approximately 5.5 hours following a single oral (100 mg) or parenteral (50 mg) dosage. After oral single or repeated 100mg dosages, the M1 metabolite's t½β values were 6.69 and 6.98 hours, respectively.[56] Individuals having hepatic or renal impairment had a ≈2-fold increase in t½β. The t½β of tramadol was lowered by almost 50% when it was administered concurrently with carbamazepine, an inducer of hepatic enzymes.[57]

XIII. PHARMACOKINETIC PROFILE OF PENTAZOCINE

Pentazocine's absorption, metabolism, and excretion are all well investigated. Although pentazocine is effectively taken in via all the standard modes of administration, blood levels in any given patient exhibit significant individual variation and a propensity to vary. [58]The blood levels attained correlate well with the start, duration, and degree of analgesia in every instance, although absorption is slower following oral treatment than following parenteral administration. Post intramuscular treatment, peak blood levels are attained 15 to 60 minutes later, yet not until 1 to 3 hours after oral administration. [59] Oral 75 mg or intramuscular 40 mg provide similar blood levels. Pentazocine's plasma half-life is around two hours following intravenous or intramuscular dosing. Personal variations in the rate of metabolism are clearly the cause of the intersubject diversity in the blood levels achieved. Just 2 to 12% of the prescribed dosage is eliminated as the unaltered medication due to the liver's substantial metabolism of pentazocine. [60] Pentazocine is more extensively metabolised when administered orally compared to when administered parenterally because of the slower rate of absorption; up to 25% of the medication has been identified in the plasma as a byproduct following oral treatment, however, this byproduct did not exist following intramuscular delivery. Hepatic biotransformation in humans produces the "cis"-alcohol and "trans"-acid metabolites by oxidising the methyl groups. [61]Certain individuals have larger amounts of the unmodified medication due to individual variations in their capacity to metabolise pentazocine, which results in a stronger and more intense pharmacological impact. This might explain variations in the prevalence of adverse effects and individual variability in the drug's therapeutic effectiveness. [62] All the unaltered and metabolised forms of pentazocine are mostly eliminated in the urine. Most of the medicine is eliminated within the first 12 hours, indicating fast elimination. When the medication is taken orally, parenterally, or rectally, less than 2% of the supplied dosage is excreted in the feces. Pentazocine is more unlikely than pethidine to penetrate the human placental barrier. [63]

XIV. MECHANISM OF ACTION OF PENTAZOCINE

Pentazocine exerts its pain-relieving properties by acting as both an agonist and an antagonist on opioid receptors. It acts as an agonist at kappa and sigma opioid receptors but exhibits a little antagonistic effect at mu receptors. [64] The complicated action of the medication includes the relationship with several receptors in the central nervous system (CNS) and peripheral tissues. [15] By competing for identical receptor sites, especially the opioid mu receptor, pentazocine reverses the effects of opioids, according to the overwhelming body of data. [65]

XV. MECHANISM OF ACTION OF TRAMADOL

Tramadol is an opioid; thus, like other opioids, it is more readily bound to different opiate receptors in the central nervous system (CNS). Tramadol is changed by the liver enzyme CYP2D6 into its active metabolite M1, which binds to the mu receptor more strongly than its inactive counterpart. [66] The M1 metabolite has up to six times the analgesic efficacy of tramadol. Tramadol does not bind to the mu receptor as firmly as morphine does. [67] Unlike other opioids, tramadol may not completely change its effects upon naloxone administration. The painkilling effect is also caused by the antinociceptive effect in the descending pathway, which is brought on by inhibiting serotonin and norepinephrine reuptake. [68]

XVI. PHARMACOLOGICAL PROFILE OF TRAMADOL

Tramadol is a product of aminomethyl cyclohexanol that has been phenyl-substituted. It is a centrally acting analgesic that has little risk of physical dependency and a very slight depressive impact on the respiratory system. [69] Although tramadol has a minimal sensitivity for opiate receptors, it does have opiate-like properties. Tramadol has been demonstrated to raise the threshold for latencies in tail-flick and hot-plate tests, similar to various morphinomimetics. It also lessens the perception of pain from a variety of sources. [70] Q Tramadol's analgesic impact is somewhat lower than buprenorphine in reducing pain after surgery, but it is somewhat comparable to that of metamizole and pentazocine. Moreover, tramadol is not responsible for respiratory depression like morphine is. It is commonly recognised that opioids have an antinociceptive effect when administered intrathecally in the Tail flick and Hotplate tests.

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[71] In a comparable manner, when administered intrathecally, tramadol likewise has a brief analgesic effect. Additionally, Carlsson and Jurna I4 have demonstrated a supraspinal site of action for tramadol. Researchers have demonstrated that the talflick delay, which had been counteracted by naloxone before treatment, is prolonged when tramadol is introduced into the periaqueductal grey matter (PAG). [72]Furthermore, because tramadol stimulates afferent C and A delta fibres in the tiny nerves, it suppresses both spontaneous activity in ascending axons at extremely high doses (20 and 40 mg/kg, i.v). It is currently being demonstrated that each of the noradrenergic, serotonergic, and cholinergic systems modulates tramadol's analgesic action. As a result, it is clear that tramadol and morphine work in essentially comparable ways. [73]

XVII. PHARMACOLOGY OF PENTAZOCINE

The standard animal test techniques used to investigate opiate analgesics are insufficient to establish the analgesic impact of opiate antagonists. They counteract the effects of opiates. [74] Nonetheless, it has been demonstrated that these substances may prevent mice and rats from writhing when phenyl quinone is administered, and that their ability to reduce writhing is consistent with their estimated analgesic effectiveness in humans. [75] Based on mass, pentazocine exhibited around one-fifth the action of morphine in this test. Pentazocine has one-fifth to one-fourth the analgesic effectiveness of morphine, according to the Flinch Jump test in rats. [76] It was demonstrated that the effectiveness of opiate antagonist action was one-sixth to one-hundredth that of nalorphine. [77] Combined with further pharmacological evidence, these findings suggested that pentazocine would have analgesic effects comparable to those of morphine but mild opiate negative activity, which may render it less prone to cause dependency on opiates. [78]

XVIII. CLINICAL PHARMACOLOGY OF TRAMADOL

The drug morphine has been shown to trigger the human body to produce histamine, Healthy participants were administered 100 mg intravenously of tramadol; no change in plasma histamine levels or anaphylactoid response was noted. [79] Despite any aberrant ECG, there was a brief increase in heart rate and blood pressure. The outcomes of the double-blind experiment were comparable. [80] 22 Regular participants were used to test the cardiovascular effects of tramadol. Within the first 15 minutes afterwards intravenous tramadol administration, a substantial rise in cardiac index, heart rate, and mean arterial blood pressure was noted among these healthy volunteers under nitrous oxide/oxygen anaesthesia. Following ten minutes, however, there was little change in haemodynamic parameters, and the cardiovascular stability was preserved. [81]

XIX. CLINICAL PHARMACOLOGY OF PENTAZOCINE

The typical plasma half-life following an intravenous injection of 30 mg of pentazocine is 135 minutes, with a peak blood level of around 200 mg per millilitre. [82] The highest plasma levels of pentazocine were 243 ng/ml at 15–60 minutes after an intramuscular injection of 45 mg/70 kg body weight, with a half-life of 120 minutes. 60–180 minutes after ingesting 75 mg of pentazocine, maxima of 110–300 ng/ml were observed. [83] Individual differences in pentazocine blood levels following oral administration indicate that the drug's "first pass metabolism" varies greatly. [84] Therefore, upon parenteral administration, pentazocine rapidly achieves effective blood levels and has a half-life of around two hours. Following oral pentazocine administration, blood levels are less constant and might differ from person to person. [85]

XX. DEPENDENCE LIABILITY OF PENTAZOCINE

According to the preliminary clinical assessment and the research on pentazocine's dependence liability, there was very little chance of both physical and psychological reliance. Pentazocine has been sold in more than 100 countries worldwide since its inception, when it was thought to have a reduced potential for misuse than morphine, codeine, or propoxyphene. [86] Based on the drug's experience, about 2.8 billion doses of pentazocine have been given out and administered to over 250 million patients since 1967. It is feasible to draw the conclusion from this experience that parenterally given pentazocine misuse does happen and will result in both physical and psychological dependency. [87] According to the preliminary clinical assessment and the research on pentazocine's dependence liability, there was very little chance of both physical and psychological dependence. Pentazocine has been sold in more than 100 countries worldwide since its inception, when it was thought to have a lesser chance for misuse than morphine, codeine, or propoxyphene. [87][88] Based on the drug's experience, about 2.8 billion doses of pentazocine have been administered to over than 250 million patients since 1967. It is feasible to draw the conclusion from this encounter that parenterally given pentazocine misuse does happen and leads to physical as well as mental dependency. [89]

XXI. DEVELOPMENT OF DEPENDENCE AND TOLERANCE WITH TRAMADOL

It is well established that all opiates cause tolerance and dependency in humans as well as mammals. Therefore, it was deemed reasonable to use animal tests to examine tramadol's acceptability and physical dependency. [90]Tramadol was supplied either in fixed dosage or in progressively rising doses; the development of dependency was not shown following quick removal of the medication. [91] Furthermore, tramadol's long-term treatment did not affect the intramitochondrial structure of adrenocortical cells in comparison to morphine. Although compared to tramadol, long-term morphine usage resulted in hypertrophy of the zona fasciculata and reticularis and growth of the adrenal glands. [92]

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➢ *Drug Interaction of Pentazocine*

Table 2 Drug interaction of Pentazocine

S.No	Drug	Interaction
1.	1,2-Benzodiazepine	Combining pentazocine plus 1,2-benzodiazepines may enhance the likelihood or intensity of side effects. (93)
2.	Acetazolamide	Acetazolamide and pentazocine together may enhance the likelihood or intensity of CNS depression. (94)
3.	Acetophenazine	Acetophenazine, as well as pentazocine, together may increase the incidence or severity of hypotension and central nervous system depression. (95)
4.	Aclidinium	Combining Aclidinium plus Pentazocine may enhance the likelihood or intensity of side effects. (96)
5.	Agomelatine	Combining pentazocine plus agomelatine may enhance the likelihood or intensity of depression in the brain. (97)

➢ *Drug Interactions of Tramadol*

Table 3 Drug interaction of Tramadol

S.No	Drug	Interaction
1.	1,2-Benzodiazepine	Combining 1,2-Benzodiazepines plus Tramadol may enhance the likelihood or intensity of CNS depression. (98)
2.	Abacavir	Tramadol may slow down the pace at which abacavir is excreted, raising the serum level. (99)
3.	Abametapir	Combining Tramadol and Abametapir may raise the drug's serum levels. (100)
4.	Abatacept	Combining Abatacept plus Tramadol can speed up its metabolism. (101)
5.	Abiraterone	Combining Abiraterone and Tramadol may slow down its metabolism. (102)

XXII. FOOD INTERACTIONS OF TRAMADOL

- Steer clear of booze. Alcohol may intensify tramadol's central nervous system impacts when taken together.
- It can be taken alone or alongside meals. Pharmacokinetics is unaffected by the combined administration. (103)

XXIII. FOOD INTERACTIONS OF PENTAZOCINE

- Steer clear of booze.
- It can be taken alone or alongside meals. The rates of absorption are not greatly impacted by meals. (104)

XXIV. PHARMACODYNAMIC PROFILE OF PENTAZOCINE

Pentazocine is a powerful painkiller that, when delivered orally in a 50 mg dose, appears comparable in therapeutic impact to 60 mg (1 grain) of codeine. Sufficient analgesia often starts to take effect 15 to 30 minutes after oral administration, and it usually lasts for three hours or more. (105)The instances of the dosage as well as the intensity of pretreatment pain are associated with the onset, duration, and level of pain alleviation. Furthermore, producing an insufficient reversal of the cardiovascular, respiratory, as well as behavioural declines brought on by morphine and meperidine, pentazocine partially counteracts their analgesic effects. The antagonistic activity of pentazocine is around 1/50 that of nalorphine. It possesses a calming effect as well. (106)

XXV. PHARMACODYNAMICS PROFILE OF TRAMADOL

By interacting with progenitor and M1 metabolites to μ-opioid receptors along with weakly inhibiting the absorption of serotonin and norepinephrine, tramadol alters the central nervous system's cascading pain pathways. corresponding to other opioids, tramadol can lead to a range of side effects in addition to analgesia, such as nausea, constipation, dizziness, somnolence, sweating, and itching. (107)

➢ *Central Nervous system*

Compared to morphine, tramadol has never been demonstrated to produce histamine, while utilised in therapeutic dosages, it does not affect cardiac index, left ventricular activity, or heart rate. Yet there have been reports of orthostatic hypotension. By specifically impacting the respiratory sites in the brain stem, tramadol suppresses breathing, which includes a decrease in the brain stem centres' reactivity to electrical stimulation and rises in CO2 tension. Tramadol also suppresses the cough reflex by directly acting on the cough centre in the medulla. Antitussive effects may arise at amounts below those typically needed for pain relief. (108)

➢ *Gastrointestinal tract and other Smooth Muscle.*

Throughout the duodenum and stomach antrum, tramadol increases the tone of smooth muscles while decreasing movement. Propulsive spasms are reduced, and the breakdown of foods in the small intestine is postponed. Decrease in the colon's propulsive peristaltic motion and a potential increase in tone to the point of spasm cause constipation. Other potential opioid-induced adverse effects include sphincter of Oddi spasm, transient elevations in

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serum amylase, and a reduction in biliary, stomach, and liver outputs. [109]

- *Endocrine System*

By altering the hypothalamic-pituitary-adrenal or gonadal axes, opiates may cause changes such as increases in serum prolactin and decreases in plasma cortisol and testosterone. [110] In rare instances, hyponatraemia can be linked to tramadol utilise, usually in patients with predisposing risk factors, such as elderly patients and/or patients taking concurrent medications that can trigger hyponatraemia (e.g., antidepressants, benzodiazepines, and diuretics). In other cases, hyponatraemia seemed to be caused by the syndrome of insufficient production of antidiuretic hormones (SIADH), which was settled with tramadol and suitable therapy (e.g. fluid constraints). [111]

XXVI. CONCLUSION

According to this review, the general comparison between pentazocine and Tramadol in postoperative pain management highlights the difference in their efficacy, pharmacological profile, safety, as well as side effects. Tramadol is a centrally acting opioid and serotonin norepinephrine reuptake inhibitor and has demonstrated effectiveness in managing moderate to severe pain, while it has a lower risk of respiratory depression and dependency compared to traditional opioids. On the other hand, pentazocine works as a mixed agonist-antagonist opioid, and it was widely used for pain relief, through its analgesic celling effect, and potential for dysphoria limits its effectiveness at higher doses. Then both these drugs produce adverse effects. Pentazocine is associated with drowsiness, respiratory issues, and may lead to dependency with long-term use, whereas Tramadol possesses adverse effects with high risk, such as seizures and serotonin syndrome, most often in combination with serotonergic drugs. These studies conclude that Tramadol may offer superior pain relief in the immediate postoperative period when compared to pentazocine; individual responses may vary. In clinical practice, the choice of drugs between pentazocine and tramadol should be guided based on patient-specific factors, which include comorbidities, pain severity, and their risk of adverse drug reactions. In this case, tramadol was most often used due to its tolerability and balanced analgesic activity, whereas pentazocine has unique receptor activity and hemodynamic stability may offer more advantages. Ongoing research on analgesics remains essential for optimising pain management strategies.

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