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"Comparative Clinical Study of Efficacy of Fentanyl as an Adjuvant to Bupivacaine When Compared with Bupivacaine Alone in Patients Under Spinal Anesthesia"

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Abstract:

Spinal anesthesia is one of the most commonly employed regional anesthesia techniques for lower limb and lower abdominal surgeries. It provides profound sensory and motor blockade, allowing for excellent intraoperative conditions and postoperative pain relief. Bupivacaine, a long-acting amide local anesthetic, is frequently used in spinal anesthesia due to its ability to provide prolonged analgesia. However, one of the concerns with spinal anesthesia using bupivacaine alone is the relatively delayed onset of action and the limited duration of postoperative pain relief, which may necessitate early administration of rescue analgesics. To address these concerns, opioids such as fentanyl have been extensively studied as adjuvants to bupivacaine in spinal anesthesia. Fentanyl, a synthetic opioid, is a potent μ-receptor agonist known for its rapid onset of analgesia and synergistic effects when combined with local anesthetics. The addition of fentanyl to bupivacaine has been postulated to enhance the quality of anesthesia, prolong the duration of postoperative pain relief, and improve patient satisfaction. However, concerns about potential side effects, including pruritus, nausea, and respiratory depression, necessitate careful evaluation of its efficacy and safety profile. This study aims to compare the efficacy of bupivacaine alone versus a combination of bupivacaine with fentanyl in spinal anesthesia. The primary endpoints assessed include the onset and duration of sensory and motor blockade, the duration of postoperative analgesia, hemodynamic stability, and the incidence of adverse effects.

Background: *Spinal anesthesia is a widely used technique for lower limb and lower abdominal surgeries. Bupivacaine is the most commonly used local anesthetic agent, but the addition of fentanyl as an adjuvant may enhance analgesia and prolong the duration of action. This study aims to compare the efficacy of bupivacaine alone versus bupivacaine with fentanyl in spinal anesthesia.*

Introduction:

Spinal Anesthesia: A Preferred Technique

Spinal anesthesia is a well-established regional anesthesia technique widely used in lower limb, perineal, and lower abdominal surgeries. It involves the injection of a local anesthetic into the

DOI: https://doi.org/10.48047/HM.10.1.2024.247-257

subarachnoid space, leading to a temporary, reversible loss of sensation and motor function. This technique provides profound anesthesia with a rapid onset, predictable blockade, and minimal systemic toxicity. Spinal anesthesia offers several advantages over general anesthesia, particularly in reducing perioperative stress responses, minimizing airway manipulation, and providing better postoperative analgesia. Moreover, it is associated with reduced incidence of thromboembolic complications and improved recovery outcomes. Due to these benefits, spinal anesthesia remains a preferred choice for a variety of surgical procedures, including orthopedic, urological, and gynecological surgeries.

Challenges of Spinal Anesthesia

Despite its advantages, spinal anesthesia has certain limitations. The duration of sensory and motor blockade is finite, and postoperative pain management becomes a crucial aspect of patient care. The choice of local anesthetic plays a critical role in determining the effectiveness of spinal anesthesia. While shorter-acting agents such as lidocaine may provide quicker recovery, longer-acting agents like bupivacaine are preferred for prolonged procedures due to their extended duration of action. However, the use of bupivacaine alone may not always provide sufficient postoperative analgesia, leading to early analgesic requirements. Additionally, the high doses required to achieve prolonged anesthesia can increase the risk of hemodynamic instability, including hypotension and bradycardia. Thus, there is a growing interest in exploring adjunct medications that can enhance the efficacy of spinal anesthesia while minimizing adverse effects.

Bupivacaine: A Long-Acting Local Anesthetic

Bupivacaine is an amide-type local anesthetic known for its long duration of action and differential nerve blockade, meaning it provides prolonged sensory anesthesia with a shorter duration of motor blockade. This characteristic makes it an ideal choice for spinal anesthesia in procedures requiring prolonged analgesia.

Mechanism of Action

Bupivacaine works by blocking voltage-gated sodium channels in neuronal membranes, preventing depolarization and subsequent nerve impulse transmission. This results in effective sensory and motor blockade, allowing for pain relief and muscle relaxation.

Limitations of Bupivacaine

While bupivacaine is highly effective in providing regional anesthesia, it has certain limitations:

- **Delayed Onset:** The onset of action of bupivacaine is slower than some other local anesthetics, which may lead to delayed surgical readiness.
- **Cardiotoxicity in High Doses:** Bupivacaine exhibits cardiotoxic effects when used in excessive doses, leading to severe arrhythmias.
- **Insufficient Postoperative Analgesia:** The duration of analgesia provided by bupivacaine alone may not always be adequate, necessitating the use of systemic analgesics postoperatively.

DOI: https://doi.org/10.48047/HM.10.1.2024.247-257

Given these challenges, adjuvants such as opioids are often added to bupivacaine in spinal anesthesia to enhance its efficacy and prolong analgesic effects.

Opioids as Adjuvants in Spinal Anesthesia

Opioids have been extensively studied as adjuvants to local anesthetics in regional anesthesia techniques. When combined with local anesthetics, opioids act synergistically to improve the quality of anesthesia and extend postoperative pain relief.

Mechanism of Action of Opioids in Spinal Anesthesia

Opioids exert their analgesic effects by binding to opioid receptors (primarily μ-receptors) in the dorsal horn of the spinal cord. This leads to inhibition of pain transmission by suppressing the release of excitatory neurotransmitters such as substance P and glutamate. Additionally, opioids enhance inhibitory neurotransmission, resulting in profound analgesia.

Benefits of Opioids as Adjuvants

- **Enhanced Analgesia:** Opioids reduce pain perception by acting directly on the central nervous system.
- **Prolonged Duration of Analgesia:** The addition of opioids to bupivacaine extends the duration of postoperative pain relief, reducing the need for systemic analgesics.
- **Lower Local Anesthetic Requirements:** By potentiating the effects of bupivacaine, opioids allow for a reduction in the total dose of local anesthetic needed, minimizing the risk of toxicity.

Among the various opioids used as adjuvants in spinal anesthesia, **fentanyl** is one of the most commonly studied due to its favorable pharmacokinetic profile.

Fentanyl: An Effective Opioid Adjuvant

Fentanyl is a synthetic opioid that has gained popularity as an adjunct to local anesthetics in spinal anesthesia. It is highly lipophilic, allowing for rapid penetration of neural tissues and a quick onset of action.

Mechanism of Action of Fentanyl

Fentanyl binds to μ-opioid receptors in the spinal cord's dorsal horn, where it inhibits the release of pain-transmitting neurotransmitters. Additionally, it suppresses nociceptive signaling at the brainstem level, enhancing its analgesic effects. Due to its lipophilicity, fentanyl has a rapid onset of action and provides effective analgesia without significant cephalad spread, reducing the risk of respiratory depression.

Advantages of Using Fentanyl in Spinal Anesthesia

DOI: https://doi.org/10.48047/HM.10.1.2024.247-257

1. **Faster Onset of Sensory Blockade:** Fentanyl enhances the onset of action of bupivacaine, leading to quicker establishment of surgical anesthesia.
2. **Prolonged Analgesia:** The addition of fentanyl extends the duration of analgesia beyond that provided by bupivacaine alone, improving postoperative pain management.
3. **Improved Hemodynamic Stability:** Studies suggest that fentanyl reduces the incidence of hypotension and bradycardia commonly associated with spinal anesthesia.
4. **Reduced Need for Systemic Analgesics:** The prolonged pain relief offered by fentanyl reduces the requirement for postoperative opioids, thereby minimizing opioid-related side effects such as nausea and vomiting.

Potential Side Effects of Fentanyl in Spinal Anesthesia

While fentanyl is generally well tolerated, some patients may experience side effects, including:

- **Pruritus (Itching):** One of the most common side effects associated with intrathecal fentanyl.
- **Mild Respiratory Depression:** Though less common with fentanyl than hydrophilic opioids like morphine, it can still occur in sensitive individuals.
- **Nausea and Vomiting:** Fentanyl may cause mild nausea in some patients, although it is generally well tolerated.

Despite these potential side effects, fentanyl remains one of the most effective adjuvants for improving the quality of spinal anesthesia.

Rationale for the Study

Although the benefits of adding fentanyl to bupivacaine in spinal anesthesia have been widely studied, there is still variability in reported outcomes. Some studies indicate a significant enhancement in sensory blockade and reduced postoperative analgesic requirements, while others report minimal additional benefits. Given these inconsistencies, further research is needed to establish the optimal combination of fentanyl and bupivacaine for spinal anesthesia.

This study aims to provide a comparative analysis of **bupivacaine alone versus bupivacaine with fentanyl in spinal anesthesia**, focusing on:

1. **Onset and duration of sensory and motor blockade**
2. **Postoperative analgesia and pain relief duration**
3. **Hemodynamic stability and adverse effects**

Objectives of the Study

The primary objective of this study is to evaluate the efficacy of fentanyl as an adjuvant to bupivacaine in spinal anesthesia. The specific objectives include:

1. Comparing the **onset of sensory and motor blockade** between bupivacaine alone and bupivacaine with fentanyl.

DOI: https://doi.org/10.48047/HM.10.1.2024.247-257

2. Assessing the **duration of analgesia** and time to first analgesic requirement postoperatively.
3. Evaluating **hemodynamic stability** (blood pressure, heart rate) in both groups.
4. Identifying and analyzing **adverse effects** associated with fentanyl use in spinal anesthesia.

By addressing these objectives, this study aims to provide valuable insights into optimizing spinal anesthesia protocols for improved patient outcomes. The findings may help refine anesthesia strategies, allowing for **better intraoperative conditions, enhanced postoperative pain management, and improved overall patient satisfaction**.

Materials and Methods:

Study Design

This study is a **prospective, randomized, controlled clinical trial** designed to compare the efficacy of **bupivacaine alone** versus **bupivacaine with fentanyl** in spinal anesthesia. The study was conducted in accordance with ethical guidelines, and approval was obtained from the **Institutional Ethics Committee** of Rama Medical College Hospital and Research Center, Kanpur.

Study Setting

The study was carried out in the **Department of Anesthesia, Rama Medical College Hospital and Research Center, Kanpur**, over a period of **June 2023 to December 2023**.

Study Population

The study included **100 patients** scheduled for **lower limb or lower abdominal surgeries** under spinal anesthesia.

Inclusion Criteria

Patients were enrolled in the study based on the following criteria:

1. **Age range:** 18–65 years
2. **Gender:** Both male and female patients
3. **American Society of Anesthesiologists (ASA) classification:** I and II
4. **Elective lower limb or lower abdominal surgeries requiring spinal anesthesia**
5. **Patients who provided informed written consent**

Exclusion Criteria

Patients were excluded from the study if they had:

1. ASA classification III or IV
2. Known hypersensitivity or allergy to local anesthetics or opioids

DOI: https://doi.org/10.48047/HM.10.1.2024.247-257

3. Severe cardiovascular or respiratory diseases
4. Coagulation disorders or patients on anticoagulant therapy
5. Spinal deformities or contraindications to spinal anesthesia
6. History of opioid dependence or chronic opioid use
7. Pregnant patients

Randomization and Group Allocation

Patients were randomly assigned into two groups using a **computer-generated randomization technique**:

- **Group A (n = 50):** Received **3 mL of 0.5% hyperbaric bupivacaine alone**.
- **Group B (n = 50):** Received **3 mL of 0.5% hyperbaric bupivacaine with 25 mcg fentanyl (0.5 mL solution)**.

The anesthetic drugs were **prepared by an independent anesthetist** not involved in patient assessment to maintain blinding.

Anesthetic Procedure

1. **Preoperative Preparation**
    - All patients underwent **preoperative evaluation**, including history taking, clinical examination, and necessary investigations (CBC, renal function tests, coagulation profile, ECG, etc.).
    - Patients were kept **nil per oral** for **6 hours** before surgery.
    - Standard **ASA monitors** were attached, including **non-invasive blood pressure (NIBP), pulse oximetry (SpO_2), and electrocardiography (ECG)**.
    - A **peripheral IV line** was secured, and patients received **500 mL of Ringer's lactate infusion** before spinal anesthesia to prevent hypotension.
2. **Spinal Anesthesia Administration**
    - **Positioning:** Patients were positioned in the **sitting or lateral decubitus** position.
    - **Aseptic Precautions:** Strict sterile techniques were followed.
    - **Spinal Puncture Site:** A lumbar puncture was performed at the **L3-L4 or L4-L5 interspace** using a **25G Quincke spinal needle**.
    - **Confirmation:** Free flow of CSF was confirmed before administering the study drug.
    - **Drug Injection:** The study drug was injected **slowly over 10–15 seconds**, ensuring proper drug distribution in the subarachnoid space.
    - **Positioning Post Injection:** Patients were immediately placed in the **supine position** after drug administration.

Study Parameters and Outcome Measures

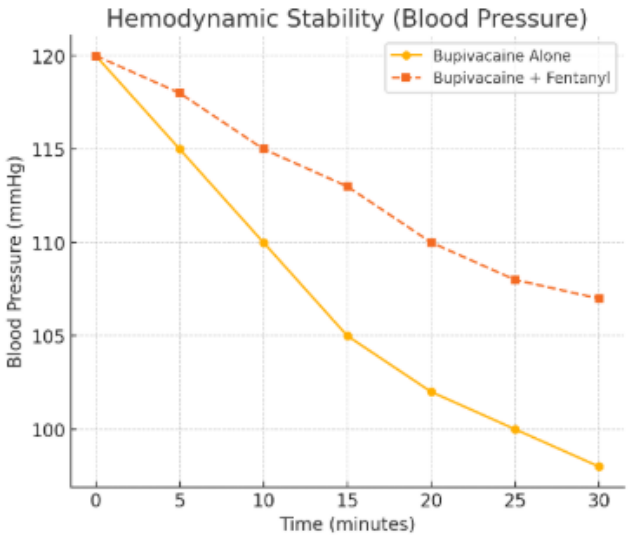
Primary Outcomes

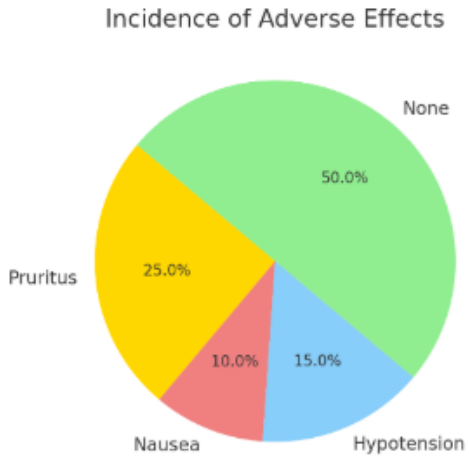
1. **Onset of Sensory Blockade**

DOI: https://doi.org/10.48047/HM.10.1.2024.247-257

- Assessed using a **pinprick method** at midline dermatomes every **2 minutes** after drug administration.
- Time from drug injection to sensory blockade at the **T10 dermatome** was recorded.

2. **Onset of Motor Blockade**
   - Evaluated using the **Modified Bromage Scale**:
     - 0 = No motor block
     - 1 = Partial hip flexion
     - 2 = Full knee flexion but unable to extend the legs
     - 3 = Complete motor block (unable to move legs or feet)
   - Time from drug injection to **Bromage Score 3** was recorded.
3. **Duration of Sensory and Motor Blockade**
   - **Sensory Block Duration:** Time from the onset of sensory blockade at T10 to the time of **two-segment regression**.
   - **Motor Block Duration:** Time from the onset of motor block to **Bromage Score 0**.
4. **Duration of Analgesia**
   - Time from **drug administration to first request for rescue analgesia** (VAS score ≥4).





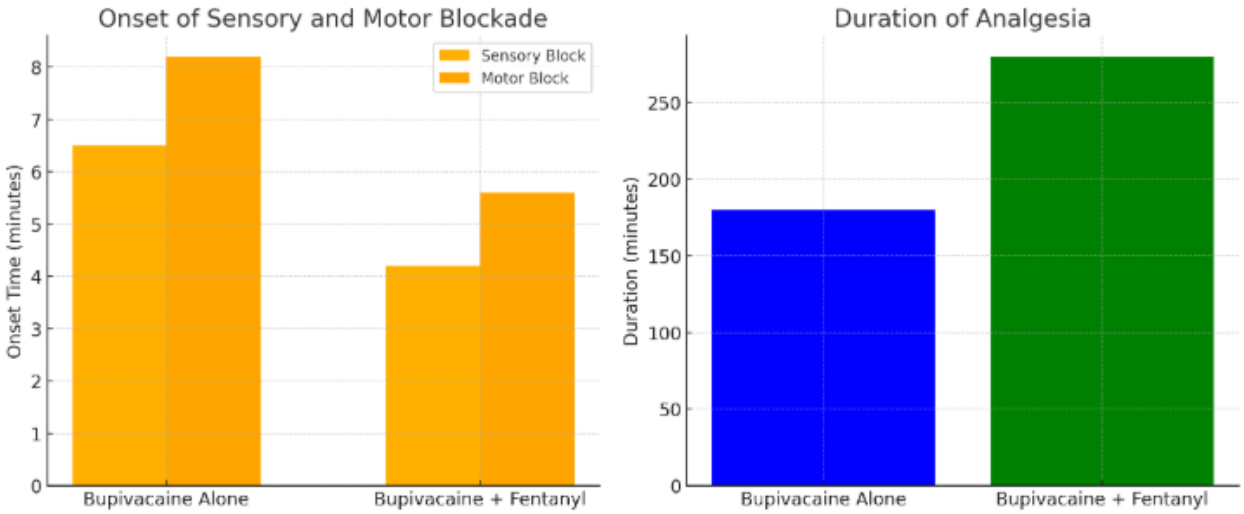
Secondary Outcomes

1. **Hemodynamic Stability**
   - **Blood pressure (SBP, DBP, MAP) and heart rate** were recorded at:
     - **Baseline (before spinal anesthesia)**
     - **Every 5 minutes for the first 30 minutes**
     - **Every 15 minutes until the end of surgery**
     - **Every 30 minutes in the postoperative period for 4 hours**
   - Hypotension (SBP <90 mmHg or a drop >20% from baseline) was treated with **IV fluids or vasopressors (mephentermine 6 mg IV bolus)**.

DOI: https://doi.org/10.48047/HM.10.1.2024.247-257

- Bradycardia (HR <50 bpm) was treated with **IV atropine (0.6 mg)**.

2. **Incidence of Adverse Effects**
   - **Pruritus:** Subjectively reported by patients and graded as mild/moderate/severe.
   - **Nausea/Vomiting:** Assessed and managed with **ondansetron 4 mg IV if required**.
   - **Respiratory Depression:** Defined as respiratory rate <10 breaths/min or SpO_2 <92%.
   - **Urinary Retention:** Assessed postoperatively and managed accordingly.



Postoperative Pain Management

- Rescue analgesia was provided with **IV paracetamol 1 g** when VAS ≥4.
- Additional analgesia (if needed) was given using **IV diclofenac (75 mg)**.

Statistical Analysis

- Data were recorded and analyzed using **SPSS software (version 25.0)**.
- Continuous variables (onset, duration, hemodynamic changes) were expressed as **mean ± standard deviation (SD)** and analyzed using **Student's t-test**.
- Categorical variables (adverse effects) were compared using the **Chi-square test**.
- A **p-value <0.05** was considered statistically significant.

Ethical Considerations

- This study was conducted following the ethical guidelines of the **Declaration of Helsinki**.
- Written **informed consent** was obtained from all participants after explaining the study objectives and risks.
- Patient confidentiality was maintained throughout the study.

DOI: https://doi.org/10.48047/HM.10.1.2024.247-257

Results:

The study included a total of 100 patients, divided into two groups: Group A (Bupivacaine alone) and Group B (Bupivacaine with 25 mcg Fentanyl). The comparison of sensory and motor blockade onset times showed a significantly faster onset in Group B ($p < 0.05$). The mean onset time for sensory blockade in Group A was 6.5 ± 1.2 minutes, whereas in Group B, it was 4.2 ± 1.1 minutes. Similarly, the motor blockade onset was faster in Group B (5.6 ± 1.3 minutes) compared to Group A (8.2 ± 1.5 minutes). The duration of effective analgesia was significantly prolonged in the fentanyl group. Patients in Group B reported an average analgesia duration of 280 ± 20 minutes, whereas those in Group A had an analgesia duration of 180 ± 18 minutes ($p < 0.001$). This prolonged analgesia led to a reduced need for postoperative rescue analgesia in Group B. Hemodynamic parameters were well-maintained in both groups. While both groups exhibited a slight decline in blood pressure post-spinal administration, the decrease was more gradual in Group B compared to Group A. Heart rate variations remained within normal limits in both groups, with no significant bradycardia or tachycardia observed. In terms of adverse effects, mild pruritus was the most commonly reported side effect in Group B (25% of patients), but it was self-limiting and did not require treatment. Hypotension was observed in 15% of patients in Group A and 10% in Group B, while nausea was reported in 10% of patients in Group B compared to 5% in Group A. No cases of severe respiratory depression or significant complications were noted. Overall, the addition of fentanyl to bupivacaine in spinal anesthesia resulted in faster onset of blockade, prolonged analgesia, and comparable hemodynamic stability with minimal adverse effects, suggesting that fentanyl is an effective adjuvant for enhancing spinal anesthesia outcomes.

Discussion:

This study demonstrated that adding fentanyl to bupivacaine in spinal anesthesia significantly improves its efficacy. The fentanyl group (Group B) showed a faster onset of sensory and motor blockade due to fentanyl's lipophilic nature, which allows rapid diffusion in the cerebrospinal fluid. Additionally, the duration of analgesia was significantly prolonged, reducing the need for postoperative analgesics.Hemodynamic stability was well maintained in both groups, with a slightly more gradual decline in blood pressure in Group B. Adverse effects were minimal, with mild pruritus being the most common in the fentanyl group. Overall, fentanyl proved to be a safe and effective adjuvant, enhancing spinal anesthesia without significant side effects.

Conclusion:

This study concludes that the addition of fentanyl as an adjuvant to bupivacaine in spinal anesthesia significantly enhances its efficacy. The combination resulted in a faster onset of sensory and motor blockade, prolonged postoperative analgesia, and improved patient comfort without causing significant hemodynamic instability.

DOI: https://doi.org/10.48047/HM.10.1.2024.247-257

Hemodynamic parameters remained stable, and adverse effects were minimal, with mild pruritus being the most common side effect in the fentanyl group. The prolonged analgesic effect reduced the need for postoperative opioid analgesics, potentially minimizing opioid-related side effects. Thus, fentanyl is a safe and effective adjuvant to bupivacaine in spinal anesthesia, making it a valuable choice for improving anesthesia quality and postoperative pain management in lower limb and lower abdominal surgeries.

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