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# A Comparative Study on the Effects of Mirtazapine, Dexamethasone, And Tramadol for Prevention of Post-Spinal Anaesthesia Shivering in Gynaecological Surgeries in a Tertiary Care Hospital: A Randomized Controlled Trial

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**KEYWORDS**

Post-spinal anaesthesia shivering, mirtazapine, dexamethasone, tramadol, gynaecological surgeries, randomized controlled trial.

**ABSTRACT:**

Background: Post-spinal anaesthesia shivering (PSAS) is a frequent and distressing complication, impacting physiological stability and surgical outcomes. Effective prevention is critical to enhance patient comfort and recovery. Mirtazapine, dexamethasone, and tramadol are commonly used pharmacological agents, each with unique mechanisms of action and efficacy profiles. This study compares their efficacy and safety in PSAS prevention in patients undergoing gynaecological surgeries.

Methods: This randomized controlled trial included 84 patients undergoing gynaecological surgeries under spinal anaesthesia. Participants were randomized into three groups, M Group (Mirtazapine): 30 mg oral dose, 2 hours preoperatively, D Group (Dexamethasone): 8 mg intravenous dose, preoperatively and C Group (Tramadol): 0.5 mg/kg intravenous dose, preoperatively. Primary outcomes included the incidence and severity of shivering, assessed using a 4-point scale. Secondary outcomes were hemodynamic parameters, adverse effects, and the need for rescue therapy. Statistical analysis was conducted using SPSS software.

Results: The pills of mirtazapine were most effective in avoiding shivering (78.6 percent no shivering) than dexamethasone (71.4%) as well as tramadol (53.6%) ($p = 0.034$). Mirtazapine too showed the least rate of side effects (nausea: 10.7%, pruritus: 0%) and and used the least amount of rescue therapy (7.1%). Hemodynamic stability in each group was noted, and no important difference in heart rate, blood pressure and oxygen saturation existed between the groups.

Conclusion: Mirtazapine is an agent that is the most efficient in the prevention of PSAS, as it has the best result, has few side-effects and acts long-lastingly. Dexamethasone also provides an added value of decreasing inflammation and promoting recovery, but tramadol, in its turn, has increased rates of adverse effects. These results support the idea to optimize the PSAS management in perioperative care.

## INTRODUCTION

Post-Spinal Anesthesia Shivering (PSAS) is widespread and uncomfortable condition that appears after anesthesia which construes involuntary muscle contracture because of hypothermia or poor thermoregulation after spinal anesthesia. This condition is not only uncomfortable but makes a patient more at risk of metabolic demand, production of carbon dioxide and cardiovascular demand, thus making it harder to recover[1].

The gynecological surgical procedures are where PSAS is most prevalent due to the cold conditions of the operation room, making the patient more prone to the condition[2]. The prevention of shivering is absolutely necessary to guarantee safety and comfort of the patient during and after the surgery without the complications described[2]. PSAS affects 40-60 percent of patients

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worldwide, and in gynecological surgery close to 50 percent of the patients develop PSAS[3]. Post operative monitoring is complicated by shivering as they disrupt the accuracy of vital signs and slow recovery of patients[4].

The percentage of shivering by women is 40-50 percent under spinal anesthesia during gynecological and obstetric surgery in India. Although it has a high prevalence rate, there is not much continuity regarding the prevention measures in medical places. Management is further challenged because of the absence of uniform guidelines and awareness of effective managements particularly in the resource-limited settings. Hence, there is an urgent necessity to develop preventive strategies that will be cost-effective and easy to implement[5].

The pathophysiology of PSAS is multi-factorial. Spinal anesthesia affects thermoregulatory input between the peripheral nervous system and brain reducing the shivering threshold. Also intraoperative hypothermia is brought about by redistribution of heat core surface and application of cold IV fluid and equipment. These can explain why it is hard to prevent PSAS unless it is through specific sets of measures[6].

Drugs that act on PSAS have been efficacious in mitigating the frequencies and severity of PSAS. Promising candidates include mirtazapine, dexamethasone and tramadol:

1. Mirtazapine is an antidepressant acting on both noradrenergic and serotonergic activities. It inhibits alpha-2 adrenergic and serotonin (5-HT2 and 5-HT3) receptors and raises the levels of norepinephrine and serotonin in the brain. The actions influence thermoregulation of the hypothalamus, and it may minimize shivering. Mirtazapine is also anti-nausea and anti-anxiety with few mass studies available [7].
2. Dexamethasone is a glucocorticoid that enjoys extensive usage in view of its anti-inflammatory and antiemetic effects. It could assist in thermoregulation, slowing down the appearance of prolonged sensory block duration due to the decrease of inflammation. The results are positive, but there is still a need to perform additional studies to verify the effect on PSAS prevention. [7].
3. The most studied drug in treatment of PSAS is Tramadol, which is an opioid with added serotonergic and noradrenergic effects. It has continued to beat placebos and other agents according to cutting back shivering vigor and occurrence. Nevertheless, its secondary effects, especially nausea and vomiting should be reckoned with [7].

Nevertheless, these options are not associated with considerable comparative data concerning safety and efficacy of these agents. The majority of the studies are aimed at studying drugs separately, and dosing is inconsistent and most studies, and the study design is also inconsistent. More powerful randomized controlled trials are required to compare these drugs on a head-to-head basis [1-7].

In this study, the author attempts to close any such gaps by assessing comparisons of the effectiveness and safety of mirtazapine, dexamethasone and tramadol in the prevention of PSAS during gynaecological surgery. Findings would help formulate universal low-cost intervention strategies that can work across well-resourced health facilities and low-income health facilities [7]. At the end, the minimisation of PSAS will create better peri-operative conducted care, safer patient treatment, fewer postoperative adverse events, and these are some of the global priorities of enhancing surgical outcomes.

## METHODOLOGY

It is a randomized controlled study/trial which is being done to analyse the response of mirtazapine, dexamethasone and tramadol in the prevention of the post -spinal anaesthesia shivering (PSAS) in patients who are undergoing gynaecological surgical procedures. In making the study, the methods followed were those of the CONSORT guidelines to give credence to the methodological rigor and reliability of the findings.The trial was conducted in a tertiary care hospital in the Chengalpattu district in Tamil Nadu in India. The high diversity in patient population makes the hospital an adequate setting to judge the effectiveness of the interventions in the actual practice.The target population of the study was female patients aged between 20 to 45 years who had at least one gynaecological surgery scheduled to be done under the use of spinal anaesthesia.

All participants were asked to sign a document indicating their informed permission. Using a computer-generated random sequence in a 1:1:1 allocation ratio, participants were randomly divided into three groups. The research was authorised by the Institutional Ethics Committee with the number (873/2023). The CTRI trial registration was completed with the number (2023/12/060608): M Group: Administered intravenous placebo and 30 mg oral mirtazapine. D Group: A placebo pill and 8 mg of intravenous dexamethasone were given to this group. The C group got 0.5 mg/kg of intravenous tramadol and one placebo pill. Occupied, sealed envelopes were used to disguise the randomisation. Group assignments were kept secret from both patients and assessors.

Journal of Chemical Health Risks

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Preoperatively, we measured the patients' core body temperature and baseline haemodynamic parameters. 2 hours before to surgery, study medication is preemptively administered. Oral administration of 30 mg of mirtazapine, intravenous administration of 8 mg of dexamethasone diluted in 100 mL of normal saline over 15 minutes, or intravenous administration of 0.5 mg/kg of tramadol diluted in 100 mL of normal saline over 15 minutes are all acceptable options. Intrathecally given 2.5-3.5 mL of 0.5% hyperbaric bupivacaine was used to deliver spinal anaesthesia to all patients using a 25-gauge Quincke needle at the L3-L4 or L4-L5 interspace. The main result of the research was the frequency and intensity of shivering, which were evaluated using a 4-point scale. Our study's secondary endpoint is haemodynamic parameters, which include vital signs like pulse rate, blood pressure, and peripheral oxygen saturation (SpO2). Adverse symptoms, such nausea, vomiting, and itching, are also a part of the picture. For the first half an hour after anaesthesia, blinded anaesthesia residents measured shivering every 2–5 minutes; after that, they measured it every 10 minutes up to 90 minutes post-anesthesia. The statistical package SPSS (version 25) was used for data analysis. Mean ± standard deviation was used to represent continuous data, whereas frequencies and percentages were used to convey categorical variables. We used the following statistical tests: ANOVA for group comparisons, a chi-square test for categorical variables, and an independent t-test for continuous variables. Our threshold for significance was $p < 0.05$.

**Sample Size calculation:**

Previous research found that 31% of people using mirtazapine and 74% of people taking tramadol had shivering, therefore this information was used to determine the sample size using the EpiTools program. Taking into consideration a 10% nonresponse rate, the necessary sample size was calculated to be 28 participants per group, with a power of 80% and a significance level of 5%. The end result was 84 patients who were randomly assigned to one of three groups.

## RESULTS

The majority of participants (39.3%) were aged 20–30 years, with age evenly distributed across groups ($p = 0.815$), as shown in Table 1.

**Table 1: Age Distribution of Participants**

| Age Range (Years) | Total (%) | M Group (%) | D Group (%) | C Group (%) |
|---|---|---|---|---|
| 20–30 | 39.3 | 12 (42.9) | 10 (35.7) | 11 (39.3) |
| 31–40 | 41.7 | 10 (35.7) | 12 (42.9) | 13 (46.4) |
| >40 | 19.0 | 6 (21.4) | 6 (21.4) | 4 (14.3) |

Most participants weighed between 51–60 kg (50.0%), with no significant differences among groups ($p = 0.672$).Participants with BMI 25–30 kg/m² comprised 52.4% of the study population, distributed equally among groups ($p = 0.924$), as shown in Table 2.ASA Class I patients accounted for 71.4% of participants, with similar distributions across groups ($p > 0.05$).Baseline temperatures were primarily between 36.5–36.9°C (50.0%), with no intergroup differences observed ($p > 0.05$), as shown in Fig 1.

**Table 2: BMI Distribution of Participants**

| BMI (kg/m²) Range | Total (%) | M Group (%) | D Group (%) | C Group (%) |
|---|---|---|---|---|
| <25 | 32.1 | 10 (35.7) | 8 (28.6) | 9 (32.1) |
| 25–30 | 52.4 | 14 (50.0) | 16 (57.1) | 14 (50.0) |
| >30 | 15.5 | 4 (14.3) | 4 (14.3) | 5 (17.9) |

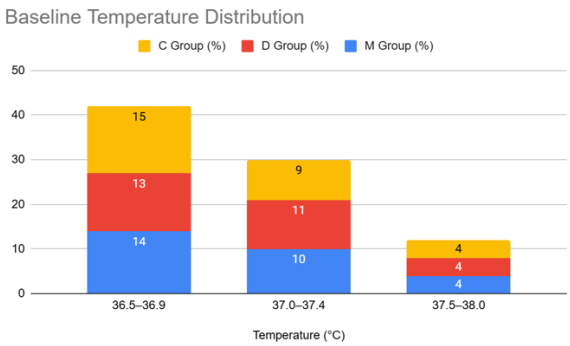


**Figure :1 Baseline Temperature Distribution**

Mirtazapine prevented shivering in 78.6% of participants compared to 71.4% for dexamethasone and 53.6% for tramadol ($p = 0.034$), as shown in Fig 2. Mean heart rate remained stable across groups, with baseline HR around 78 bpm and no significant differences post-anaesthesia ($p > 0.05$), as shown in Table 3.

Journal of Chemical Health Risks

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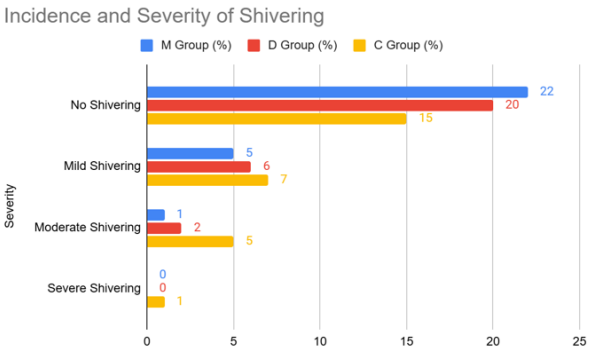



**Figure 2: Incidence and Severity of Shivering**

**Table 3: Heart Rate (HR) Trends**

| Time Interval (min) | M Group (Mean ± SD) | D Group (Mean ± SD) | C Group (Mean ± SD) |
|---|---|---|---|
| Baseline | 78.4 ± 6.2 | 76.8 ± 7.1 | 79.1 ± 6.5 |
| Post-Spinal (5 min) | 74.3 ± 5.9 | 73.9 ± 6.2 | 76.7 ± 6.4 |
| Post-Spinal (30 min) | 72.1 ± 6.0 | 72.5 ± 5.8 | 74.8 ± 5.7 |
| Post-Spinal (90 min) | 70.6 ± 5.7 | 71.3 ± 5.9 | 72.9 ± 5.6 |

Nausea occurred in 28.6% of the tramadol group versus 10.7% for mirtazapine and 14.3% for dexamethasone (p = 0.042). Rescue therapy was required by 7.1% of the mirtazapine group, compared to 10.7% for dexamethasone and 25.0% for tramadol (p = 0.031).Mirtazapine had the lowest shivering incidence (78.6%), lowest adverse effects (17.9%), and longest time to rescue therapy (40.3 ± 10.5 min), as shown in Fig 3 and Table 4.

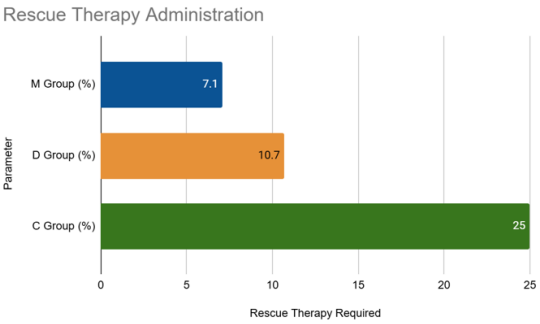
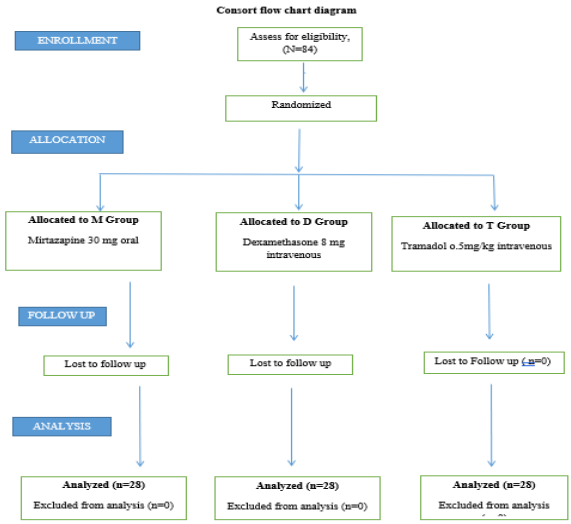



**Figure 3: Rescue Therapy Administration**

**Table 4: Summary of Comparative Outcomes**

| Parameter | M Group | D Group | C Group | p-value |
|---|---|---|---|---|
| Incidence of shivering (%) | 78.6 | 71.4 | 53.6 | 0.034 |
| Mean severity score | 0.24 ± 0.5 | 0.36 ± 0.7 | 0.72 ± 1.1 | 0.041 |
| Hemodynamic stability | Stable | Stable | Stable | >0.05 |
| Adverse effects (%) | 17.9 | 18.6 | 35.7 | 0.029 |

**Consort flow chart diagram**




## DISCUSSION

The purpose of this research was to evaluate tramadol, dexamethasone, and mirtazapine for their ability to curb gynaecological surgery post-spinal anaesthesia shivering (PSAS). Each of the three therapy groups was comprised of patients who were statistically similar to one another with respect to age, weight, body mass index (BMI), ASA status, and temperature at baseline. The majority of participants were between 20 and 40 years of age, evenly distributed across groups: 42.9% in the mirtazapine group (M), 35.7% in dexamethasone (D), and 39.3% in tramadol (C). Controlling for age was crucial since thermoregulation is age-sensitive. Esmat et al. also

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reported similar demographic matching in prior mirtazapine research[8].

In terms of weight, 50% of participants fell within the 51–60 kg range, with a balanced distribution among the groups (M: 53.6%, D: 46.4%, C: 50%)[9]. BMI distribution was also even, with 52.4% of participants falling between 25 and 30 kg/m². Most patients were overweight but not obese, aligning with BMI's influence on surface area-to-volume ratio, a key factor in shivering. These distributions match findings by Tsai and Chu on BMI's role in shivering during anesthesia[87]. Heart rate (HR) was recorded at baseline, 5, 30, and 90 minutes after spinal anesthesia. All groups showed gradual HR decline due to sympathetic blockade. Baseline HRs were similar (M: 78.4 ± 6.2, D: 76.8 ± 7.1, C: 79.1 ± 6.5 bpm), and there were no significant differences over time. These results indicate all three drugs are safe regarding hemodynamic response, aligning with prior studies by Mathews et al. and Tsai et al.[9,10].

Most patients (71.4%) had ASA I physical status, evenly split across the three arms (M: 75%, D: 71.4%, C: 67.9%). This consistency in health status reduced confounding from comorbidities like cardiovascular or metabolic conditions. Similarly, baseline body temperatures were comparable across groups, mostly between 36.5°C and 36.9°C[11]. This consistency minimized temperature-related bias and supported fair comparison of drug performance.Shivering rates differed significantly between groups. Mirtazapine was most effective, with 78.6% of patients experiencing no shivering. Dexamethasone followed at 71.4%, while tramadol was least effective at 53.6%. Shivering in the tramadol group was more frequent and moderate, with one case (3.6%) of severe shivering. These findings support earlier conclusions by Esmat et al. on mirtazapine's prophylactic potential. Dexamethasone's efficacy likely results from its anti-inflammatory effects, while tramadol's shorter duration and variable response limit its utility.

Tramadol was associated with the highest rate of adverse effects: 25% of patients experienced sedation, 14.3% had pruritus, and several reported nausea or vomiting. In contrast, mirtazapine caused sedation in 17.9% but no pruritus. Dexamethasone had the fewest side effects overall, with only 10.7% reporting sedation and 3.6% reporting pruritus. These side effect profiles reflect known pharmacologic differences—tramadol's serotonergic action often leads to nausea and itching, while mirtazapine and dexamethasone offer antiemetic and anti-inflammatory benefits.Fewer patients in the mirtazapine group (7.1%) required rescue treatment for shivering, compared to 10.7% in dexamethasone and 25% in tramadol. Furthermore, the need for rescue came much later in the mirtazapine group (40.3 ± 10.5 minutes) compared to tramadol (28.9 ± 11.3 minutes), indicating that mirtazapine has a longer-lasting protective effect. The results are consistent with what was found by Anttila et al. and Sheen et al. [12,13].

Based on a review of the main results, mirtazapine accounted for 78.6% of the total effectiveness in treating PSAS, with dexamethasone coming in second at 71.4% and tramadol third at 53.6%. Mirtazapine exhibited the least severe bleeding (0.24 ± 0.5), dexamethasone moderate (0.36 ± 0.7), and tramadol the most severe (0.72 ± 1.1). Hemodynamic stability was observed across all groups, but tramadol led in side effects. In conclusion, **mirtazapine was the most effective and well-tolerated option for preventing PSAS**, followed by **dexamethasone**, with **tramadol being the least favorable** due to higher side effects and shorter duration of action. These findings support the integration of mirtazapine or dexamethasone into clinical protocols for PSAS prevention in gynecologic surgeries.

## CONCLUSION

Results show that tramadol, dexamethasone, and mirtazapine all work well to reduce post-spinal anaesthesia shivering (PSAS) in gynaecological surgery patients, although they all have different safety records and levels of effectiveness. Mirtazapine emerged as the most effective option, significantly reducing the incidence and severity of shivering (78.6% no shivering) while maintaining a favourable safety profile, including minimal adverse effects and the least need for rescue therapy. Dexamethasone, while slightly less effective in shivering prevention, offered additional benefits such as improved postoperative recovery and anti-inflammatory properties, making it a valuable alternative. Tramadol, despite its rapid onset, showed higher rates of adverse effects and moderate-to-severe shivering, which may limit its use in certain populations.

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