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Original Article

Pharmacology Section

Pattern of Adverse Drug Reactions Linked to Anaesthetic Agents Used for Regional Anaesthesia: A Prospective Observational Study from a Tertiary Care Teaching Hospital in South Assam, India

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ABSTRACT

Introduction: Regional Anaesthesia (RA) is widely employed across surgical specialities owing to its benefits for perioperative analgesia, haemodynamic stability, and reduced Postoperative Nausea and Vomiting (PONV). Despite these advantages, Adverse Drug Reactions (ADRs) linked to Local Anaesthetics (LAs) and their adjuvants remain an important consideration, particularly in settings with limited pharmacovigilance resources.

Aim: To determine the incidence and study the pattern, causality, and severity of adverse drug reactions associated with anaesthetic agents used in regional anaesthesia in a tertiary care teaching hospital in South Assam, India.

Materials and Methods: A prospective, observational study was conducted at the Department of Pharmacology in collaboration with the Department of Anaesthesiology in Silchar Medical College and Hospital, Silchar, Assam, India, from November 2023 to October 2024, among 385 adult patients who underwent surgery under RA. ADRs occurring within 24 hours of RA administration were identified through direct clinical observation, patient interviews, and review of medical records. Causality was evaluated using the World Health Organisation–Uppsala Monitoring Centre (WHO–UMC) Causality Assessment Scale, while severity was categorised according to the Hartwig and Siegel Severity Assessment Scale. Data were summarised using descriptive statistics. Data were summarised using descriptive statistics in Microsoft® Excel® 2021 (version 2604, 64-bit).

Results: Out of 385 patients monitored, 54 patients experienced a total of 54 ADRs during the study period, representing an overall ADR incidence of 14.03%. Hypotension was the most commonly reported ADR, 28 (51.85%), followed by PONV 12 (22.22%). The majority of ADRs occurred within the first six hours after RA administration 46 (85.18%). Hyperbaric bupivacaine accounted for the greatest proportion of ADRs, 42 (77.78%), followed by ropivacaine heavy (11.11%). According to WHO-UMC criteria, most ADRs were classified as "possible" (94.44%), while a smaller proportion were deemed "probable" (1.85%). All ADRs were categorised as mild based on Hartwig's severity scale.

Conclusion: ADRs associated with RA in this cohort were generally mild, occurred early, and were most frequently linked to hyperbaric bupivacaine. Although no severe reactions were observed, these findings underscore the importance of early postoperative monitoring, judicious drug selection, and strengthened pharmacovigilance to support patient safety.

Keywords: Causality assessment, Hartwig severity scale, Pharmacovigilance, Treatment outcome

INTRODUCTION

Pharmacovigilance is defined by the World Health Organisation (WHO) as the science and activities concerned with the detection, assessment, understanding, and prevention of Adverse Drug Reactions (ADRs) and other drug-related problems [1]. It plays a crucial role in ensuring patient safety, improving therapeutic outcomes, and promoting the rational use of medicines. Spontaneous reporting systems form the backbone of pharmacovigilance by enabling early detection of safety signals and identification of previously unrecognised adverse effects. In India, the Pharmacovigilance Programme of India (PvPI) was launched in 2010 by the Ministry of Health and Family Welfare (MoHFW) to monitor ADRs and safeguard public health [2]. The program is coordinated by the Indian Pharmacopoeia Commission, which serves as the National Coordination Centre. PvPI functions through a network of ADR Monitoring Centres (AMCs) across the country, facilitating the collection, analysis, and reporting of ADR data. Furthermore, it contributes to the global pharmacovigilance database maintained by the WHO-UMC, thereby strengthening international drug safety surveillance [3].

Regional anaesthesia has become a central element of contemporary perioperative practice because of its recognised advantages, which include superior analgesia, reduced postoperative nausea and vomiting, earlier mobilisation, and improved patient satisfaction when compared with general anaesthesia [4]. Progress in the field, particularly with the wider use of ultrasound guidance, fascial plane techniques, and catheter-based approaches, has broadened the scope and safety of regional techniques, allowing their application across a range of surgical populations [5]. Evidence from nationwide surveys in India similarly indicates a steady rise in the use of regional anaesthesia in clinical practice [5,6].

Despite these benefits, regional anaesthesia is not free from drug-related risks. LAs and various adjuvant agents can lead to adverse drug reactions. The WHO defines an adverse drug reaction as a harmful and unintended response to a medicine given at standard therapeutic doses [7]. Anaesthesiologists are particularly likely to encounter such reactions because multiple drugs are administered in a short period and the physiological responses of patients under anaesthesia may alter the presentation of early warning signs [8]. ADRs may range from minor cutaneous manifestations to serious events such as

anaphylaxis, cardiovascular compromise, or Local Anaesthetic Systemic Toxicity (LAST) [8,9].

The incidence of anaesthesia-related ADRs is often cited as between one in ten thousand and one in twenty thousand, with a reported mortality approaching 10% [8]. These figures may underestimate the true burden, partly because of under-reporting and the masking of early clinical indicators in anaesthetised patients; it remains a rare but serious complication. Its estimated incidence varies from 0.03% to 1.8 per one thousand blocks and depends on the drug, its dosage, and the technique employed [9,10]. Presentations may involve neurological or cardiovascular disturbances, and atypical patterns are well described, which can delay recognition and timely treatment [9,10].

Neurological adverse events following regional anaesthesia, although uncommon, are clinically important. They may result from needle trauma, intraneural injection, neurotoxicity, haematoma, or infection. Most are temporary, but persistent deficits have occasionally been reported [11]. Even with ultrasound guidance, which has improved accuracy and safety, complications such as vascular puncture, infection, nerve injury, allergic reactions, and systemic toxicity may still occur [12].

While international literature provides extensive insights into adverse events associated with regional anaesthesia, there is comparatively limited information from India [5,13-15]. Variations in institutional practice, technique, patient demographics, and resource availability may influence the occurrence and reporting of ADRs. Understanding the local pattern of these reactions is therefore critical for strengthening pharmacovigilance and improving patient safety.

The present prospective study was undertaken in a tertiary care teaching hospital in South Assam to assess the incidence and pattern of ADRs associated with anaesthetic agents used in regional anaesthesia, with particular emphasis on their type, causality, and severity.

MATERIALS AND METHODS

A prospective, observational study was conducted at the Department of Pharmacology in collaboration with the Department of Anaesthesiology in Silchar Medical College and Hospital, Silchar, Assam, India, from November 2023 to October 2024. Patients were recruited at the preoperative stage from the Departments of General Surgery, Obstetrics and Gynaecology, and Orthopaedics, scheduled to undergo operative procedures under regional anaesthesia. Ethical approval for the research was officially granted by the Institutional Ethics Committee (IEC) of Silchar Medical College and Hospital during its committee meeting held in October 2023 (IEC approval number: SMC/ETHICS/M2/2023/71) prior to the initiation of study recruitment in November 2023. Written, voluntary informed consent was obtained from all participants in English or the local vernacular language according to IEC guidelines. Confidentiality and anonymity were ensured throughout, and all data were anonymised before entry into the study database.

Inclusion criteria: During the study period, all patients who underwent Operative Theatre (OT) procedures under RA were systematically assessed for eligibility. To be included in the study, patients were required to have their surgeries performed under specific regional anaesthetic techniques, namely spinal anaesthesia, epidural anaesthesia, or a supraclavicular block. Additionally, eligible participants had to demonstrate a willingness to provide written, voluntary informed consent. From a clinical health standpoint, inclusion was strictly limited to patients classified as either American Society of Anaesthesiologists (ASA) physical status I (a normal, healthy patient) or ASA II (a patient with mild systemic disease without functional limitations), according to the ASA Physical Status Classification System [16].

Exclusion criteria: Conversely, the study established strict exclusion criteria to eliminate confounding factors and ensure participant safety. Patients undergoing surgery under general anaesthesia were excluded, as were those receiving infiltration blocks or undergoing purely diagnostic procedures. Due to the unique physiological changes and safety considerations associated with pregnancy and breastfeeding, pregnant or lactating women were also barred from participation. Finally, any patient who demonstrated an unwillingness to provide written, voluntary informed consent was excluded from the study.

Sample size calculation: Sample size was calculated using Daniel's formula [17]:

$N = [Z^2 \times p(1-p)] / d^2$, with Z set at 1.96 corresponding to a 95% confidence level, p assumed at 0.5, and the margin of error (d) at 0.05. The calculated sample size was 384.16, which was rounded to 385. A total of 385 patients undergoing a variety of surgical procedures under RA were therefore included in the final analysis.

Study Procedure

The approach was selected to capture real-world patterns of use of anaesthetic agents in RA and to identify any ADRs associated with these agents in routine clinical practice. After administration of the anaesthetic agent, each patient was observed continuously in the OT for any immediate adverse manifestations. Monitoring continued in the recovery area and wards for up to 24 hours postoperatively. During this period, members of the research team assessed each patient for suspected ADRs through direct observation, review of clinical records, interviews with patients, and monitoring of vital parameters. For every suspected adverse drug reaction, details regarding its onset and clinical features and parameters (blood pressure, heart rate, oxygen saturation, postoperative temperature, respiratory rate, headache, backache, any limb weakness) were recorded. Causality was evaluated using the WHO-UMC Causality Assessment Scale [18], (categories are: Certain, Probable/Likely, Possible, Unlikely, Unclassified and • Unclassifiable) and Severity was assessed using the Hartwig and Siegel Severity [19] based on the level of clinical intervention required and the effect on patient outcomes. Assessment scale as follows

- Level 1: ADR requiring no change in treatment;
- Level 2: ADR requiring the suspected drug to be withheld, discontinued, or otherwise changed, with no antidote or additional treatment required and no increase in hospital stay;
- Levels 3–4 (Moderate): ADR requiring additional treatment and/or resulting in prolonged hospitalisation;
- Levels 5–7 (Severe): ADR requiring intensive medical care, resulting in permanent harm, or contributing to death.

STATISTICAL ANALYSIS

All collected data were entered into Microsoft Excel 2021 MSO (Version 2604 Build 16.0.19929.20172) 64-bit, cleaned, and tabulated. Frequencies and percentages were calculated using Microsoft Excel 2021. Continuous variables were expressed as Mean ± Standard Deviation (SD).

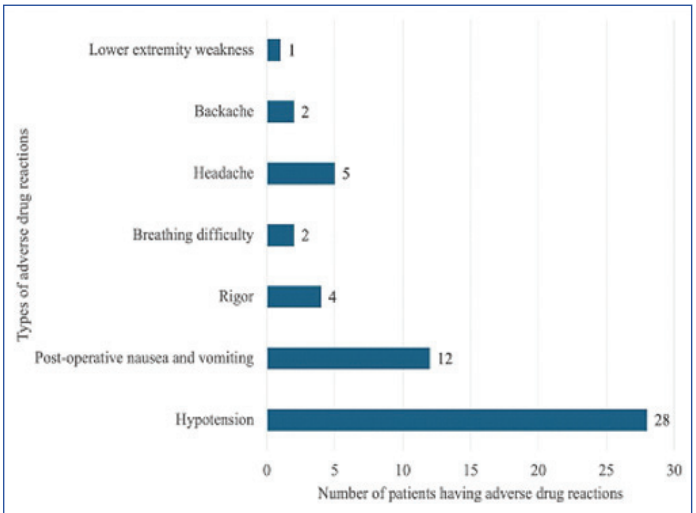
RESULTS

Mean age of the patients was 39.49±17.39 years. Female patients were 194 (50.39%) and male patients were 191 (49.61%). The OT procedures like fracture repair, fibroid and uterovaginal prolapse repair, recurrent appendicitis with inguinal hernia repair were performed in Orthopaedics, Gynaecology and General Surgery OTs respectively under supraclavicular, spinal and epidural anaesthesia.

Out of 385 patients monitored, 54 patients experienced ADRs during the study period, among patients who received RA and

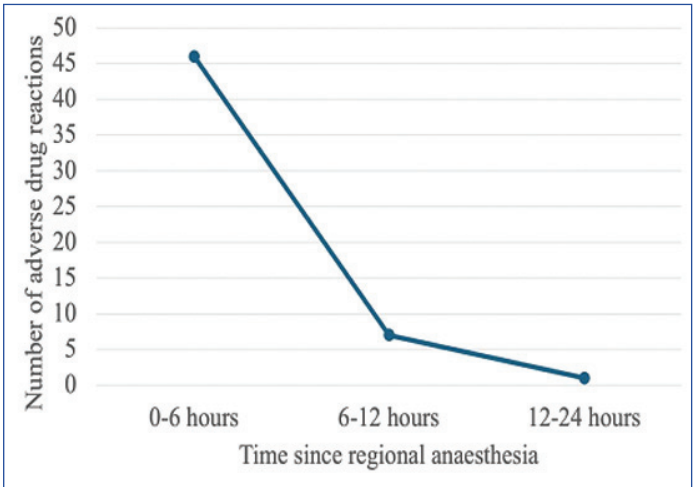
resolved without the need for significant intervention, representing an overall ADR incidence of 14.03%.

Types of ADRs: Hypotension was the most frequently documented reaction, accounting for 51.85% of all events (n=28). This was followed by postoperative nausea and vomiting, which contributed 22.22% of reactions. The overall distribution of ADRs is depicted in [Table/Fig-1].



[Table/Fig-1]: Distribution of types of ADRs associated with anaesthetic agents used in RA.

Time of onset of ADRs: Most reactions occurred within the first six hours (0-6 hours) following administration of RA, representing 46 (85.18%) of the total (n=54). 7 (12.96%) ADRs, developed between 6-12 hours postoperative period, and only 1 (1.85%) ADR developed between 12-24 hours postoperatively. These findings are presented in [Table/Fig-2].



[Table/Fig-2]: Distribution of ADRs according to time since administration of RA.

ADRs attributable to primary anaesthetic agents: Hyperbaric bupivacaine (Avg. dose-5 mg/mL (3.3 mL)…Intrathecal route… frequency once) was associated with the majority of ADRs 42, (77.78%). Ropivacaine heavy (7.5 mg/mL, 3.5 mL administered intrathecally once accounted for a further six reactions (11.11%). The complete distribution of reactions in relation to the primary anaesthetic agent is summarised in [Table/Fig-3].

Causality assessment: According to the WHO-UMC Causality Assessment Scale, most reactions were classified as possible 51 (94.44%). No reaction was categorised as certain. The detailed causality profile is shown in [Table/Fig-4].

Severity assessment: All 54 ADRs were graded as mild on the Hartwig and Siegel Severity Assessment Scale. No moderate or severe reactions were observed. The severity assessment is presented in [Table/Fig-5].

DISCUSSION

In the present prospective evaluation of ADRs associated with RA, out of 385 patients monitored, 54 patients experienced a total of 54 ADRs during the study period, representing an overall ADR incidence of 14.03%. Most of these were mild and resolved without the need for significant intervention. Hypotension emerged as the most frequent reaction, 28 (51.85%), a finding that aligns well with established literature demonstrating that sympathetic blockade from neuraxial techniques commonly leads to vasodilatation and haemodynamic instability [4,5]. The predominance of hypotension in the present study may also be linked to the extensive use of hyperbaric bupivacaine, which is known to produce a dense sympathetic block and dose-dependent cardiovascular effects [9]. PONV was the second most common reaction, consistent with earlier observations that it can occur even with RA in the presence of hypotension, opioid adjuvants, or individual patient susceptibility [4,8]. One ADR (and not multiple) was reported per patient, and hence the manuscript uses patients and ADRs interchangeably for the Figure 4 and Figure 5.

Most reactions, 46 (85.18%), were observed within the first six hours after RA was administered, underscoring the need for heightened monitoring during this early postoperative period. This observation supports the guidance from the American Society of Regional Anaesthesia and Pain Medicine (ASRA), which highlights the immediate post-block phase as a period of increased risk for haemodynamic and neurological instability [20]. Hyperbaric Bupivacaine accounted for the largest proportion of reactions, reflecting its well-documented pharmacological profile and evidence from previous studies that report higher rates of haemodynamic changes and potential systemic toxicity, particularly when inadvertent intravascular injection occurs [9,21]. Although ropivacaine is recognised to have a more favourable cardiotoxicity profile than bupivacaine, it was not entirely free of adverse reactions in the present study. This finding is in keeping with evidence that all LA agents may produce adverse effects depending on the administered dose, the technique employed, and patient-specific factors [22].

Causality assessment using the WHO-UMC scale classified 51 (94.44%) of reactions as “possible”, reflecting the interplay of surgical, clinical, and pharmacological variables that may obscure definitive attribution in the perioperative setting [8,12]. Similarly, severity grading using the Hartwig scale revealed that all reactions were mild, with no moderate or severe events recorded. Although this differs from reports describing a small but meaningful incidence of serious complications such as LAST, the absence of such events in the current study is consistent with literature indicating that severe reactions are uncommon when RA is administered in well-monitored clinical environments [9,21,23]. Macfarlane and colleagues have emphasised the importance of prompt recognition and lipid emulsion therapy in the management of LAST, while ASRA guidance [20] further stresses the necessity of structured monitoring protocols and preparedness for emergencies in RA

ADR type	Bupivacaine heavy	Ropivacaine heavy	Isobaric ropivacaine	Ropivacaine + lignocaine	Ropivacaine + lignocaine + adrenaline	Total
Hypotension	28	0	0	0	0	28
PONV	8	3	0	1	0	12
Rigor	1	1	0	2	0	4

Breathing difficulty	0	2	0	0	0	2
Headache	4	0	0	0	1	5
Backache	0	0	1	0	1	2
Lower extremity weakness	1	0	0	0	0	1
Total	42	6	1	3	2	54

[Table/Fig-3]: Distribution of ADRs attributable to the primary anaesthetic agent used.
PONV: Postoperative nausea and vomiting

Causality category	n (%)
Certain	0
Probable	1 (1.85%)
Possible	51 (94.44%)
Unlikely	2 (3.70%)
Total	54 (100%)

[Table/Fig-4]: Distribution of ADRs based on WHO–UMC causality assessment.

Severity category	n (%)
Mild (Level 1–2)	54 (100%)
Moderate (Level 3–4)	0
Severe (Level 5–7)	0
Total	54 (100%)

[Table/Fig-5]: Distribution of ADRs based on Hartwig's severity assessment scale.

practice [21,23]. Taken together, the pattern of reactions observed in the present study mirrors findings from national and international reports, reinforcing that RA is generally safe when performed by trained practitioners with adherence to recommended monitoring and safety standards. The apparent discrepancy between the incidence of anaesthesia-related ADRs reported in the literature (approximately 1 in 10,000 to 1 in 20,000 anaesthetic administrations) [8] and the incidence observed in the present study, 54/385 (14.0%), arises primarily from differences in case definitions and outcome measures. The published estimates [8-10] generally refer to rare, severe, and life-threatening anaesthesia-related reactions such as perioperative anaphylaxis, LAST, or other major drug-induced complications. In contrast, the present study employed active surveillance and included all suspected ADRs occurring during the perioperative period, including common and expected pharmacological effects such as Hypotension, PONV, Rigour, Breathing difficulty, Headache, Backache, Lower extremity weakness, etc., that fulfilled ADR reporting criteria. Consequently, the higher incidence observed in the current study reflects the broader spectrum of ADRs captured rather than an increased occurrence of serious anaesthesia-related drug reactions. The strengths of the present study include its prospective design, systematic assessment of ADRs using validated WHO-UMC and Hartwig scales, and its conduct in a busy tertiary care teaching hospital where findings reflect real-world clinical practice.

Limitation(s)

Several limitations of the study must also be acknowledged, including its single centre design, relatively short follow-up period of 24 hours, and the exclusion of high-risk patients, which may limit generalisability and under represent delayed or rare reactions. From a clinical perspective, the findings highlight the importance of vigilant early postoperative monitoring, especially during the first six hours after block administration, careful dose selection when using local anaesthetic agents, and strengthening Institutional pharmacovigilance systems. Adoption of ASRA-recommended safety practices, including preparedness for local anaesthetic systemic toxicity and wider use of ultrasound guidance, may further enhance the safety of RA. Future research should focus on multicentric studies with longer follow-up, assessment of safer adjuvant strategies, and development of digital reporting systems to support stronger pharmacovigilance and improve patient outcomes.

CONCLUSION(S)

In the prospective study, after evaluating ADRs associated with RAs, we conclude that most reactions were mild, occurred early after administration, and were predominantly linked to hyperbaric bupivacaine. Although serious events such as LAST were not encountered, the findings reinforce the need for vigilant early monitoring, cautious dose selection, and adherence to established safety protocols to optimise patient outcomes. Strengthening pharmacovigilance practices and adopting guideline-driven monitoring frameworks may further enhance the safety profile of RA in similar clinical settings.

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