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REVIEWER'S REPORT

Manuscript No.: IJAR-56522

Title: A Fatal Case Of Bupivacaine Induced Central Nervous System Toxicity Presenting As Super Refractory Status EpilepticusÂ : Case Report

Recommendation:

Accept as it is .....

Accept after minor revision.....

Accept after major revision .....YES.....

Do not accept (*Reasons below*) .....

Rating	Excel.	Good	Fair	Poor
Originality		√		
Techn. Quality			√	
Clarity				√
Significance		√		

Reviewer's ID: JPR-094

Detailed Reviewer's Report

Reviewer's Report

1. Strengths of the Manuscript

Rare clinical presentation

The manuscript describes a rare complication of intrathecal Bupivacaine resulting in **super-refractory Status Epilepticus**, which has been reported only in a few cases in literature.

Severe and unusual outcome

Unlike most reported cases where patients recovered, this case resulted in **fatal outcome with multi-organ complications** including:

Rhabdomyolysis

This adds clinical value and highlights the potential severity of LAST.

Detailed clinical timeline

The case description provides chronological clinical events including ICU management, EEG findings, laboratory parameters, and pharmacological treatment.

ISSN(O): 2320-5407 | ISSN(P): 3107-4928
International Journal of Advanced Research
Publisher's Name: Jana Publication and Research LLP
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Clinical relevance

The report raises awareness among anesthesiologists and critical care physicians regarding **rare but potentially fatal complications of spinal anesthesia**.

Literature support

The discussion cites previous case reports and provides context regarding the incidence and pathophysiology of LAST.

2. Weaknesses of the Manuscript

Language and grammatical issues

The manuscript contains numerous grammatical errors, inconsistent punctuation, and typographical mistakes which affect readability and professionalism.

Abstract not properly structured

The abstract does not fully follow the recommended structured format (Background, Case Presentation, Outcome, Conclusion).

Formatting inconsistencies

Spacing errors and inconsistent units

Repeated references (e.g., reference duplication)

Inconsistent drug formatting (e.g., "Injection phenytoin 500mg").

Insufficient differential diagnosis discussion

Although some differential diagnoses are mentioned, the manuscript should better discuss exclusion of conditions such as:

Malignant Hyperthermia

Thyroid Storm

Pheochromocytoma

ISSN(O): 2320-5407 | ISSN(P): 3107-4928
International Journal of Advanced Research
Publisher's Name: Jana Publication and Research LLP
www.journalijar.com

Limited pathophysiological explanation

The discussion on mechanisms of CNS toxicity from intrathecal bupivacaine is brief and could be expanded with more recent references.

Figures and imaging details unclear

The manuscript refers to EEG figures but they are not described in sufficient detail.

Speculative statements

The suggestion that drug impurity might have caused toxicity is speculative and not supported by laboratory evidence.

3. Significance of the Study

This case report is **clinically significant** because it highlights a rare and severe neurological complication following spinal anesthesia with Bupivacaine.

The report emphasizes:

Early recognition of Local Anesthetic Systemic Toxicity

Importance of rapid administration of lipid emulsion therapy

Need for advanced ICU support in cases of refractory seizures

The fatal outcome further stresses the **unpredictable nature of LAST even with standard dosing**.

4. Recommendation

Decision: Major Revision

Reasons for Major Revision

Significant language and grammar correction required.

Abstract needs restructuring according to journal guidelines.

Discussion section requires expansion with updated literature.

ISSN(O): 2320-5407 | ISSN(P): 3107-4928
International Journal of Advanced Research
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REVIEWER'S REPORT

Figures and EEG descriptions should be improved.

After addressing these issues, the manuscript may become suitable for publication as a **rare fatal case report of bupivacaine-induced CNS toxicity**.

Overall Recommendation:
Major Revision before reconsideration for publication.

Justification for Major Revision

Title (Line 1–2)

Issue:
Title formatting and grammar problems; unnecessary capitalization and spacing.

Justification:
Scientific titles must follow standard formatting and clarity. The title should also include "case report" clearly and avoid inconsistent capitalization.

Abstract

Line 5

Issue:
"Use of local anaesthetic agent for spinal anaesthesia is routinely done…" is grammatically weak and lacks scientific precision.

Justification:
The opening sentence should clearly present the clinical background of Local Anesthetic Systemic Toxicity with proper academic language.

Line 6–7

ISSN(O): 2320-5407 | ISSN(P): 3107-4928
International Journal of Advanced Research
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www.journalijar.com

REVIEWER'S REPORT

Issue:
Sentence structure is unclear and punctuation errors are present.

Justification:
The statement about toxicity occurring despite appropriate dosage requires clearer wording and literature support.

Line 7–9

Issue:
The abstract lacks structured format (Background, Case presentation, Outcome, Conclusion).

Justification:
Most medical journals require a structured abstract following CARE reporting guidelines for case reports.

Line 9

Issue:
"central nervous system toxicity manifesting as super refractory status epilepticus" lacks citation and clearer description.

Justification:
Rare presentations like super-refractory Status Epilepticus require supporting literature in introduction and

Line 10

Issue:
Complications listed without clinical context.

Justification:
Conditions such as

Rhabdomyolysis

ISSN(O): 2320-5407 | ISSN(P): 3107-4928
International Journal of Advanced Research
Publisher's Name: Jana Publication and Research LLP
www.journalijar.com

REVIEWER'S REPORT

Acute Kidney Injury

Acute Respiratory Distress Syndrome

should briefly explain their relationship with prolonged seizures or toxicity.

Line 11

Issue:
Phrase "patient couldn't be saved" is not appropriate scientific language.

Justification:
Medical manuscripts should use formal wording such as "the patient expired despite intensive management."

Line 12–13

Issue:
Conclusion sentence is vague and lacks clinical insight.

Justification:
The abstract conclusion should highlight the **clinical lesson and importance of early recognition and management of LAST**.

Keywords (Line 16)

Issue:
Keywords are not formatted as per indexing standards.

Justification:
Keywords should include standardized medical terms such as:

Bupivacaine

ISSN(O): 2320-5407 | ISSN(P): 3107-4928
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REVIEWER'S REPORT

Local Anesthetic Systemic Toxicity

Status Epilepticus

for better indexing in databases.

Introduction

Line 19–21

Issue:
Introduction is very brief and lacks epidemiological data.

Justification:
The introduction should include incidence and clinical significance of Local Anesthetic Systemic Toxicity.

Line 23

Issue:
Statement regarding "only 7 case reports" lacks comprehensive literature review.

Justification:
Rare complication claims must be supported by updated systematic literature review.

Case History

Line 28

Issue:
Geographical information ("sub district hospital in Kashmir") may not be necessary.

ISSN(O): 2320-5407 | ISSN(P): 3107-4928
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REVIEWER'S REPORT

Justification:

Case reports should focus on clinical details rather than unnecessary location identifiers.

Line 29

Issue:

Body mass index formatting incorrect.

Justification:

Standard format should be used (kg/m²).

Line 33

Issue:

Sentence incomplete regarding ASA grading.

Justification:

The statement describing ASA classification must be grammatically complete.

Line 37–38

Issue:

Dose of Bupivacaine is mentioned but rationale is missing.

Justification:

Authors should explain whether the dose was within recommended safety limits.

Line 39–40

Issue:

Clinical symptoms are described but differential diagnosis is not considered.

ISSN(O): 2320-5407 | ISSN(P): 3107-4928
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www.journalijar.com

REVIEWER'S REPORT

Justification:

Symptoms like agitation and myoclonus may also be seen in conditions such as:

Malignant Hyperthermia

Thyroid Storm

Pheochromocytoma

These should be discussed.

Line 41–43

Issue:

Drug administration details are poorly formatted.

Justification:

Drug names, doses, and routes must follow standardized clinical reporting style.

Line 44

Issue:

Airway management description incomplete.

Justification:

The reason for intubation and sedation protocol should be clearly stated.

Line 52–54

Issue:

Laboratory values presented without interpretation.

Justification:

Authors should interpret ABG findings such as metabolic acidosis.

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REVIEWER'S REPORT

Line 56

Issue:

Dose and administration protocol of lipid emulsion unclear.

Justification:

Guidelines for treating LAST recommend specific dosing protocols which should be referenced.

Line 59–61

Issue:

EEG findings are mentioned but figure explanation is inadequate.

Justification:

EEG images should include detailed captions and interpretation.

ICU Course

Line 67–71

Issue:

Clinical deterioration described but pathophysiological explanation insufficient.

Justification:

The relationship between prolonged seizures and organ failure needs clarification.

Line 77–78

Issue:

Diagnosis of Acute Respiratory Distress Syndrome not explained.

Justification:

Diagnostic criteria for ARDS should be mentioned.

ISSN(O): 2320-5407 | ISSN(P): 3107-4928
International Journal of Advanced Research
Publisher's Name: Jana Publication and Research LLP
www.journalijar.com

REVIEWER'S REPORT

Line 83–84

Issue:

Cause of death described vaguely.

Justification:

Authors should clarify whether death resulted from multi-organ failure, refractory seizures, or severe toxicity.

Discussion

Line 88–89

Issue:

Incidence data lacks proper citation formatting.

Justification:

Statistical information must be supported by recent literature.

Line 94–96

Issue:

Mechanism of CNS toxicity insufficiently explained.

Justification:

Discussion should elaborate on pharmacological neurotoxicity of Bupivacaine.

Line 114–115

Issue:

Differential diagnoses briefly listed but not discussed.

ISSN(O): 2320-5407 | ISSN(P): 3107-4928
International Journal of Advanced Research
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REVIEWER'S REPORT

Justification:

Conditions like:

Malignant Hyperthermia

Thyroid Storm

Pheochromocytoma

should be systematically ruled out.

Line 131–133

Issue:

Literature review on previous cases is limited.

Justification:

Comparison with previous reported cases should be expanded.

Line 144–146

Issue:

Speculative explanations (drug impurity, lack of ECMO) lack supporting evidence.

Justification:

Scientific discussions must avoid unsupported speculation.

Conclusion (Line 161–166)

Issue:

Conclusion contains grammatical errors and speculative statements.

ISSN(O): 2320-5407 | ISSN(P): 3107-4928
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REVIEWER'S REPORT

Justification:
Conclusions should focus on key clinical lessons rather than hypothetical causes such as drug impurity.

References

Issue:

Some references outdated

Inconsistent citation style

Formatting errors

Justification:
References must follow journal formatting guidelines and include recent literature.

CARE Checklist

Issue:
CARE checklist marked "Yes" for several items that are not fully addressed.

Justification:
Authors must verify compliance with CARE guidelines before submission.

Overall Reason for Major Revision

Major revision is recommended due to:

Numerous language and grammar errors.

Abstract not structured properly.

Insufficient differential diagnosis discussion.

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REVIEWER'S REPORT

Incomplete explanation of pathophysiology.

Formatting and referencing issues.

Speculative statements without evidence.

Limited literature review.

Reviewer Recommendation:

Major Revision before reconsideration for publication.