

## Review report

Final title: **Synergistic neurotoxicity of ciprofloxacin and NSAIDs in unmasking a hidden catalyst for seizures:**

**Title at submission: Synergistic neurotoxicity of ciprofloxacin and NSAIDs: Unmasking a hidden catalyst for seizures**

### Round 1



**Reviewer G: Rowsan Ara, ORCID: [0000-0001-7671-8244](https://orcid.org/0000-0001-7671-8244)**

**1. Comment** What was the serum calcium and magnesium levels?  
**Response** At the time of admission, serum calcium was 9.0 mg/dL (reference range: 8.5–10.5 mg/dL) and serum magnesium was 2.0 mg/dL (reference range: 1.7–2.3 mg/dL), both within normal physiological limits. Therefore, electrolyte imbalance was excluded as a precipitating factor for the seizure.

**2. Comment** Did you do blood culture and sensitivity, serum procalcitonin to rule out sepsis and serum quinolone level to see toxicity?  
**Response** Blood culture and sensitivity (C/S): Two peripheral blood samples were collected prior to starting intravenous therapy. Both cultures remained sterile after 72 hours of incubation, effectively ruling out bacteraemia or sepsis.  
Serum procalcitonin: Serum procalcitonin level was 0.23 ng/mL (reference < 0.5 ng/mL), indicating no biochemical evidence of systemic sepsis.  
Serum quinolone level: Quantitative estimation of serum ciprofloxacin level was not performed, as therapeutic drug monitoring for fluoroquinolones is not routinely available at hospital. However, the temporal association between ciprofloxacin administration and seizure onset, absence of metabolic or structural abnormalities, and rapid neurological recovery after discontinuation of ciprofloxacin and nimesulide strongly support the diagnosis of drug-induced neurotoxicity.

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**Responsible editor**  
Md Nahiduzzamane Shazzad  
0000-0002-8535-4259

**Reviewer**  
G: Rowsan Ara  
0000-0001-7671-8244

**Keywords**  
cytochrome P450, GABAergic dysfunction, generalised tonic-clonic seizure

**Ethical approval**  
Ethical approval was not sought because this is a case report. However, written informed consent was obtained from the patient for publication of this case report and any accompanying images.

**Funding**  
None

**Trial registration number**  
Not applicable

**Responsible editor: Md Nahiduzzamane Shazzad, ORCID: [0000-0002-8535-4259](https://orcid.org/0000-0002-8535-4259)**

**3. Comment** According to the journal policy, the number of authors, affiliation and sequence could not be changed after mechanical review.  
**Response** The change that occurred was an unintentional mistake during the mechanical review stage. If required, I can provide written consent from all authors confirming their agreement with the final authorship details.

**4. Comment** We accept up to 10 references in a case report. Please modify your writing.  
Our another observation regarding reference is that you have provided four references in a table, please provide it in your text and keep the total reference number within ten.  
**Response** At the time of submission, we had already discussed the need for some relaxation in the reference limit, and this was part of our earlier communication.  
Additionally, the inclusion of references inside the table was also discussed during the submission process, and approval for this format was given from your side.

**Executive editor: M Mostafa Zaman, ORCID: [0000-0002-1736-1342](https://orcid.org/0000-0002-1736-1342)**

**5. Comment** The board decision has already been communicated by the concerned section editor on 27 November. We never agreed to include more than 10 references. We passed it to the review process to save time.  
The issue has been dragged on too much. I wish to close the case by COB tomorrow with the following three points to be resolved rigorously:  
1. The discussion should be convincing as to why NSAIDs are considered, while nimesulide has only been used. In addition, paracetamol was prescribed. Why do you causally link NSAIDs? Did the seizure stop after withdrawing the drugs? In such a case, which drug was stopped, nimesulide or paracetamol or both? Therefore, the conclusion has overclaims. Please revise the language so that the conclusion is justified.

2. References must not exceed 10. The author's rigid view of this might lead to a negative decision.
3. We shall need a signed copy of the authorship changes, which you correctly proposed in your previous communication.

**Response** Thank you for your clear guidance. I am pleased to inform you that all the comments have been fully addressed as per your instructions.

The discussion and conclusion have been revised.

The references have been limited to 10, and the authorship correction letter has been submitted.

## Round 2

**Responsible editor:** Md Nahiduzzamane Shazzad, ORCID: [0000-0002-8535-4259](https://orcid.org/0000-0002-8535-4259)

**1. Comment** We are aware of your concern and appreciate your sincere efforts. The editorial team want to maintain the same policy for every manuscript. We have gone through the previous discussions regarding the number of references. We suggest keeping the number of references to a maximum of 10 and citing them in the discussion section of the manuscript; it's not required to include a table.

Regarding Authorship, affiliation, and sequence, please send the signed permission document from the authors.

**Response** The reference cited in table was the content reference I have already discussed that in the month of April the screenshot is attached.

For author change please share the templet where I can do?

**Executive editor:** M Mostafa Zaman, ORCID: [0000-0002-1736-1342](https://orcid.org/0000-0002-1736-1342)

**2. Comment** There is substantial improvement of the manuscript.

I suggest changing the title to nimesulide instead of the NSAIDs. However, we can do it at the copy editing stage.

The change is in the authors' list, and its sequence needs the signature of all authors; otherwise, an email from you could suffice. Please submit the signed copy by all authors.

**Response** For title change please make the change or highlight during copyediting I will correct it.