Severe Confusion Possibly Caused by levofloxacin

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Abstract

Levofloxacin is a third generation fluoroquinolone antibiotic which is generally well tolerated, and has a very low rate of clinically relevant neurological adverse events (0.2-1.1%). The more common central nervous system (CNS) adverse effects are headache, dizziness, restlessness, tremor, insomnia, anxiety and depression. Delirium and hallucinations have been reported with fluoroquinolones as well as seizures. This case report describes changes in mental status experienced by an elderly patient who was receiving levofloxacin for presumed pneumonia. This 91 year old male was admitted to the hospital with fever, cough, and rigor and started empirically on levofloxacin for community acquired bacterial pneumonia. The patient became severely confused, agitated and combative 12 hours after the first dose of levofloxacin. The patient’s oxygen saturations were within normal limits, electrolytes within normal limits, and no other cause for his change in mental status was apparent. The patient received 2 doses of levofloxacin 750 mg administered 48 hours apart which was appropriate for his renal function. The patient received 2 doses of alprazolam and 2 doses of haloperidol because of his agitation and combative behavior. Levofloxacin was discontinued after the second dose on recommendation of the pharmacist and within 24 hours of discontinuation, the patient was alert and oriented to person, time, and place. The patient’s pneumonia improved on alternate antibiotics and the patient was able to be discharged on hospital day 4 with no sequelae. This case illustrates that, while very useful, fluoroquinolones should be used with caution in elderly patients who may be at risk for changes in mental status.

Naranjo Score = 6

Possible ADR

Background

• Most common CNS disturbances reported with levofloxacin include headache, dizziness and drowsiness, usually occur on Day 1 and resolve after discontinuation.

• Less commonly reported CNS events include increased intracranial pressure and CNS stimulation which may lead to tremors, restlessness, anxiety, lightheadedness, confusion, hallucinations, paranoia, depression, nightmares, insomnia, and suicidal thoughts/acts.

• Mechanism for levofloxacin-induced change in mental status involves inhibition of the binding of γ-aminobutyric acid (GABA) at its N-methyl-D-aspartate (NMDA) receptor site as well as activation of excitatory NMDA receptors leading to CNS excitation².

• Case reports of fluoroquinolone-induced altered mental status involving levofloxacin have been previously published.

• The reported overall trend in incidence of drug-related CNS adverse events is as follows norfloxacin > ciprofloxacin > ofloxacin > levofloxacin².

Results

<table>
<thead>
<tr>
<th>HD#1</th>
<th>HD#2</th>
<th>HD#3</th>
<th>HD#4</th>
<th>HD#5</th>
<th>HD#6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levofloxacin 750 mg IV Q48 AAO x3</td>
<td>Levofloxacin 750 mg IV Q48 AAO to self</td>
<td>Levofloxacin 750 mg IV Q48 AAO to self</td>
<td>Levofloxacin O/C AAO3</td>
<td>Ceftriaxone 1 g IV Q24 AAO3</td>
<td>Levofloxacin D/C Pl discharged to home with family</td>
</tr>
<tr>
<td>Lung sounds diminished at bases T_max = 08.45 (oral) + cough</td>
<td>Lung sounds diminished at bases T_max = 09.35 (oral) + cough</td>
<td>Lung sounds diminished at bases T_max = 03.35 (oral) + cough</td>
<td>Ceftriaxone 1 g IV Q24 AAO3</td>
<td>Azithromycin 500 mg IV Q24 AAO3</td>
<td>Pt cooperative, pleasant Pt worked with PT in afternoon</td>
</tr>
</tbody>
</table>

Discussion

• The major reported adverse effects of fluoroquinolones are gastrointestinal (3-17%) and CNS (0.9-11%) disturbances.³

• Predisposing factors for CNS related adverse events include:
  - elderly age
  - male gender
  - diabetes mellitus
  - Hypoxemia
  - any neurological illness
  - severe atherosclerosis

Conclusions

• Fluoroquinolones are an under-recognized cause of changes in mental status.

• Elderly patients should be monitored carefully for the CNS symptoms.

• Many signs of possible adverse reactions, such as confusion, weakness, loss of appetite, tremor or depression, are often mistakenly attributed to old age and may remain unreported.

• Thus, before initiating a fluoroquinolone it is important to account for the risk of neurotoxicity especially in the elderly and with patients with a past neurological history.

References


Disclosures

Authors of this presentation have the following to disclose concerning possible financial or personal relationships with commercial-entities that may have a direct or indirect interest in the subject matter of this presentation:

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