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PROCEEDINGS ABSTRACT

Suicidal ideation as an adverse effect of fluoroquinolones: a review of recent evidence

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Fluoroquinolones (including widely used agents such as ciprofloxacin, delafloxacin, levofloxacin, moxifloxacin, and ofloxacin) represent an important tool of modern therapeutics. Due to their tissue penetration ability, favourable pharmacokinetic profiles, and bactericidal activities against a broad spectrum of Gram-positive and -negative pathogens, these antibiotics remain clinically important for selected serious infections. However, the historical perception of fluoroquinolones as having benign safety profiles is now being challenged by a growing body of clinical evidence. Over the last decade, this shifting landscape has redirected medical focus toward a spectrum of severe (and often debilitating) neuropsychiatric adverse drug reactions, with global regulatory authorities (including the FDA) issuing warnings in order to highlight the potential of this class of antibiotics for causing serious central nervous system (CNS) toxicities. Suicidal ideation and suicidal behaviour have been recognised by regulatory product information as rare potential outcomes of fluroquinolone-associated psychiatric reactions, although neither their frequency nor their period of risk can currently be quantified. This narrative review attempts to synthesize current clinical evidence, pharmacovigilance data, and the findings of mechanistic research in order to assess the intricate relationship between fluoroquinolones and the risk of severe neuropsychiatric adverse events [1]. We have, herein, placed particular emphasis on assessing the fluoroquinolone-associated risks of suicidal ideation as well as those of acute psychosis and major depression. Clinical evidence reveals a distressing pattern of rapid-onset psychiatric decompensation, and several cases indicate that severe neuropsychiatric symptoms can manifest even after a few doses of fluoroquinolones in patients with no prior history of psychiatric disease or identified psychological vulnerabilities. Case reports and some spontaneous-reporting analyses support a potential association between fluroquinolones and serious psychiatric reactions, including suicidal ideation; however, the findings from pharmacovigilance and population-based studies are inconsistent, and the incidence and magnitude of any excess risk remain uncertain [2,3]. The reported symptoms exist on a broad and unpredictable continuum that ranges from insidious insomnia and mild anxiety to profound psychomotor agitation, vivid hallucinations, and suicidal behavior. Potential susceptibility factors described in the literature include advanced age, renal impairment, concomitant medicines, and pre-existing neuropsychiatric conditions; however, evidence identifying reliable predictors of suicidal ideation remains limited. Proposed mechanisms include antagonism of gamma-aminobutyric acid-mediated inhibitory neurotransmission, altered excitatory neurotransmission involving *N*-methyl-D-aspartate receptors, and oxidative or mitochondrial effects. However, the relative contribution of these mechanisms to individual psychiatric reactions, particularly suicidal ideation, remains uncer-

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tain. Until future studies manage to identify genetic markers and / or biological signatures that can accurately predict individual susceptibility to these rare but life-threatening fluoroquinolone-induced neuropsychiatric adverse events, clinicians will need to prioritize the identification of high-risk patient phenotypes and to exercise judicious prescribing practices for this class of antibiotics, particularly in the cases of uncomplicated infections for which alternative therapeutic options exist. Patients and caregivers should also be counselled to seek immediate medical advice if new or worsening psychiatric symptoms (including depression, psychosis, or suicidal thoughts) occur, and treatment should be discontinued promptly when a serious psychiatric reaction develops.

Keywords

adverse drug reaction; fluoroquinolones; neuropsychiatric symptoms; pharmacovigilance; suicidal ideation

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Conflicts of interest statement

None to declare.

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