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Original Investigation

January 13, 2025

Antiviral Medications for Treatment of Nonsevere Influenza

A Systematic Review and Network Meta-Analysis

Ya Gao, PhD^{1,2,3,4}; Yunli Zhao, MD^{5,6}; Ming Liu, PhD^{3,4}; [et al](#)

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Editorial
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Key Points

Question What is the optimal antiviral drug in the treatment of patients with nonsevere influenza virus infection?

Findings In this systematic review and network meta-analysis of 73 trials involving 34 332 participants, baloxavir might have reduced the risk of admission to hospital for high-risk patients, probably reduced time to alleviation of symptoms, and did not increase adverse events related to treatment, but might have increased emergence of resistance. Oseltamivir had little or no effect on mortality and admission to hospital, likely had no important effect on time to alleviation of symptoms, and likely increased adverse events related to treatments.

Meaning Baloxavir may be superior to standard care or placebo in reducing the risk of admission to hospital for high-risk patients with nonsevere influenza virus infection and probably decreases time to alleviation of symptoms with few or no adverse effects.

Abstract

Importance The optimal antiviral drug for treatment of nonsevere influenza remains unclear.

Objective To compare effects of antiviral drugs for treating nonsevere influenza.

Data Sources MEDLINE, Embase, CENTRAL, CINAHL, Global Health, Epistemonikos, and ClinicalTrials.gov were searched from database inception to September 20, 2023.

Study Selection Randomized clinical trials comparing direct-acting influenza antiviral drugs to placebo, standard care, or another antiviral drug for treating people with nonsevere influenza.

Data Extraction and Synthesis Paired reviewers independently performed data extraction and risk of bias assessment. A frequentist network meta-analysis was performed to summarize the evidence and the certainty of evidence was evaluated using the GRADE approach.

Main Outcomes and Measures Mortality, admission to hospital, admission to the intensive care unit, duration of hospitalization, time to alleviation of symptoms, emergence of resistance, and adverse events.

Results Overall, 73 trials with 34 332 participants proved eligible. Compared with standard care or placebo, all antiviral drugs had little or no effect on mortality for low-risk patients and high-risk patients (all high certainty). All antiviral drugs (no data for peramivir and amantadine) had little or no effect on hospital admission for low-risk patients (high certainty). For hospital admission in high-risk patients, oseltamivir (risk difference [RD], -0.4%; 95% CI, -1.0 to 0.4; high certainty) had little or no effect and baloxavir may have reduced risk (RD, -1.6%; 95% CI, -2.0 to 0.4; low certainty); all other drugs may have had little or uncertain effect. For time to alleviation of symptoms, baloxavir probably reduced symptom duration (mean difference [MD], -1.02 days; 95% CI, -1.41 to -0.63; moderate certainty); umifenovir may have reduced symptom duration (MD, -1.10 days; 95% CI, -1.57 to -0.63; low certainty); oseltamivir probably had no important effect (MD, -0.75 days; 95% CI, -0.93 to -0.57; moderate certainty). For adverse events related to treatment, baloxavir (RD, -3.2%; 95% CI, -5.2 to -0.6; high certainty) had few or no adverse events; oseltamivir (RD, 2.8%; 95% CI, 1.2 to 4.8; moderate certainty) probably increased adverse events.

Conclusions and Relevance This systematic review and meta-analysis found that baloxavir probably reduced risk of hospital admission for high-risk patients and may reduce time to alleviation of symptoms, without increasing adverse events related to treatment in patients with nonsevere influenza. All other antiviral drugs either probably have little or no effect, or uncertain effects on patient-important outcomes.

Editor's Note

The Limited Role for Antiviral Therapy in Influenza

JAMA Internal Medicine

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[The evidence on baloxavir](#)

Fabian Desimpel, Medical Doctor | Berlin School of Public Health, Berlin, Germany

Dear Editor, we read with interest the systematic review and network meta-analysis by Gao et al. regarding antivirals for the treatment of nonsevere influenza. The authors concluded that baloxavir probably reduced symptom duration with one day, and that baloxavir may have reduced the risk of hospital admission in high-risk patients.[1]

1) Regarding the conclusion that baloxavir probably reduced symptom duration, it is important to note that in all included baloxavir trials, the use of antipyretics and analgesics (except for paracetamol as "rescue therapy") was prohibited.[2-4] As such, the benefit of baloxavir may not be present in real-world practice, where the ...

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Binh Ngo, M.D. | Keck USC School of Medicine

We are grateful for this analysis of antiviral medications for treatment of nonsevere influenza by Gao et al (1) and for the comment by Dr. Desimpel suggesting modification of hazard ratios. It should also be emphasized that antiviral prophylaxis for influenza is supported by regulatory authorities. In a key article including several of the same authors, Zhao et al concluded that "Zanamivir, oseltamivir, laninamivir, and baloxavir probably achieve important reductions in symptomatic influenza in individuals at high risk of severe disease (zanamivir: risk ratio 0.35, 95% CI 0.25-0.50; oseltamivir: 0.40, 0.26-0.62; laninamivir: 0.43, 0.30-0.63; baloxavir: 0.43, 0.23-0.79; moderate certainty) ...

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