In brief

Oseltamivir (Tamiflu) use in healthcare settings

25 July 2022

Questions

1. What is the evidence that use of oseltamivir in healthcare workers with a symptomatic influenza diagnosis result in an earlier return to work and reduced absenteeism? What is the likely reduction in the duration of absenteeism?
2. What is the evidence that use of oseltamivir in adults and children with symptomatic influenza reduces influenza transmission in health care settings? (Or where this has been inferred from either reduced viral shedding or reduction in viral load in respiratory samples on therapy).

Summary

Treatment of influenza in healthcare workers with oseltamivir and its impact on absenteeism

- Evidence on the effectiveness of antivirals in reducing absenteeism in healthcare workers with symptomatic diagnosis is lacking, and data on healthcare service disruption are not readily available.[1]
- Antiviral drugs started within 48 hours of influenza onset, reduce the time until the patient is symptom-free by a mean of approximately 0.5 to 1.5 days. [2] Specifically, oseltamivir decreases the time until patients are symptom-free by approximately one day (21% reduction in time). [3]
- Oseltamivir treatment is associated with side effects including nausea and vomiting. [3] Risk of side effects need to be balanced with the marginal benefits of treatment, especially in healthy individuals.
- Observational studies with no control groups note that outbreaks appear to end quickly if affected patients and staff are treated with oseltamivir. [4, 5] A modelling study found that absenteeism decreased from 10% to 8% with oseltamivir, compared to no treatment. [6]
- There are some reports of greater staff willingness to work during influenza outbreaks where antivirals are available. [7, 8]

Treatment of influenza in healthcare settings with oseltamivir and its impact on viral transmission

- Oseltamivir treatment appears to reduce symptoms and viral shedding by around one day. [2, 3]
- There is little evidence that oseltamivir treatment for healthcare staff reduces the spread of influenza to vulnerable patients.
- A recent review on antiviral treatment (including oseltamivir) noted that: [9]
  - Evidence on the effect of antiviral treatment on influenza virus transmission are lacking.
  - Observational and clinical trial data confirm that early antiviral treatment can reduce infection risk and illness in household contacts, although the magnitude of the effect has varied widely across studies and is highly dependent on timing.
  - Epidemiologic models indicate that prompt antiviral treatment could have major indirect benefits in reducing virus transmission.
- For inpatients:
  - For adults, commencing treatment earlier with oseltamivir leads to significantly shorter viral shedding duration. [10]

  - A randomised controlled trial determined that there were no advantages to clearance of virus, mortality or tolerability when administering a double dose of oseltamivir in paediatric inpatients with severe influenza, compared to a single dose. [11]
- For residential aged care facilities:
  - One study on Influenza A (no control group) demonstrated that nearly 80% of the 150 patients showed relief in symptoms (e.g. decreasing body temperature, relief in body aches) within two days of oseltamivir treatment, around 80% of the patients did not have a viral shedding detected on RT-PCR by the seventh day. [12]
  - In a randomised controlled trial, a 'treatment plus prophylaxis' strategy was more effective in reducing outbreak duration and influenza attack rate than treatment alone (23% versus 36%, p=0.002). [13]
- Most studies investigating viral transmission in the community contribute to the evidence that oseltamivir appears to lead to faster decline in viral load in infected individuals. [14-16] However, a 2012 Cochrane review on children, noted that the benefit of oseltamivir in preventing the transmission of influenza in households, is modest and based on weak evidence. [17]
- Regarding viral shedding, randomised controlled trials in community settings have demonstrated that:
  - Oseltamivir decreased viral shedding (79 hours for the oseltamivir group versus 84 hours for the placebo group, p=0.34) but not time to resolution of clinical symptoms. [18]
  - Oseltamivir treatment was associated with a significant reduction period of infectiousness (inferred by shorter period for replicant-competent viral shedding). [19]
  - Median virus titre areas under curves were lower by 30–40% during the first four days of treatment in the oseltamivir groups than in a placebo group. Changes in median virus titre after 24 hours of treatment were significant (p=0·0004). [20]
- Notably, a pharmaceutical study (WV15799) concluded that oseltamivir could prevent influenza in contacts by interrupting transmission from index cases, however, authors of a systematic review have highlighted problems with the study design. [21]

Grey Literature

- Relevant international clinical guidelines do not comment on this topic specifically. [22-24]

Background

- Oseltamivir (Tamiflu) is a neuraminidase inhibitor used in influenza treatment and prophylaxis.
- Many studies evaluating influenza prevention or reductions in transmission are not high quality, making it difficult to distinguish the role of individual variables. Multimodal infection control policies are thought to be most effective in reducing healthcare-associated influenza infections. [25]
- However, understanding the role of antivirals in influenza management, both for patients and for staff, is important for forming policy and stockpiling medicines.

Methods

To inform this brief, PubMed and Google searches were conducted using terms related to influenza and oseltamivir on 27 June 2022.

References

1. Tadount F, Laghdir Z, Quach C. Antiviral use in healthcare workers—A systematic review. Infect Control Hosp Epidemiol. 2022;43(4):518-23. DOI: 10.1017/ice.2021.79
2. Lehnert R, Pletz M, Reuss A, et al. Antiviral Medications in Seasonal and Pandemic Influenza. Dtsch Arztebl Int. 2016 Nov 25;113(47):799-807. DOI: 10.3238/arztebl.2016.0799
3. Dobson J, Whitley RJ, Pocock S, et al. Oseltamivir treatment for influenza in adults: a meta-analysis of randomised controlled trials. Lancet. 2015 May 2;385(9979):1729-37. DOI: 10.1016/s0140-6736(14)62449-1
4. Gaillat J, Dennetière G, Raffin-Bru E, et al. Summer influenza outbreak in a home for the elderly: application of preventive measures. J Hosp Infect. 2008 Nov;70(3):272-7. DOI: 10.1016/j.jhin.2008.07.009
5. Raymond NJ, Berry N, Blackmore TK, et al. Pandemic influenza A(H1N1) 2009 in hospital healthcare workers in New Zealand. Infect Control Hosp Epidemiol. 2012 Feb;33(2):196-9. DOI: 10.1086/663705
6. Lee VJ, Chen MI. Effectiveness of neuraminidase inhibitors for preventing staff absenteeism during pandemic influenza. Emerg Infect Dis. 2007 Mar;13(3):449-57. DOI: 10.3201/eid1303.060309
7. Devnani M. Factors associated with the willingness of health care personnel to work during an influenza public health emergency: an integrative review. Prehosp Disaster Med. 2012 Dec;27(6):551-66. DOI: 10.1017/s1049023x12001331
8. Garrett AL, Park YS, Redlener I. Mitigating absenteeism in hospital workers during a pandemic. Disaster Med Public Health Prep. 2009 Dec;3 Suppl 2:S141-7. DOI: 10.1097/DMP.0b013e3181c12959
9. Hayden FG, Asher J, Cowling BJ, et al. Reducing Influenza Virus Transmission: The Potential Value of Antiviral Treatment. Clin Infect Dis. 2022 Feb 11;74(3):532-40. DOI: 10.1093/cid/ciab625
10. Ling LM, Chow AL, Lye DC, et al. Effects of early oseltamivir therapy on viral shedding in 2009 pandemic influenza A (H1N1) virus infection. Clin Infect Dis. 2010 Apr 1;50(7):963-9. DOI: 10.1086/651083
11. South East Asia Infectious Diseases Clinical Research Network. Effect of double dose oseltamivir on clinical and virological outcomes in children and adults admitted to hospital with severe influenza: double blind randomised controlled trial. BMJ. 2013;346:f3039. DOI: 10.1136/bmj.f3039
12. Gandhoke I, Rawat DS, Rai A, et al. Pandemic Influenza A (H1N1) 2009 in India: duration of virus shedding in patients under antiviral treatment. Indian J Med Microbiol. 2011 Jan-Mar;29(1):37-41. DOI: 10.4103/0255-0857.76522
13. Booy R, Lindley RI, Dwyer DE, et al. Treating and preventing influenza in aged care facilities: a cluster randomised controlled trial. PLoS One. 2012;7(10):e46509. DOI: 10.1371/journal.pone.0046509
14. Fielding JE, Kelly HA, Mercer GN, et al. Systematic review of influenza A(H1N1)pdm09 virus shedding: duration is affected by severity, but not age. Influenza Other Respir Viruses. 2014 Mar;8(2):142-50. DOI: 10.1111/irv.12216
15. Cheung DH, Tsang TK, Fang VJ, et al. Association of Oseltamivir Treatment With Virus Shedding, Illness, and Household Transmission of Influenza Viruses. J Infect Dis. 2015 Aug 1;212(3):391-6. DOI: 10.1093/infdis/jiv058
16. Mattila J-M, Vuorinen T, Waris M, et al. Oseltamivir treatment of influenza A and B infections in infants. Influenza Other Respir Viruses. 2021;15(5):618-24. DOI: https://doi.org/10.1111/irv.12862
17. Wang K, Shun-Shin M, Gill P, et al. Neuraminidase inhibitors for preventing and treating influenza in children (published trials only). Cochrane Database Syst Rev. 2012 Apr 18;2012(4):Cd002744. DOI: 10.1002/14651858.CD002744.pub4

18. Beigel JH, Manosuthi W, Beeler J, et al. Effect of Oral Oseltamivir on Virological Outcomes in Low-risk Adults With Influenza: A Randomized Clinical Trial. Clin Infect Dis. 2020 May 23;70(11):2317-24. DOI: 10.1093/cid/ciz634
19. Fry AM, Goswami D, Nahar K, et al. Efficacy of oseltamivir treatment started within 5 days of symptom onset to reduce influenza illness duration and virus shedding in an urban setting in Bangladesh: a randomised placebo-controlled trial. Lancet Infect Dis. 2014 Feb;14(2):109-18. DOI: 10.1016/s1473-3099(13)70267-6
20. Nicholson KG, Aoki FY, Osterhaus AD, et al. Efficacy and safety of oseltamivir in treatment of acute influenza: a randomised controlled trial. Neuraminidase Inhibitor Flu Treatment Investigator Group. Lancet. 2000 May 27;355(9218):1845-50. DOI: 10.1016/s0140-6736(00)02288-1
21. Jefferson T, Jones M, Doshi P, et al. Oseltamivir for influenza in adults and children: systematic review of clinical study reports and summary of regulatory comments. BMJ. 2014 Apr 9;348:g2545. DOI: 10.1136/bmj.g2545
22. Centers for Disease Control and Prevention. Influenza Antiviral Medications: Summary for Clinicians [Government Report]. United States: CDC; 2021 [cited 2022 Jul 1]. Available from: https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm
24. Association of Medical Microbiology and Infectious Disease Canada. Guidance on the use of antiviral drugs for influenza in the COVID-19 pandemic setting in Canada [Internet]. Canada: AMMI; 2021 [cited 2022 July 1]. Available from: https://jammi.utpjournals.press/doi/full/10.3138/jammi-2022-01-31
25. Most ZM. Beyond personal protective equipment: adjunctive methods for control of healthcare-associated respiratory viral infections. Curr Opin Infect Dis. 2020 Aug;33(4):312-8. DOI: 10.1097/qco.0000000000000655

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