INAHTA Briefs

Issue 2010/159

Title **Amantadine, Oseltamivir and Zanamivir for the Prophylaxis of Influenza (Including a Review of Existing Guidance No. 67): A Systematic Review and Economic Evaluation**

Agency **NETSCC, HTA, NIHR Evaluation and Trials Coordinating Centre**
Alpha House, University of Southampton Science Park, Southampton, SO16 7NS, United Kingdom;
Tel: +44 2380 595 586, Fax: +44 2380 595 639; hta@soton.ac.uk, www.hta.ac.uk

Reference Volume 13.11. ISBN 1366-5278. www.hta.ac.uk/project/1686.asp

Aim

To evaluate the clinical effectiveness and incremental cost effectiveness of amantadine, oseltamivir, and zanamivir for seasonal and postexposure prophylaxis of influenza.

Conclusions and results

All 3 interventions showed some efficacy for seasonal and postexposure prophylaxis. However, weaknesses and gaps in the clinical evidence base are directly relevant to the interpretation of the health economic model and rendered the use of advanced statistical analyses inappropriate. The clinical effectiveness review included 26 published references relating to 22 randomized controlled trials (RCTs) and 1 unpublished report (8, 6, and 9 RCTs were included for amantadine, oseltamivir, and zanamivir respectively). Study quality varied, and gaps in the evidence base limited the assessment of the clinical effectiveness of the interventions. For seasonal prophylaxis, limited evidence supported the efficacy of amantadine in preventing symptomatic, laboratory-confirmed influenza (SLCI) in healthy adults (relative risk [RR] 0.40, 95% confidence interval [CI] 0.08–2.03). Oseltamivir was effective in preventing SLCI, particularly when used in at-risk elderly (RR 0.08, 95% CI 0.01–0.63). The preventative efficacy of zanamivir was most notable in at-risk adults and adolescents (RR 0.17, 95% CI 0.07–0.44), and healthy and at-risk elderly (RR 0.20, 95% CI 0.02–1.72). For postexposure prophylaxis, data on amantadine use were again limited: in adolescents an RR of 0.10 (95% CI 0.03–0.34) was reported for the prevention of SLCI. Oseltamivir was effective in households of mixed composition (RR 0.19, 95% CI 0.08–0.45). The efficacy of zanamivir in postexposure prophylaxis in households was also reported (RR 0.21, 95% CI 0.13–0.33). Interventions appeared to be well tolerated. Limited evidence supported the effectiveness of the interventions in preventing complications and hospitalization and in minimizing length of illness and time to return to normal activities. No clinical effectiveness data were identified for health-related quality of life or mortality outcomes. With the exception of at-risk children, the incremental cost-utility of seasonal influenza prophylaxis is expected to range between 38 000 and 428 000 pounds sterling (GBP) per QALY gained (depending on subgroup). The cost-effectiveness ratios for oseltamivir and zanamivir as postexposure prophylaxis are expected to be below GBP 30 000 per QALY gained in healthy children, at-risk children, healthy elderly, and at-risk elderly individuals. Despite favorable clinical efficacy estimates, the incorporation of recent evidence of viral resistance to amantadine led to it being dominated in every economic comparison.

Recommendations

See link www.hta.ac.uk/project/1686.asp.

Methods

A systematic review was undertaken and an independent health economic model developed, based on clinical advice and a detailed review of existing cost-effectiveness models. The model draws on a broad spectrum of evidence relating to the costs and consequences of influenza and its prevention.

Further research/reviews required

1) Additional RCTs of influenza prophylaxis in subgroups for which data are currently lacking; 2) RCTs where follow-up extends beyond the duration of prophylaxis; 3) head-to-head RCTs that directly compare clinical effectiveness of interventions in different subgroups; 4) quality-of-life studies to inform future economic decision modeling; 5) further research on the incidence and management of influenza complications.

Written by Mr Paul Tappenden, SCHARR, University of Sheffield, NETSCC, United Kingdom

ISSN 1654-501X