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BMJ. 2013 May 30;346:f3039. doi: 10.1136/bmj.f3039.

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.

South East Asia Infectious Disease Clinical Research Network.

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Abstract

OBJECTIVE: To investigate the validity of recommendations in treatment guidelines to use higher than approved doses of oseltamivir in patients with severe influenza.

DESIGN: Double blind randomised trial.

SETTING: Thirteen hospitals in Indonesia, Singapore, Thailand, and Vietnam.

PARTICIPANTS: Patients aged ≥ 1 year admitted to hospital with confirmed severe influenza.

INTERVENTIONS: Oral oseltamivir at double dose (150 mg twice a day/paediatric equivalent) versus standard dose (75 mg twice a day/paediatric equivalent).

MAIN OUTCOME MEASURE: Viral status according to reverse transcriptase polymerase chain reaction (RT-PCR) for influenza RNA in nasal and throat swabs on day five.

BMJ. 2013; 346: f3039. PMCID: PMC3668094
Published online 2013 May 30. doi: 10.1136/bmj.f3039

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

South East Asia Infectious Disease Clinical Research Network

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Accepted 2013 May 7.

Abstract

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Main outcome measure Viral status according to reverse transcriptase polymerase chain reaction (RT-PCR) for influenza RNA in nasal and throat swabs on day five.

Results Of 326 patients (including 246 (75.5%) children aged <15), 165 and 161 were randomised to double or standard dose oseltamivir, respectively. Of these, 260 (79.8%) were infected with influenza virus A (133 (40.8%) with A/H3N2, 72 (22.1%) with A/H1N1-pdm09, 38 (11.7%) with seasonal A/H1N1, 17 (5.2%) with A/H5N1) and 53 (16.2%) with influenza virus B. A further 3.9% (13) were false positive by rapid antigen test (negative by RT-PCR and no rise in convalescent haemagglutination inhibition titers). Similar proportions of patients were negative for RT-PCR on day five of treatment: 115/159 (72.3%, 95% confidence interval 64.9% to 78.7%) double dose recipients versus 105/154 (68.2%, 60.5% to 75.0%) standard dose recipients; difference 4.2% (−5.9 to 14.2); P=0.42. No differences were found in clearance of virus in subgroup analyses by virus type/subtype, age, and duration of illness before randomisation. Mortality was similar: 12/165 (7.3%, 4.2% to 12.3%) in double dose recipients versus 9/161 (5.6%, 3.0% to 10.3%) in standard dose recipients. No differences were found between double and standard dose arms in median days on supplemental oxygen (3 (interquartile range 2-5) *v* 3.5 (2-7)), in intensive care (4.5 (3-6) *v* 5 (2-11), and on mechanical ventilation (2.5 (1-16) *v* 8 (1-16)), respectively. No important differences in tolerability were found.

Conclusions There were no virological or clinical advantages with double dose oseltamivir compared with standard dose in patients with severe influenza admitted to hospital.