DIMDI Deutsches Institut für Medizinische Dokumentation und Information

Im Geschäftsbereich des Bundesministeriums für Gesundheit und Soziale Sicherung

HTA REPORT | ABSTRACT

Neuraminidase inhibitors in the treatment and post exposure prevention of influenza

Braun S, Behrens T, Kulp W, Eberle A, Greiner W, Ahrens W, Graf von der Schulenburg JM

Introduction

Influenza is a viral respiratory infection which presents itself as an acute febrile disease. It is contracted by virus-laden respiratory secretions from infected individuals. Symptoms usually last three to seven days and are accompanied by severely limited activities during this time. A definite diagnosis, however, can only be made by laboratory analysis. Every year, about 20 % of children and 5 % of adults develop symptomatic influenza of the serotypes A or B worldwide. Typical complications of influenza include viral or bacterial infections, as well as deterioration of an existing cardio-vascular or respiratory disease which may lead to hospitalization and death. Current policy recommends that individuals, who are at-risk of developing serious complications (patients over sixty years of age or patients with concomitant chronic diseases), as well as people in direct contact with high risk patients (i.e. nursing staff in living and care facilities), should be annually vaccinated with inactivated influenza strains. Various pharmaceutical agents for the treatment and prophylaxis of influenza have been approved. Amantadine, which inhibits the viral M2-ion channel, is only effective in influenza-serotype A. Neuraminidase inhibitors (NI) represent a new class of antivirals for prophylaxis and treatment of influenza A and B. NI interrupt various central functions that are vital for the life cycle and spreading of the virus. Two drugs of this substance class, Zanamivir (Relenza™) and Oseltamivir (Tamiflu®), are licensed for the treatment of influenza. For adults and teenagers over thirteen years of age Oseltamivir is also approved for the prophylaxis of influenza. Zanamivir is a powder which needs to be inhaled, whereas Oseltamivir is licensed as a capsule for oral administration. M2-inhibitors and NI are only effective at an early stage of the influenza infection, i.e. during the first 36 to 48 hours after symptom onset, before replication and spread of the virus begin.

Objective

The effectiveness of NI during treatment and post exposure prophylaxis (PEP) of an influenza infection are analyzed from a medical and an economical perspective. The effectiveness of NI in seasonal prophylaxis is not investigated in this report. Safety aspects of the drugs are also discussed.

Methods

The relevant literature was identified by a systematic, structured bibliographic data base review. In addition, a manual search of relevant journals was conducted. The structured electronic data base analysis was supported by DIMDI and comprised the bibliographic data bases MEDLINE, HealthStar, Current Contents / Clinical Medicine, EMBASE, DA-RA, Cochrane Library, CancerLit, as well as Dissertation Abstracts for the period between 1999 and September 2004. Predefined key words were linked by AND / OR operators. A manual search of the Cochrane register was conducted for the time period before September 1999. Relevant medical journals were also handsearched from January to November 2004. Quantitative reviews, randomized, double-blind clinical trials (RCT), and cost-benefit-analyses were considered as relevant if they fulfilled predefined inclusion criteria.

Results

As compared to placebo, NI shortened the median duration of symptoms by approximately one day in meta-analyses, when the drug was taken within 48 hours after the onset of symptoms. The symptom reduction for other subgroups (such as patients who are at-risk for complicated influenza courses) was even greater. For children under twelve, however, this was not the case. However, the incidence of severe influenza courses which led to hospitalization or death was low in the controlled studies. Pooled analyses nevertheless showed a tendency of a possible benefit of NI with respect to the hospitalization rate. Regarding PEP in homes with one infected household member, the reviewed studies showed a prophylactic effect of inhaled Zanamivir and Oseltamivir if a person started chemoprophylaxis within 48 hours after contact with an infected person.

13 out of 14 international publications evaluated the cost-effectiveness of NI as treatment for influenza. Only one study analyzed the cost-effectiveness of NI in the PEP of influenza. Only two evaluations considered neither Zanamivir nor Oseltamivir to be cost-effective. However, the assumptions made by these two studies were comparatively conservative. All other analyses indicated at least certain circumstances, under which the active agents can be considered cost-effective. NI only saved costs only in a few models under certain assumptions. We identified only one study that evaluated the cost-effectiveness of NI within the German health care system.

DIMDI
Waisenhausgasse 36-38a
50676 Köln

www.dimdi.de

Tel.: 0221 - 47 24 1
Fax: 0221 - 47 24 444
E-Mail: posteingang@dimdi.de

Discussion

Evidence from the investigated studies supported the view that NI are clinically effective under study conditions with regard to the reduction of the duration of symptoms. However, there is considerable uncertainty when these results are transferred into general medical practice. Economic studies try to take into account the uncertainty of diagnoses, while clinical studies oftentimes underestimate this issue and also neglect the fact that treatment with NI is required within the first 48 hours after the onset of symptoms.

In senior citizens and high risk patients the cost-effectiveness of NI depends on the reduction of complications and associated hospitalizations and mortality. The medical evaluation, however, did not demonstrate sufficient evidence with regard to these issues. In addition to the problems concerning the medical evaluation, problems arise with regard to the economical evaluation when results of international studies are transferred to the German health care system. Therefore we can only draw limited conclusions about the cost-effectiveness of NI based on the results of international studies.

Clinical studies demonstrated the effectiveness of NI in post exposure prophylaxis. Cost-effectiveness, however, can only be assessed based on limited evidence, because, so far, no economic model has been proposed for Germany. In addition, we identified only one international study regarding the cost-effectiveness of NI in PEP.

Conclusion

From a medical viewpoint, NI are effective in the treatment and PEP of influenza. The clinical relevance, however, is hard to judge. A one-day reduction of the duration of symptoms alone does not justify a general prescription of NI. This decision rather depends on individual factors such as unsuccessful primary prophylaxis (e.g. influenza vaccination) and the risk for complications. NI seem to be economically efficient when a fair amount of diagnostic accuracy is present. Further research is required for the definition of cost-effectiveness and economic evaluation of NI in post exposure prophylaxis of influenza.

All HTA reports are available for free as full texts in the DAHTA database (only in German). (www.dimdi.de – HTA)

Contact at DAHTA@DIMDI

Head: Dr. Alric Rüther

E-Mail: dahta@dimdi.de

German Agency for Health Technology Assessment at the German Institute of Medical Documentation and Information