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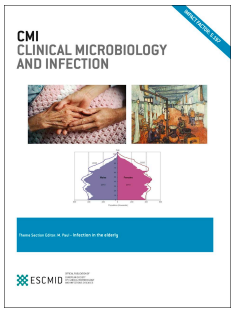

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Neuraminidase inhibitors: who, when, where?

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[2,113 words]

Up until 1999, influenza management involved vaccination for primary prevention, and use of M2-inhibitors (amantadine and rimandatine) for prophylaxis and treatment. The latter were problematic medicines to use, owing to rapid emergence of resistance (especially when used for treatment and prophylaxis in the same setting and in immunocompromised patients),[1,2] absence of activity against influenza B, and frequent central nervous system side-effects (most often observed with amantadine; e.g. anxiety, hallucinations, nightmares and confusion), particularly so in elderly subjects in whom the elimination half-life may be doubled.[3]

From 1999 onwards, the neuraminidase inhibitors (NIs), zanamivir and oseltamivir, have offered new prospects for influenza management, being active against influenza A and B and with, overall, a more benign side-effect profile (albeit with a very common reported incidence of headache and nausea for oseltamivir).[4] Notwithstanding, up until the A(H1N1)pdm09 pandemic in 2009, adoption and usage of NIs had been low in all territories except Japan. The 'Achilles Heel' of the NIs has always been their rather modest effect on symptom reduction,[4] and somewhat limited historical evidence of their ability to reduce complications.[5] The combination of needing rapid access to treatment after symptom onset, and poor discriminatory powers of physicians to distinguish influenza clinically from a variety of other common respiratory virus infections, adds on further logistic and clinical challenges.[6-8] Taken together, the latter two elements could encourage inappropriate use of primary care services for non-serious, self-limiting respiratory virus infections, produce logistic hurdles in terms of rapid access to treatment, and result in NIs being used to 'treat' a variety of non-influenza related respiratory virus infections. The response of guidance authorities to this clinical conundrum has, in general, been to attempt to rationalise limited use of NIs in situations where, diagnostic certainty of influenza is enhanced, access to treatment is timely, and the patient is less likely to have a trivial influenza infection[9] – essentially periods when influenza is known to be circulating widely, and use in high-risk patients who can be treated rapidly after symptom onset.

The above scenario was in sharp contrast to policy evolution over use of NIs in the event of a pandemic. In this arena, in 2005, responding to the pandemic threat posed by avian influenza A(H5N1) in particular, the World Health Organization recommended the establishment of a global stockpile of antiviral drugs;[10] and that countries with sufficient resources should also acquire individual national stockpiles.[10] These stockpiles were subsequently deployed widely during the 2009 pandemic, albeit not against A(H5N1) but the much less virulent A(H1N1)pdm09 virus. In the aftermath of this event, further questions have been raised about the rationale of stockpiling NIs for pandemic usage, and their clinical effectiveness. Recent debate has been polarised by an updated Cochrane review,[11] which