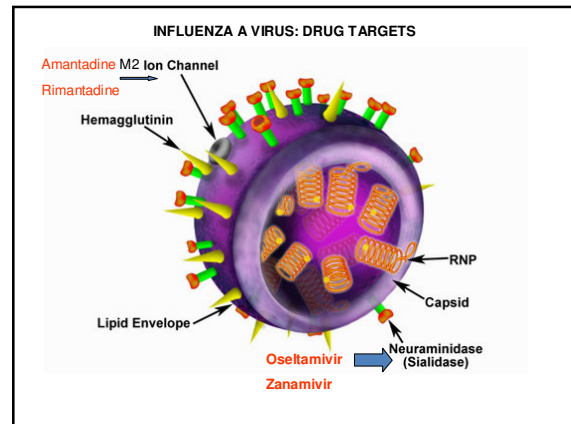


Issues in pharmacotherapy of 2009 H1N1 infection

YK Gupta



Anti-influenza therapy

- Adamantanes
 - Amantadine
 - Rimantadine
- Neuraminidase inhibitors
 - Oseltamivir
 - Zanamivir

Oseltamivir & Zanamivir

- O. Phosphate (prodrug) → O. Carboxylate (Active)
- Zanamivir (Active)
- MOA
 - Inhibits Neuraminidase enzyme
 - Inhibits all 9 NA subtypes
 - Oseltamivir: IC_{50} 1.9 to 69.2 nanomolar
 - Zanamivir: IC_{50} 2.2 to 30.1 nanomolar

Search for still lower IC_{50} ongoing

Future NAIs in pipeline

- For I.V. Preparation
- For very sick patients
- For oseltamivir resistant cases
- For favourable AE profile

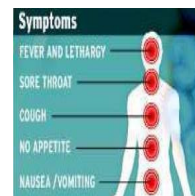
- Peramivir (phase III)
- Laninamivir (pre-clinical)
- A-315675 (pre-clinical)

Symptom management....

Which antipyretic?

No aspirin for children and adolescents (<18years): risk of Reye's syndrome

-Paracetamol is DOC



Antiviral therapy...When?

- Hospitalization or **antiviral therapy is not required** for most patients
- Clinicians/care-givers should take into account:
 - ❖ Signs of clinical deterioration
 - ❖ Underlying conditions: chronic cardiovascular, pulmonary, diabetes, immunodeficiency
- Young children, elderly and pregnant women warrant close observation and early antiviral treatment

Which Antiviral for 2009 H1N1?

The 2009 H1N1 virus is currently

- **Susceptible to - NAIs (oseltamivir and zanamivir)**
- **Resistant to - M2-inhibitors (amantadine and rimantadine)**

How efficacious are NAIs?

- NAIs might reduce severity and duration and might contribute to prevent progression of severe disease and death due to 2009 H1N1 (based on seasonal influenza and H5N1 influenza studies)
- **Results from large, adequately powered, well designed clinical trials for 2009 H1N1 still awaited**

	Oseltamivir	Zanamivir
Formulation	Capsules or oral suspension	Powder in 5-mg blister on Rotadisk; requires Diskhaler inhalation device
Adverse effects	Nausea, vomiting, Abdominal pain (10-15%)	Bronchospasm in patients with underlying airway diseases
Dose adjustments	Required in patients with creatinine clearance < 30 ml/min	Not required

Adverse effect profile of NAIs

Oseltamivir

- Headache, nausea, vomiting, insomnia, vertigo, pyrexia, rash, toxic epidermal necrolysis, confusion, arrhythmia, unstable angina, seizure, aggravation of DM, hepatitis, pseudomembranous coliti

Zanamivir

- Wheezing and bronchospasm
- Not recommended for treatment of patients with underlying airway disease

Neuropsychiatric events particularly in the paediatric age group reported

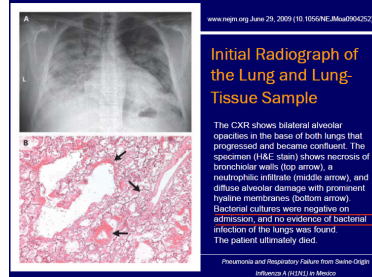
What is the AE profile in Indians?

- No data of AE of NAIs in 2009 H1N1 Indian patients
- Proactive pharmacovigilance: an urgent need
- Cohort event monitoring
- Registry and prescription analysis---telephonic follow up of patients
 - Resource intensive
 - Higher data quality than spontaneous reports

Will restricted use of NAIs reduce resistance?

- Unrestricted availability
 - Emergence of resistance ??
 - Japan: NAIs widely used --- resistance 3%
 - Norway: NAIs rarely used--- resistance 67%
- Highly restricted use: Not feasible
 - Increasing incidence
 - Widespread demand

Are concomitant antibiotics required ??



In USA, the evidence suggests NOT NEEDED

But Indian Scenario ???

Affordability issue

- Indian version is 1/3rd costly than US

BUT

