Amantadine use in influenza outbreaks in long-term care facilities

Even when immunization programs are implemented, outbreaks of influenza can occur in long-term care facilities because of poor vaccine response in elderly people. The antiviral drug amantadine is used to abort influenza A outbreaks in this setting.[1–3]

Amantadine is 70% to 90% effective in preventing illness caused by influenza A viruses but is ineffective against influenza B.[2] When amandatine is given simultaneously to all residents as soon as an influenza A outbreak is recognized, the outbreak usually stops abruptly. For this strategy to work well, however, the facility must be well prepared.

Contingency plans and amantadine orders

Long-term care facilities should develop contingency plans to start amantadine prophylaxis rapidly.[4] Options include obtaining physician orders in advance (e.g., each fall or as each resident is admitted) that can be activated by the advisory physician or infection control committee as the need arises. The advisory physician or committee should also have authority to stop amantadine prophylaxis at the appropriate time.

Amantadine has few side effects when the dosage is calculated carefully. The recommended prophylactic dose for people over age 65 is 100 mg once daily, but this is excessive for many frail residents. The annual National Advisory Committee on Immunization statement on influenza vaccination contains a dosage table with adjustments for renal impairment (Table 1). Determining each resident's creatinine clearance and amantadine dosage before the influenza season is most helpful; the facility's pharmacist will often do the calculations. In an emergency, however, residents may be prescribed an initial 100-mg dose while the creatinine level is being obtained.[4]

Deciding whether amantadine should be used

When a confirmed or suspected outbreak of influenza A occurs in a long-term care facility, amantadine prophy-

Table 1: Recommended amantadine hydrochloride dosage by age and renal status

	Patient age, yr; dosage		
Renal status	1–9*	10–64	≥ 65
No recognized renal disease	5 mg/kg once daily or, divided, twice daily; total daily dose not to exceed 150 mg	200 mg once daily or, divided, twice daily†	100 mg once daily‡
Recognized renal disease; creatinine clearance,§ mL/min · 1.73 m^{-2}			
≥ 80	NA	100 mg twice daily	100 mg once daily
60–79	NA	Alternating daily doses of 200 and 100 mg	Alternating daily doses of 100 and 50 mg
40–59	NA	100 mg once daily	100 mg every 2 days
30–39	NA	200 mg twice weekly	100 mg twice weekly
20–29	NA	100 mg three times weekly	50 mg three times weekly
10–19	NA	Alternating weekly doses of 200 and 100 mg	Alternating weekly doses of 100 and 50 mg

*Use in children under 1 year of age has not been evaluated adequately.
†Reduction of dosage to 100 mg/d is recommended for people with a seizure disorder because they may be at risk for more frequent seizures when the dosage is 200 mg/d.
‡The reduced dosage is recommended to minimize the risk of toxic effects because renal function generally declines with age and because side effects have been reported more frequently in elderly people.
§Calculation of estimated creatinine clearance:

$$\text{Male: CrCl mL/min} = \frac{(140 - \text{age}) \times \text{weight (kg)}}{\text{serum creatinine level } (\mu\text{mol/L}) \times 0.81}$$

$$\text{Female: CrCl mL/min} = 0.85 \times \text{CrCl (male)}$$

NA = not applicable.

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laxis should be started as soon as possible, preferably in consultation with the local public health department. If prophylaxis is delayed, many more residents may become ill. Rapid testing of nasopharyngeal swabs can confirm the diagnosis quickly, although false negative results can occur. Starting amantadine before laboratory confirmation is reasonable if the symptoms are compatible with influenza and the medical officer of health advises that influenza A is circulating in the area.

Amantadine should be given to all residents simultaneously, regardless of vaccination status. However, amantadine will not benefit and should not be given to residents who have already been ill for longer than 48 hours or who have already recovered. Amantadine may also be offered to unvaccinated staff. Prophylaxis should continue for at least 2 weeks or until approximately 1 week after the onset of the last case.

If large numbers of people continue to become ill, suggesting another cause of the outbreak or the development of resistance, amantadine should be stopped.

Monitoring side effects

Residents receiving amantadine should be monitored carefully; dosages should be modified or the drug discontinued if serious side effects occur.[2,3] Side effects are usually mild and diminish after the first week. Amantadine may cause both central nervous system and gastrointestinal symptoms. Occasional serious side effects include marked behavioural changes, delirium, hallucinations, agitation and seizures. These occur more frequently in elderly people and in people with seizure disorders, psychiatric disorders or renal insufficiency. When dosages are tailored to creatinine clearance, serious side effects are uncommon.

Treating ill residents

In young healthy adults amantadine decreases fever and shortens the duration of illness, but its effectiveness in preventing complications in patients at high risk is unknown.[2] Furthermore, amantadine-resistant viruses may emerge during treatment and lead to further cases of influenza.[5,6] Amantadine treatment for residents with acute influenza should be limited to 3 to 5 days; these patients must be isolated to whatever extent is possible from residents receiving amantadine prophylaxis.[3,4]

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