Targeted Antiviral Prophylaxis With Oseltamivir in a Summer Camp Setting

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Objective: To describe the effectiveness of containment of novel influenza A(H1N1) infection at a summer camp.

Design: Targeted use of oseltamivir phosphate by individuals in close contact with influenza-confirmed cases.


Participants: A total of 171 campers, 48 camp counselors, and 27 camp staff.

Interventions: Campers with confirmed influenza received oseltamivir and were immediately isolated and sent home. All boys and counselors in the infected child’s adjoining cabins received prophylactic oseltamivir for 10 days, including 8 campers at higher risk for influenza infection (eg, those with asthma, seizure disorder, or diabetes). Alcohol-based hand sanitizer was provided at each of the daily activities, in the boys’ cabins, and in the dining hall, and counselors were educated by the medical staff on the spread of influenza and its prevention through good hand hygiene. All cabins, bathrooms, and community sports equipment were sprayed or wiped down with disinfectant each day.

Main Outcome Measure: Virologic confirmation of influenza.

Results: Three of the 171 campers tested positive for influenza A during the course of the 2-week fourth session, for an attack rate of 1.8%. The probability of observing 3 or fewer infected campers if the attack rate was 12% is less than 1 in 100,000,000 (P<.0000001). An exact 95% confidence interval based on 3 events among 171 individuals estimates the attack rate to be between 0.3% and 5.0%. While 31% to 57% of campers, counselors, or staff experienced nausea with the treatment, this did not result in discontinuation of therapy. No campers tested positive for influenza A after returning home at the end of the camp session.

Conclusion: In conjunction with comprehensive hand sanitization and surface decontamination, a targeted approach to antiviral prophylaxis contained the spread of influenza in a summer camp setting.


Since the emergence of the novel influenza A(H1N1) virus in spring 2009, millions of Americans have been infected with the virus and thousands of people have died.1 Children have been particularly at risk for infection with and complication by this pandemic strain. Hospitalization rates for children exceed those of any adult age group, and one-third of influenza-associated pediatric deaths that occurred during the current influenza season were due to the novel influenza A(H1N1) virus.2 In a most unusual development, influenza continued to spread and cause disease throughout the 2009 summer months, with approximately one-third of states reporting widespread or regional influenza activity and half reporting sporadic activity.

With large numbers of children from disparate locales coming together and living in communal settings, summer camps are uniquely suited to experience outbreaks of novel influenza A(H1N1) and potentially to contribute to the virus’ ongoing spread during a period of the year when influenza typically is very uncommon. While state health departments and the Centers for Disease Control and Prevention (CDC) have not systematically tracked summer camp outbreaks of influenza-like illness (ILI), as of August 26, 2009, the CDC had identified 240 camps with ILI activity through self-reporting and media channels (Daphne Copeland, MD, CDC, written communication, August 28, 2009). Some camps have reported that 30% to 40% of their campers have been infected, although a true attack rate cannot

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be calculated at this time because formal studies have not been completed (Jacquelyn Polder, RN, MPH, CDC, written communication, August 28, 2009). At least 80 summer camps either closed altogether or operated for more limited periods than they otherwise would have owing to widespread IILI. To date, no coordinated approaches to the challenges posed by novel influenza A(H1N1) have been advocated by the CDC, state health agencies, or organizations such as the American Camp Association.

With very rare exception,3 novel influenza A(H1N1) has retained sensitivity to oseltamivir phosphate. It is worth noting, though, that resistance to date apparently has developed more readily when oseltamivir is used prophylactically rather than therapeutically.4 This is presumably owing to lower drug exposures among people receiving once-daily prophylactic dosing, which allows for selection of resistant isolates. While oseltamivir generally is a safe medication, approximately 20% of pediatric subjects enrolled in clinical trials of oseltamivir experienced gastrointestinal adverse events (eg, nausea, vomiting, diarrhea), with other adverse effects being much less common.5 Oseltamivir has been proven to be effective in the prevention of seasonal influenza spread in household settings6,7 and within closed environments such as nursing homes.8,9 However, targeted antiviral prophylaxis has not been described in the similarly closed habitat of a summer camp. We describe our successful efforts in containing novel influenza A(H1N1) from spreading within a boys' camp in northeastern Alabama during late July 2009 using a targeted antiviral prophylaxis approach to minimize drug exposure as much as possible.

METHODS

STUDY POPULATION

Camp Laney is a boys' camp in Mentone, Alabama, that was established in 1959. Located in the southernmost portions of the Appalachian mountain chain near Chattanooga, Tennessee, it has four 2-week sessions with approximately 200 boys per session. There are 16 cabins, each of which sleeps 12 to 14 campers and 2 or 3 counselors; 6 of the cabins share an adjoining bathroom between them, while the 10 cabins for the older campers have their own private bathroom facilities and do not join another cabin. Campers range in age from 8 through 14 years. Boys in adjoining cabins attend all activities as a group.

In the final 3 days of the third session of camp in mid July 2009, 12 campers became ill with IILI, including fever plus respiratory symptoms. At least 4 of these campers tested positive for influenza A using the QuickVue Influenza A + B rapid diagnostic test (Quidel Corp, San Diego, California). In an effort to interrupt the spread of the virus between the Friday close of the third session and the Sunday start of the fourth session, all counselors and staff began receiving oseltamivir prophylaxis at the end of the third session and continued to receive prophylaxis as the fourth session began. The fourth session ran from July 19 to 31, 2009. As in the previous sessions in 2009, alcohol-based hand sanitizer was provided throughout the fourth session at each of the daily activities, in the boys' cabins, and in the dining hall. All boys were required to use hand sanitizer at least 13 times per day, and this was monitored by an adult counselor. Counselors were educated by the medical staff on the spread of influenza and its prevention through good hand hygiene. In addition, all cabins, bathrooms, community sports equipment, and the health center were sprayed or wiped down with disinfectant each day.

STUDY DESIGN AND OBJECTIVES

Throughout the fourth session, when campers presented to the health center with fever and/or upper respiratory tract symptoms they were tested with the QuickVue Influenza A + B rapid diagnostic test per the manufacturer's specifications. If a child tested negative but still had upper respiratory tract symptoms or a temperature higher than 99.5°F, the camper was held in the health center for up to 24 hours before being released back to camp activities. If a child tested positive, he received oseltamivir at a dosage specified in the package insert and was immediately isolated in the health center until his parents could pick him up. At the time of diagnosis, the cabin of the infected camper, the bathroom, and the adjoining cabin (if present) were immediately disinfected. Influenza-infected boys were allowed to return to camp after receiving oseltamivir for at least 4 days and being symptom-free for at least 24 hours. With parental permission, all boys in the infected child's cabin as well as the adjoining cabin that shared a common bathroom (if present) received a 10-day prophylactic course of oseltamivir. All children were monitored carefully by the camp physicians (T.A.S., D.W.K.), 3 camp nurses (J.E., J.G., J.O.), and counselors for signs of illness and tolerance of medication.

Following completion of this clinical management of campers during the fourth session, approval was obtained from the University of Alabama at Birmingham Institutional Review Board to survey staff and camper families. Staff and counselors completed their brief surveys using paper forms, while families received an e-mail from the camp director requesting that they complete a short survey using a link to SurveyMonkey (SurveyMonkey.com, Portland, Oregon). All survey tools were anonymous and completely voluntary, and questions addressed medication use, compliance, and adverse events.

STATISTICAL ANALYSIS

Owing to the small number of influenza cases observed, exact binomial calculations were used to estimate the probability of the observed events under various assumptions. An exact 95% binomial confidence interval was calculated to estimate the infection rate. To assess association between the number of doses missed and the number of observed adverse events, Cochran-Mantel-Haenszel tests were used.

RESULTS

CLINICAL COURSE

The total number of campers at the fourth session was 171, and none had also been at the third session. Of these 171 campers, 3 (camper A, aged 8 years; camper B, aged 10 years; and camper C, aged 14 years) tested positive for influenza A during the course of the 2-week fourth session, for an attack rate of 1.8%. Using attack rates of 12% (similar to household transmission and military recruits) or 30% to 40% (as seen in other camps across the nation with sentinel influenza cases) would have accounted for a possible 21 to 68 of the 171 campers becoming ill with IILI. The probability of observing 3 or fewer infected campers if the attack rate was 12% is less than 1 in 10 000 000 (P < .0000001). If the infection rate was
between 30% and 40%, the probability of observing 3 or fewer infections in 171 campers would be even less. An exact 95% confidence interval based on 3 events among 171 individuals estimates the attack rate to be between 0.3% and 5.0%, well below the reported ranges of 12% to 40%.

Campers A and B became ill on the second and fourth days of the camp session, respectively. Camper A had spent the night 2 nights before camp started (3 nights before he became ill) with a boy who tested positive for influenza A the following day. Camper B did not have a known exposure, but the timing of onset of illness within 4 days of arriving at camp suggests that it was an imported infection that the camper brought with him from home. Camper C became ill on day 9 of the 2-week session, suggesting spread within the closed camp facility. This subject had a broken finger and wore a splint on his hand, which impeded hand washing and full use of the posted hand sanitizers. All 3 campers were in separate cabins that did not adjoin each other. As an older camper, camper C did not have activities with either camper A or camper B.

Cabinmates of the 3 ill campers began receiving oseltamivir prophylaxis within 12 hours of the diagnosis of influenza in the respective index case. Medication was administered at the approved doses once daily via directly observed therapy accomplished by the camp nurses and doctors. Hand sanitization was maintained for these cabins as well as the remainder of the camp throughout the session. When the second case was identified on day 4 of the session and before it was known whether the infection had been contained, all high-risk campers (eg, campers with asthma who currently were receiving controller medication, with a seizure disorder resulting from encephalitis diagnosed the previous year, or with diabetes) also received oseltamivir prophylaxis (n=8). The total number of campers who began oseltamivir prophylaxis during the session was 68, or 40% of all campers at the session. No campers receiving antiviral prophylaxis developed influenza disease.

When the third case was identified early in the second week of the session, counselor and staff oseltamivir prophylaxis was extended from 10 days to 14 days, not to limit spread (as had been the rationale when it was first started) but to protect key personnel from becoming ill so that the camp could continue to function with appropriate counselor supervision. Dances with 2 girls’ camps in the area were canceled, but campers were allowed to go on trips to raft down rivers in North Carolina and to visit the Tennessee Aquarium in Chattanooga. On these trips, all campers stayed together and did not interact with noncampers. The buses that transported the campers were not used by other camps, and hand sanitizer was administered to campers by their adult counselors on boarding and disembarking the buses.

After the end of the session, 57 parents (33%) completed the online survey. Three of the 56 boys (5%) experienced fever and upper respiratory tract symptoms within 4 days of returning home (1, 3, and 4 days), but none tested positive for influenza A.

### ADVERSE EVENTS

Forty-one of 48 counselors and 27 of 27 staff completed the survey. Of the 68 counselors and staff combined who completed the survey, 39 (57%) experienced stomach discomfort or nausea that they associated with the medication, 34 (50%) experienced headache, and 19 (28%) experienced loose stools or diarrhea (Table 1); all counselors and staff received the capsule formulation of the medication. Questioning of campers receiving oseltamivir prophylaxis revealed that 21 of 68 (31%) had nausea that they related to the medication, 17 of whom received the liquid formulation of the drug. All doses of medication were administered at mealtime. No one receiving oseltamivir prophylaxis presented to the health center with dehydration during the period of drug administration.

Two subjects (1 camper and 1 staff member) had diabetes controlled by insulin injections, and both reported that they experienced difficulty maintaining control of their blood glucose level (hypoglycemia) while receiving oseltamivir.

### MEDICATION COMPLIANCE

All counselors took at least 1 dose of oseltamivir compared with 89% of the staff. The median number of missed doses was 1 (mean, 1; range, 0-12) for the college-aged counselors and was the same for the somewhat older staff (median, 1; mean, 1; range, 0-4). The percentage who missed at least 1 dose of oseltamivir was 66% for the counselors and 38% for the staff (Table 2). Medication noncompliance was not associated with the number of adverse events a subject experienced (Cochran-Mantel-

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### Table 1. Types of Adverse Events Likely Related to Oseltamivir Prophylaxis

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Counselors (n=41)</th>
<th>Staff (n=27)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stomach discomfort or nausea</td>
<td>39/41 (95%)</td>
<td>19/27 (70%)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>2/41 (5%)</td>
<td>2/27 (7%)</td>
</tr>
<tr>
<td>Loose stools or diarrhea</td>
<td>19/41 (46%)</td>
<td>6/27 (22%)</td>
</tr>
<tr>
<td>Headache</td>
<td>34/41 (83%)</td>
<td>27/27 (100%)</td>
</tr>
</tbody>
</table>

### Table 2. Frequency of Medication Compliance and Adverse Events

<table>
<thead>
<tr>
<th>Medication Compliance and Adverse Events</th>
<th>Counselors (n=41)</th>
<th>Staff (n=27)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oseltamivir phosphate compliance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Took ≥1 dose, No./Total No. (%)</td>
<td>41/41 (100)</td>
<td>24/27 (89)</td>
</tr>
<tr>
<td>Missed ≥1 dose, No./Total No. (%)</td>
<td>27/41 (66)</td>
<td>9/24 (38)</td>
</tr>
<tr>
<td>No. of missed doses</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Median (range)</td>
<td>1 (0-12)</td>
<td>1 (0-4)</td>
</tr>
<tr>
<td>Adverse events, No.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>1.5</td>
<td>2</td>
</tr>
<tr>
<td>Median (range)</td>
<td>1.5 (0-4)</td>
<td>2 (0-3)</td>
</tr>
</tbody>
</table>

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Only 1.8% of campers in the fourth session developed ILI and tested positive for influenza A, compared with 12% of family members in household settings, 6 11% of military recruits, 10 and up to 30% to 40% of campers in camps without this level of aggressive monitoring and intervention (Jacquelyn Foldes, RN, MPH, CDC, written communication, August 28, 2009). No campers were known to test positive for influenza A within the first weeks after returning home. Among persons receiving prophylaxis, the majority of staff and counselors (51 of 65 [78%]) experienced 1 or more adverse events (nausea, headache, loose stools or diarrhea, or vomiting) that may have been related to the medication. A smaller percentage of campers (31%) had nausea likely related to prophylactic oseltamivir. All persons received their oseltamivir doses at mealtime to decrease the likelihood of gastrointestinal adverse effects. Limiting use of oseltamivir prophylaxis to campers at increased risk for exposure, while continuing universal hand sanitization and surface decontamination, resulted in fewer campers having adverse effects from the drug. Based on the percentages of campers (31%) and counselors and staff (78%) who had adverse effects while receiving treatment, 32 to 80 of the 103 campers who did not receive oseltamivir prophylaxis may have had nausea or other adverse effects if oseltamivir had been administered less discriminately. At an active boys’ camp with numerous outdoor activities in the heat of the summer, minimizing events that could contribute to decreased fluid intake and dehydration is desirable. Additionally, the cost of oseltamivir for the 136 campers, counselors, and staff receiving prophylaxis was already approximately $16 000 (data not shown), and providing it for 113 additional campers would have increased this expense by 43%. Discriminate use of antiviral prophylaxis also lessens the likelihood that antiviral resistance may develop. Two cases of oseltamivir resistance were reported in a girls’ camp in North Carolina during a mass chemoprophylaxis program in which approximately 600 campers and staff members received oseltamivir or zanamivir. 11

The rationale for using oseltamivir prophylactically in the closed environment of a boys’ camp is based on documented benefit of prophylaxis in nursing homes. 8, 9 Using oseltamivir in a targeted fashion to provide protection of persons closest to the index case was possible at this camp because the boys in adjoining cabins went to all activities as a group. Thus, there was less exposure of campers in one cabin to those in a nonadjoining cabin, although exposure still occurred during change of activities, at mealtime, at snack breaks in the mornings and afternoons, and during free time in the evenings. Our rationale for using targeted prophylaxis was based on the experience of ring vaccination in smallpox eradication.12, 13 In this approach, the intervention (eg, vaccination for smallpox, antiviral prophylaxis for influenza) is targeted to those persons in closest contact with the source case. By providing protection to this ring of potential exposures, the overall spread of the infection is limited within the larger population.

Several potential weaknesses exist in our study. Our efforts to contain the spread of influenza A within the camp setting developed rapidly once the experience of having a dozen campers with ILI at the end of the third session was recognized. Data on effective influenza disease management in summer camp settings were not available, and indeed the extent of camp outbreaks during the 2009 summer was not recognized because influenza transmission during summer months in the Northern Hemisphere previously was extremely rare. As such, we were unable to involve other camps and randomize them to differing interventions to more rigorously prove that this approach resulted in the observed benefit of markedly diminished transmission. Additionally, the sensitivity of influenza rapid tests for novel influenza A(H1N1) is 40% to 69%, 14 which could have resulted in underrecognition of disease in our camp or among campers once they returned home. However, we used the QuickVue Influenza A + B rapid diagnostic test, which has a sensitivity on the higher end of the range (69%), 14 and we monitored all campers with any fever in an isolation room in the health center regardless of the influenza A test result. No other campers were identified with clinical illness consistent with influenza disease but a negative rapid test result. Influenza illness following completion of the fourth session of camp was self-reported via the SurveyMonkey online tool, and as such underreporting could have occurred. Finally, we are unable to determine which part of our intervention (targeted oseltamivir prophylaxis, hand sanitization, surface cleaning) provided the greatest benefit since all were done simultaneously. However, the rapid appearance of 12 ILI cases in the final days of the third session, at which time hand sanitization and surface cleaning were being performed with the same rigor as during the fourth session but with no antiviral prophylaxis, suggests that the targeted oseltamivir prophylaxis is what provided most of our beneficial outcomes during the fourth session.

In conjunction with aggressive hand sanitization and surface decontamination, a targeted approach to antiviral prophylaxis contained the spread of influenza in a summer camp setting. Among campers and staff receiving prophylaxis, one-third to three-quarters experienced adverse effects of treatment, further illustrating the benefit of limiting antiviral use without compromising effectiveness. Additional controlled studies randomizing camps to specific components of the interventions used here would be needed to fully understand the relative benefits of each.

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REFERENCES


