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Route of administration for antibiotics with high oral bioavailability

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National stewardship guidelines recommend that hospitals develop interventions to increase use of oral antibiotics.1 Transition from intravenous to oral route of administration for antibiotics with high oral bioavailability (HOB) is a simple intervention shown to decrease cost and length of hospitalization. We sought to determine the prevalence of use and route of administration of HOB antibiotics at children’s hospitals to determine how frequently intravenous to oral switch might be feasible and to quantify potential cost savings of this strategy in hospitalized children.

Methods

We used 2015 data from the Pediatric Health Information System (PHIS), an administrative and clinical database maintained by the Children’s Hospital Association.2 Patients were included if they were potentially eligible for intravenous to oral switch as defined by (1) receipt of an HOB antibiotic, (2) receipt of ≥1 nonantibiotic oral medication on the same day as the antibiotic, and (3) hospital stay ≥2 days. The HOB antibiotics included clindamycin, metronidazole, ciprofloxacin, levofloxacin, doxycycline, linezolid and rifampin, all of which have ≥80% oral bioavailability.3 Antimicrobials typically used for prophylaxis (azithromycin, trimethoprim-sulfamethoxazole, and azoles) were excluded because they are usually given orally and it is difficult to distinguish treatment from prophylaxis using PHIS data.

Days of therapy (DOT) for each drug were reported overall and stratified by route and hospital. Oral administration of HOB antibiotics was reported using 2 metrics: (1) the percentage of all HOB antibiotic DOT that were administered orally (% PO DOT) and (2) the percentage of all patients receiving HOB antibiotics who received doses orally, either completely or in combination with intravenous therapy. If children received antibiotic doses via both routes on the same day it was counted as an oral DOT. Specific diagnoses were identified using All Patient Refined Diagnosis Related Groups (APR-DRGs).

Antibiotic costs were estimated using institution-specific cost-to-charge ratios. Maximal cost-savings were estimated using the same institution-specific cost-to-charge ratios under the alternate case of administering all doses of HOB antibiotics orally.

Results

Data from 48 freestanding children’s hospitals were included: 38,933 children received 221,535 DOT of HOB antibiotics and at least 1 nonantibiotic oral medication, accounting for ~17% of all PHIS antibiotic use. Overall, 35.8% of all HOB DOT were administered orally, ranging from 21.3% to 63.8% across institutions. Clindamycin was the most commonly prescribed HOB antibiotic, accounting for nearly half of all HOB DOT (Table 1). However, it had the lowest percentage of oral DOT (21.7%) and the highest percentage (63.0%) of intravenous-only receipt. Cellulitis was the most common diagnosis associated with clindamycin use, for which 27.6% of DOT were oral. Other common diagnoses included pneumonia (26% oral DOT) and musculoskeletal infections (16% oral DOT).

The HOB antibiotics most likely to be prescribed orally were rifampin (80.5% of all DOT) and doxycycline (70.8% of all DOT). Fluoroquinolones were administered orally for only half of all DOT. However, there was significant variation in the proportion of oral fluoroquinolone use across institutions, ranging from 27.0% to 98.3% for ciprofloxacin and from 0 to 100% for levofloxacin. Similarly, less than one-third of linezolid DOT were administered orally, ranging from 0 to 100% across institutions.
The total hospital cost for all HOB antibiotics administered during the study period was $11,662,963. The estimated cost had all doses been administered orally was $5,891,137.

**Discussion**

Only 36% of HOB antibiotic DOT were administered orally in this cohort of children receiving other oral medications. These data suggest that intravenous to oral switch programs should be prioritized in children’s hospitals. Clindamycin should be a priority target for such programs because it is both commonly used and often administered intravenously. It is well-documented that intravenous to oral switch is safe and effective for children with osteomyelitis and complicated pneumonia. However, in this cohort, children with these diagnoses were more likely to be treated with intravenous clindamycin.

Intravenous to oral switch programs would be cost saving in this cohort of children receiving other oral medications. These data suggest that intravenous to oral switch programs should be prioritized in children’s hospitals. Clindamycin should be a priority target for such programs because it is both commonly used and often administered intravenously. It is well-documented that intravenous to oral switch is safe and effective for children with osteomyelitis and complicated pneumonia. However, in this cohort, children with these diagnoses were more likely to be treated with intravenous clindamycin.

Intravenous to oral switch programs would be cost saving in pediatrics. We estimated a nearly 50% decrease in drug cost alone. Although this represents the maximum potential savings in direct drug costs, it does not account for additional cost savings due to drug administration, shorter hospital stays, avoidance of outpatient parenteral antibiotic therapy and catheter-associated infections.

The reasons for underutilization of oral administration are uncertain. Some clinicians and parents may have the perception that intravenous antibiotics are more effective or that insurance companies mandate intravenous therapy for reimbursement of parenteral antibiotic therapy and catheter-associated infections.

The data from freestanding children’s hospitals. Clindamycin should be a priority target for such programs because it is both commonly used and often administered intravenously. It is well-documented that intravenous to oral switch is safe and effective for children with osteomyelitis and complicated pneumonia. However, in this cohort, children with these diagnoses were more likely to be treated with intravenous clindamycin.

In conclusion, we observed frequent intravenous administration of HOB antibiotics at children’s hospitals. Intravenous to oral conversion programs, with a focus on clindamycin and fluoroquinolones, are potential high-impact targets for antimicrobial stewardship.

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