

Randomized Trial of Team Pharmacist-Led Antimicrobial Time Out

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ABSTRACT

Background: The CDC has advocated for antimicrobial “time out” implementation to improve antimicrobial use, but little data exists on the impact of such interventions.
Methods: Six medicine teams were randomized to implementation of a team pharmacist-led antimicrobial time out (TO) or usual care (UC). Pharmacists in the TO group received education and used standardized questions to facilitate TOs on rounds targeting two time points: early (<72 hours after antibiotic start) and late (after early, ≤5 days after antibiotic start). Time out were performed on all patients, but only those meeting inclusion criteria were analyzed: age≥19, medicine primary, received antibiotics ≥ 48 hours. ICU days were excluded; antibiotic use was measured in days of therapy (DOT) per patient day (PD).
Results: A total of 260 (120 TO, 140 UC) patients with 290 admissions were included. Demographics were similar between groups: overall 46.9% male, 76.9% admitted to medicine, median age and Charlson score 62 and 2, respectively. Infections were similar between groups with respiratory tract (28.6%), skin-soft tissue/bone (24.1%), and genitourinary (21.7%) most common. TOs were performed 152 times; TO compliance was 72% for early and 68.8% for late. Common TO outcomes were: no change (N=80), narrow antibiotics (N=29), ID consult (N=21), and change to PO (N=13). Clinical outcomes and antibiotic use data are in Table 1. In the TO group oral conversion was more frequent (54.7% vs. 44.2%, P=0.08), time to oral conversion was earlier (2.43 vs. 3.39 days, P=0.14), the proportion of PO antibiotics prescribed increased (39.1% vs. 29.6%), and the ratio of PO to IV antibiotic days was significantly higher (1.14 vs. 0.54, P=0.01) compared to the UC group.

	Time Out (N=137)	Usual Care (N=153)	P
ID Consult	47 (34.3)	48 (31.4)	0.62
Stewardship Intervention	11 (8.1)	21 (13.7)	0.14
Readmission	34 (24.8)	48 (31.4)	0.26
ICU Transfer	17 (12.4)	16 (10.5)	0.71
<i>C. difficile</i> Infection	5 (3.7)	2 (1.3)	0.26
Any Antibiotic Adverse Event	29 (21.2)	32 (20.9)	1.00
DOT/1000 PD	1190	1101	0.39
IV DOT/1000 PD	739	780	0.98
PO DOT/1000 PD	465	326	0.44

Conclusion: Introduction of a pharmacist-led antimicrobial time out did not decrease antibiotic use, but was associated with earlier and more frequent use of oral therapy.

INTRODUCTION

- Antimicrobial use in the hospital is widespread and often inappropriate
- Antimicrobial stewardship (AS) can improve antimicrobial use but often requires dedicated personnel and expertise
 - Many patients may not be captured by traditional antimicrobial stewardship mechanisms (pre-authorization, audit/feedback, etc.) due to resource limitations
- The use of antibiotic “time-outs” (ATO) has been advocated as a broadly applicable process which can extend the reach of traditional AS and improve antibiotic use without dedicated personnel¹
 - Small, quasi-experimental, single center studies have shown some benefit to ATO but little data has been published regarding effective deployment of ATO²⁻⁴
- We developed an ATO process and implemented it in a randomized fashion to 6 medicine teams using team-based pharmacists as the initiators of the ATO

METHODS

Setting:

- Six medicine (5 internal medicine and 1 family medicine) teams at a 650-bed academic medical center
- Institutional antimicrobial stewardship team (AST) did not alter activities during the study

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METHODS, cont.

Antibiotic Time Out (ATO) Process:

- Local AST developed an ATO process with feedback from team pharmacists designed to facilitate discussion of antibiotics
- Pharmacists classified antibiotics into categories (Empiric, definitive, prophylaxis) and used algorithms to assist in discussion (Fig 1).
- ATO were targeted for 2 time periods and documented in the electronic record when performed:
 - Early (<72 hrs. after antibiotic start or <24 hrs. after transfer from ICU)
 - Late (after early and ≤5 days after antibiotic start)
 - Subsequent (any ATO after 5 days)

Implementation:

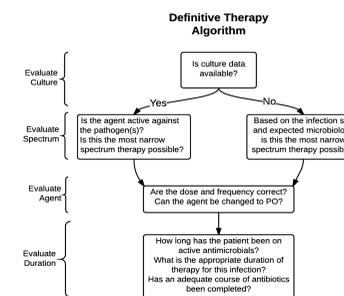
- Medicine teams were randomized to use of the ATO or usual care (UC) and outcomes measured over a 2 month period
- All team personnel were educated once per month in the management of common infectious disease syndromes (pneumonia, skin infections, etc.)
- ATO group pharmacists were educated on ATO process with weekly follow up by the local AST

Data Collection:

- ATO were performed in all patients on the medicine teams but only patients meeting the following criteria were included in the analysis: age≥19, medicine primary, received antibiotics ≥ 48 hours
 - ICU days were excluded from analysis

Data Collected:

- Demographics
- Admitting service
- Length of stay
- ICU transfer, mortality, readmission
- Infection source
- AST intervention
- Antibiotic adverse events: (*C. difficile* infection, allergic reaction, renal dysfunction, QT prolongation)
- Total and specific antibiotic days of therapy (DOT) per 1000 patient days (PD)
- Two-sample t-test and Fisher’s exact test were used to compare continuous and categorical variables between groups
- DOT rates were compared using negative binomial regression



RESULTS

- A total of 260 patients (120 ATO, 140 UC) with 290 (137 ATO, 153 UC) admissions met inclusion criteria with no differences in mortality (2.5% ATO vs. 2.9% UC, P=1.00)
- There were no significant differences in % male (51.7 ATO vs. 42.9 UC, P=0.17), median Charlson score (2 vs. 2, P=0.47), mean age (62 vs. 60, P=0.15), or race (overall 78.8% Caucasian, 16.2% African-American, 5% other)
- No differences were noted in the admitting service with 77.6% admitted to medicine and 22.4% admitted to other services (mostly ICU) and transferred to medicine (P=0.34)
- Infection sources were: respiratory tract (28.6%), skin and soft tissue/bone (24.1%), genitourinary (21.7%), intra-abdominal (12.8%), Central venous catheter (6.6%), CNS (1.4%), and other (4.8%); with no significant difference between groups (P=0.44)
- Clinical outcomes did not differ between the ATO and UC groups (Table 1)

Table 1: Clinical Outcomes

	ATO (N=137)	UC (N=153)	P
ID Consult	47 (34.3)	48 (31.4)	0.62
AST Intervention	11 (8.1)	21 (13.7)	0.14
<i>C. difficile</i> Infection	5 (3.7)	2 (1.3)	0.26
Readmission	34 (24.8)	48 (31.4)	0.24
ICU Transfer	17 (12.4)	16 (10.5)	0.71
Any Antibiotic Adverse Event	29 (21.2)	32 (20.9)	1.00

Antibiotic Use:

- Overall antibiotic use was not different between groups nor were there any differences in use of specific agents, but PO therapy was more common in the ATO group (Table 2)

Table 2: Antibiotic Use

	ATO	UC	P
DOT per 1000PD	1190.3	1101.1	0.39
IV DOT per 1000PD	739.3	780.1	0.98
PO DOT per 1000PD	465.3	324.6	0.44
PO/IV DOT Ratio	1.14	0.57	0.01
IV to PO Conversion	55.5%	44.4%	0.08
Time to PO Conversion	2.4 days	3.4 days	0.14

Antibiotic Time Outs:

- A total of 184 ATO were documented during the study period but only 152 (82.6%) were performed on patients meeting study criteria and were analyzed
- Early ATO compliance was 72%
- Late ATO compliance was 68.8% but in 53.3% of patients an ATO wasn’t indicated
 - Reasons for ATO not being indicated included: Discharged (70.2%), ID consulted (14.3%), Antibiotics already stopped or prophylaxis already evaluated (N=13.1%), Other (2.4%)
- ATO type and intervention are described in Table 3

Table 3: Antibiotic Time Out Description

Type of Therapy	All (N=152)	Early (N=96)	Late (N=44)	Subsequent (N=12)
Empiric	80 (53.0)	62 (64.6)	15 (34.9)	3 (25.0)
Definitive	67 (44.4)	30 (31.3)	28 (65.1)	9 (75.0)
Prophylaxis	4 (2.7)	4 (4.2)	0 (0.0)	0 (0.0)
Intervention				
Narrow Abx	29	19	9	1
Broaden Abx	2	2	0	0
Discontinue Abx	6	2	3	1
ID Consult	21	14	6	1
Change to PO	13	9	4	0
Adjust Dose	5	3	2	0
No Change	80	49	23	8
Other	5	3	1	1

CONCLUSION

- Implementation of a team-based pharmacist-led ATO was successful although opportunities were missed due to lack of team-based pharmacist staffing on weekends and holidays
- ATO did not decrease overall antibiotic use but appeared to precipitate more frequent and earlier transition to oral agents
- While subjective feedback regarding the ATO was positive from both teams and pharmacists more study is needed to determine:
 - Sustainability
 - Generalizability (ICU, surgical team, pediatrics, etc.)
 - Optimization (timing, personnel, format, etc.)
- To evaluate these issues UC care teams implemented ATO with similar outcomes measured for 2 months (data analysis ongoing)

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