CORRESPONDENCE

Challenges in Procalcitonin Implementation in the Real-World

To the Editor—We read with interest the article by Broyles [1] describing a pre-post, retrospective cohort study at a 50-bed community hospital. Broyles [1] describes a comprehensive and resource-intensive intervention, including the development of an evidence-based procalcitonin algorithm (PCT-A) and numerous education sessions. Unique aspects of the study intervention include electronically building the PCT-A into the electronic medical record (EMR) and oversight by pharmacists, who were authorized to order PCT and adjust antibiotic regimens per protocol, resulting in 92% adherence to the PCT-A.

To emphasize the importance of developing a comprehensive intervention to aid in the success of PCT implementation, we describe our single-center experience, when adding the PCT assay (VIDAS B.R.A.H.M.S PCT) as an in-house test. Our institution is a 473-bed academic hospital with a well established antimicrobial stewardship program (ASP). Similar to Broyles' [1] study, an evidence-based PCT-A was developed, in which antibiotics were discouraged when PCT ≤0.25 ng/mL, and lectures were provided to physicians and pharmacists. Although guidance to help interpret PCT was provided in the comments section of the EMR, the full PCT-A was not built into the EMR, and a physiologic reference range of ≤0.09 ng/mL was inadvertently selected for use in the EMR based on the package insert [2]. Consequently, any value above 0.09 ng/mL flagged as elevated. Therefore, we aimed to evaluate the influence of laboratory reporting on the interpretation of PCT results and subsequent impact on antibiotic decision making.

We performed a retrospective cohort study of adult patients admitted from November 1, 2015 to October 31, 2016 with a first PCT concentration between 0.09 ng/mL and 0.25 ng/mL. We included 274 patients in our study with a median PCT concentration of 0.15 ng/mL. Most of the patients (47%) were suspected of having pneumonia or sepsis, but no suspected infection was documented in 29% of patients. Forty-three percent of patients had an elevated white blood cell count, 26% of patients had a T_{max} > 101°F, and 38% of patients had neither sign of infection.

Procalcitonin interpretation was documented in 85 (31%) patients in progress notes. Among these patients, 61% of interpretations were inappropriate. An example of appropriate interpretation was "procalcitonin not suspicious for infection," whereas an example of inappropriate interpretation was "infection ruled out, but will continue antibiotics because of elevated procalcitonin." Patients with inappropriate interpretations received more antibiotics compared with patients with appropriate interpretations (7 versus 5 days, $P = .05$) despite having no differences in signs of infection and similar PCT values. In addition, antibiotics were more commonly initiated or broadened among patients with inappropriate interpretations (34% versus 9%, $P < .01$) (Table 1).

At our institution, implementation of PCT with a low reference range resulted in a high rate of inappropriate clinical interpretation and greater exposure to antibiotics, despite having a well established ASP, developing a PCT-A, and providing education. Our study has several limitations. First, the rate of PCT interpretations documented in the EMR was low. However, including only direct

Table 1.   Analysis Based on Appropriate Versus Inappropriate Procalcitonin Interpretation[a]

Patient Characteristic	Appropriate Interpretation N = 32	Inappropriate Interpretation N = 53	P Value
First procalcitonin, ng/mL, median (IQR)	0.13 (0.11–0.18)	0.16 (0.13–0.20)	.06
ICU admission	14 (44)	23 (43)	.98
Receipt of antibiotics	28 (88)	51 (96)	.19
Antibiotic duration of therapy, days, median (IQR)	5 (3–8)	7 (5–12)	.05
Sign of infection			
T_{max} >101°F and WBC >12 K/mcl	1 (3)	3 (6)	.99
T_{max} >101°F	6 (19)	12 (23)	.67
WBC >12 K/mcl	13 (41)	23 (43)	.80
Neither T_{max} >101°F nor WBC >12 K/mcl	14 (44)	21 (40)	.71
Antibiotic change in response to PCT value or trend			<.01
Initiate or broaden	3 (9)	18 (34)	
De-escalate or discontinue or no initiation	16 (50)	10 (19)	
No change	13 (41)	25 (47)	
Length of stay, days, median (IQR)	8 (4–27)	11 (5–25)	.38

Abbreviations: ICU, intensive care unit; IQR, interquartile range; PCT, procalcitonin; T_{max}, maximum temperature; WBC, white blood cell count.

[a]Values presented as n (%) unless otherwise noted.

interpretations strengthens our ability to attribute antibiotic changes to PCT results. Second, other variables that may have affected PCT and antibiotic management were not assessed. However, fever and leukocytosis were included in the analysis, as objective signs of infection. Third, in contrast to Broyles' [1] study, our larger academic hospital setting, with a high rate of rotation between providers and trainees, makes comprehensive education difficult. Strengths of our study, compared with Broyles' [1] analysis, include the short time frame and inclusion of only patients with a PCT result, rather than analyzing all patients receiving antimicrobials. In addition, we compared patients within the same short time frame, which reduces the risk for confounders that may have influenced antibiotic use and clinical outcomes, such as improvements in practice, especially given more recent focus on antimicrobial stewardship and shortening duration of therapy for many infections, including pneumonia, urinary tract infections, and intra-abdominal infections.

CONCLUSIONS

In the current environment of antimicrobial stewardship, many clinicians are increasingly utilizing rapid diagnostic tests and biomarkers to better differentiate infectious versus noninfectious syndromes in an effort to curb inappropriate antibiotic use. Clinical decision support tools that provide guidance at the point-of-care in the EMR can help prevent misinterpretation of laboratory results. Although our efforts were well intended, perfunctory implementation had the opposite effect of increasing antibiotic exposure. Therefore, this case study should serve as a cautionary tale to antimicrobial stewardship programs—failure to develop a robust and comprehensive intervention may result in unintended consequences.

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