Changes in Coagulation Testing During a National Shortage of Blue-Top Tubes

A Laboratory Stewardship Opportunity

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ABSTRACT

Objectives: Manufacturer recalls and altered supply chains during the coronavirus disease 2019 (COVID-19) pandemic caused a nationwide shortage of blue-top tubes (BTTs). Most non–point-of-care coagulation tests use these tubes, leaving laboratories and health care facilities in short supply. The Department of Pathology and Laboratory Medicine at Cedars-Sinai Medical Center implemented interventions to conserve supply without sacrificing patient safety.

Methods: In a retrospective quality improvement analysis, we examined coagulation testing and BTT utilization over the 3-month interval during which our interventions were applied. Our study assessed the interventions’ effectiveness by evaluating changes in BTT utilization, coagulation testing volume, and patient impact.

Results: Average daily use (ADU) of BTT before and after the intervention were 476 and 403, respectively—a 15.2% reduction. Notably, the Emergency Department had a reduction in ADU of 43.3%. Average daily volumes of coagulation assays performed decreased from 949 to 783—a 17.5% reduction. No adverse events from the Pharmacy Department were identified during the study period.

Conclusions: Interventions resulting in significant reductions were in divisions with effective management and supervision. Success in navigating the BTT shortage stemmed from timely announcements, action, and effective communication. Our recommendations established more effective coagulation assay utilization, decreased overall BTT use, and prevented patients with coagulopathic disorders from experiencing adverse consequences.

INTRODUCTION

Coagulation studies are essential for the evaluation of blood hemostatic function in patients. Coagulation studies are used in various clinical settings, including bleeding and clotting disorders, preoperative testing, and anticoagulation monitoring. Accurate coagulation testing requires that the blood specimens be collected in an appropriate collection tube that will inhibit the initiation of the coagulation cascade before reaching the laboratory for testing. The most widely used collection tube is the blue-top tube (BTT), which contains a 3.2% sodium citrate anticoagulant solution. The quantity of sodium citrate solution in the collection tube

KEY POINTS

• In this retrospective quality improvement analysis, we aimed to reduce unnecessary utilization of blue-top tubes (BTTs) in a tertiary-care hospital, initially motivated by a critical nationwide shortage.

• This quality improvement project highlights the laboratory’s ability to provide insight into clinical practices and identify areas of improvement.

• Outcomes resulted in effective coagulation assay use, reduced BTT use and unnecessary phlebotomy, and prevented adverse outcomes in patients with coagulopathic disorders.

KEY WORDS

Blue-top tubes; Shortage; COVID-19; Laboratory stewardship

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is fixed to create an appropriate ratio of 1 part sodium citrate solution to 9 parts whole blood when the tube is filled correctly. Only 2 major vendors supply US Food and Drug Administration (FDA)–approved BTTs to laboratories and health care facilities in the United States: Greiner Bio-One and Becton Dickinson (BD). In May 2021, the United States was confronted with a severe nationwide shortage of BTTs.2,3 This critical shortage was a result of several factors. The primary factor was a recall of more than 1 million BTTs by Greiner Bio-One on March 29, 2021, because of concerns for insufficient draw volume of the tubes, which could produce erroneous results.1 An additional factor contributing to the shortage was the coronavirus disease 2019 (COVID-19) pandemic.2,3 The COVID-19 pandemic altered typical vendor manufacturing and supply chains in various aspects of the laboratory, including coagulation.1,3 These factors were compounded by a significant increase in coagulation assays ordered during the COVID-19 pandemic because of the incidence of thrombotic events in patients infected with severe acute respiratory syndrome coronavirus-2 and use of anticoagulation therapy in these patients.4-6

Most non–point-of-care (POC) coagulation tests are collected in BTTs, and for many laboratories and health care facilities, use was exceeding reduced supply. In an effort to mitigate this shortage, the Department of Pathology and Laboratory Medicine at Cedars-Sinai Medical Center implemented several interventions to help conserve supply while continuing to meet demands. We performed a retrospective quality improvement study to assess the effectiveness of the implemented interventions and resulting outcomes of these interventions. The outcomes evaluated included BTT utilization, performed coagulation test quantity changes, and patient impact.

MATERIALS AND METHODS

In this retrospective quality improvement project, we examined coagulation testing and BTT utilization before and after a recommendation initiative within the Cedars-Sinai Health System. Cedars-Sinai is one of the largest health care organizations serving the diverse Los Angeles community. It includes a main medical center (883 beds), several hospital affiliations, and more than 250 primary and specialty care locations.7 Our study included the main medical center data reported from April 15, 2021, through June 16, 2021. We selected a limited 3-month time frame to minimize nonrepresentative data. Earlier data would be affected by uncharacteristic coagulation testing volumes associated with the COVID-19 pandemic, and subsequent data would be affected by the hospital’s acquisition, validation, and implementation of new BTTs ordered from a manufacturer outside the United States. For historical comparison, we also collected data during this same time interval from the past 3 years (2018, 2019, and 2020) to assess for seasonal variation. On May 12, 2021, a health care system-wide announcement was released alerting all medical staff of the critical nationwide shortage of the 3.2% sodium citrate BTTs used for coagulation assays. The announcement included information regarding significant reductions in tube allocation as well as a request for providers to limit coagulation testing for patients with active bleeding, serious coagulopathies, and baseline/monitoring of anticoagulation therapies, when indicated. In addition, the Pharmacy Department provided anticoagulation recommendations to follow to use current supply strategically without compromising patient care and safety.1

In the setting of patients requiring multiple coagulation tests, strategies could be implemented to consolidate blood draws and ultimately set standards for minimum required sodium citrate tubes. With assistance from the director of Coagulation Consultative Services, the clinicians received guidelines for the minimum required sodium citrate tubes for coagulation assays.1 These guidelines included minimum requirements for both the adult and pediatric patient populations, emphasized that tubes must be filled in appropriate quantities, and listed coagulations assays that do not require sodium citrate tubes and were therefore unaffected by the shortage (eg, serologic and molecular assays).

Alternative assays were available that could be used as a substitute to the standard assay during this shortage. This concept is best highlighted by our solutions offered with the VerifyNow Assay. The VerifyNow Assay is used to assess aspirin and adenosine diphosphate (ADP) inhibitor effect. This test required tubes provided by Greiner Bio-One, which were affected by the shortage and temporarily unavailable for ordering. The laboratory distributed information about other assays offered to assess platelet function to support patients’ needs. These assays included platelet aggregometry and thromboelastography platelet mapping, indicated for assessing aspirin and ADP inhibitor effect, and platelet function analyzer 100, indicated for assessing aspirin effect only. Because the laboratory provided alternative testing information, clinicians were able to adequately monitor patients amidst the shortage.

Using SAP Crystal Reports, version 14.1.1.1036, software interfaced with the laboratory’s Sunquest laboratory information system, we extracted the total numbers of BTTs collected. We collected the total BTT utilization data and sorted them by major departments (Emergency Department [ED], Inpatient, Outpatient, Outreach, and Surgery). In addition, weekly census data in our ED and inpatient units were collected using SAP Crystal Reports software from April 15, 2021, through June 16, 2021, to assess fluctuating hospital census as a possible confounding variable.

The assays performed in the hospital’s core laboratory and used in this analysis included prothrombin time (PT), activated partial thromboplastin time (aPTT), fibrinogen, dimerized plasmin fragment D (D-dimer), and unfractionated heparin (UFH) level. The tests performed in the hospital’s special testing laboratory (which performs PT; aPTT; and other, more specialized coagulation tests) included PT, aPTT, von Willebrand factor (VWF) level/activity, lupus anticoagulant, and platelet aggregometry. Also, this study collected data on POC testing (POCT) performed before and after the intervention. Using SAP Crystal Reports software, we extracted weekly POCT performed approximately 4 weeks before and after the intervention. POCT data included kaolin activated clotting time (ACTk) and (international normalized ratio [INR]) measurements performed on i-STAT analyzers (Abbott Diagnostics), the Hemostasis
Management System (Medtronic), and CoaguChek system (Roche Diagnostics).

To evaluate data and reduce the “noise,” of daily variations in BTTs collected and coagulation test volumes, we used a 7-day moving average. Each 7-day moving average data point was the mean of the counts of the current day plus the counts from the prior 6 days.

Per our institution’s Office of Research Compliance and Quality Improvement (ORCQI), quality improvement activities designed to assess or improve performance within the laboratory that involve no patient interaction and no accessing of protected health information apart from laboratory values do not constitute “research” or “clinical investigation” subject to institutional review board approval or certification of exemption by the ORCQI.

### RESULTS

#### BTT Utilization

Overall, BTTs collected decreased after the intervention. The daily average of BTTs collected before and after the intervention was 476 and 403, respectively, for a total reduction of 15.2%. When compared with the past 3 consecutive years, these changes were not the result of seasonal variation. Additionally, at the beginning of the pandemic, between May and June 2020, BTT utilization increased notably.

When we separated the results by department, the most significant reductions were seen in the ED, followed by inpatient units. The daily average of BTTs the ED collected before and after the intervention was 81 and 46,

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**TABLE 1** Pre- and Postintervention Laboratory Tests to Monitor and Adjust Anticoagulation Therapy

| Test Type | Preintervention | Postintervention |
|-----------|-----------------|------------------|
| aPTT/HL   | Within 24 h     | NA               |
| PT/INR    | NA              | NA               |

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**TABLE 2** Pre- and Postintervention Required Sodium Citrate Tubes for Coagulation Assays

| Test Type | Adults | Pediatric |
|-----------|--------|-----------|
| Coagulation assays (eg, PT, aPTT, anti-Xa, fibrinogen, coagulation factors, VWF) | 1 tube per coagulation assay ordered | 1 tube per 1-3 assays |
| PFA-100   | 2      | 1         |
| TEG       | 2      | 1         |
| Platelet aggregometry | 2-6 | 4 |

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**aPTT**, activated partial thromboplastin time; **DOAC**, direct oral anticoagulant; **HL**, heparin level; **ICU**, intensive care unit; **INR**, international normalized ratio; **NA**, not applicable; **PT**, prothrombin time; **PFA-100**, platelet function analyzer 100; **PT**, prothrombin time; **TEG**, thromboelastography; **VWF**, von Willebrand factor; **Xa**, factor Xa.

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**TEG** platelet mapping requires an additional lithium heparin light green–top tube.
respectively—a reduction of 43.3%. The daily average of BTT collected for inpatients before and after the intervention was 300 and 266, respectively—a reduction of 11.2%. These reductions were observed irrespective of changes in the ED and inpatient units’ census over the 3-month period. Near the end of our observed time interval, BTT usage showed trends toward backsliding. We attribute this to an increasing census of COVID-19 patients, who were managed per our COVID-19 protocol, which required more frequent patient hemostatic status assessment.

Coagulation Testing
Overall, coagulation testing performed decreased after the intervention, with significant reductions seen in the assays the core laboratory performed. The daily average volume of coagulation assays the core laboratory performed before and after the intervention was 949 and 783, respectively, for a total reduction of 17.5%. The specific assays that demonstrated postintervention reductions included PT, aPTT, and UFH. The daily average volume of PT, aPTT, and UFH assays the core laboratory performed showed a reduction of 16.3%, 25.0%, and 8.7%, respectively.
The special testing laboratory also experienced a reduction in assays performed, although to a lesser extent. In contrast, the D-dimer assay, which was used as a prognostic metric in patients with COVID-19, increased as anticipated given that we were in the midst of the COVID-19 pandemic. D-dimer assay utilization in 2020 (2,119 assays) and 2021 (2,017 assays) nearly doubled compared with the 2 years before the pandemic (1,421 assays in 2018 and 1,189 assays in 2019).

Point-of-Care Testing
Overall, POCT performed by the intensive care units (ICUs) and the Pharmacy Department demonstrated a slight increase after the intervention. The weekly average of performed POCTs (ACTk and INR) showed an increase of 19.3% and 12.5%, respectively. These results were anticipated because ACTk was used to monitor anticoagulation in patients on extracorporeal membrane oxygenation (ECMO), and there was increased use of ECMO support for patients with COVID-19. The Pharmacy Department used POCT INR to monitor vitamin K antagonist therapy. If the pharmacist had questionable results or an INR above 5.0, the sample was sent to the laboratory for confirmation.

Establishing a Task Force and Providing Guidance
Success in navigating the tube shortage stemmed from timely announcements and action. A task force was formed that included the Pathology Department chair, Clinical Laboratory Improvement Amendments director, Laboratory director, and pathologists with coagulation expertise. The committee established lines of communication between pathologists and clinicians requiring assistance with coagulation test ordering, continuously monitored tube supply and utilization by department, and initiated validation of alternative sodium citrate tubes. In addition, the task force provided recommendations and policy guidance that were distributed on May 12, 2021, ahead of the College of American Pathologists (CAP) recommendations, published June 15, 2021.

Impact of Interventions
We observed that interventions that resulted in the most significant reductions in sodium citrate tube utilization ultimately supporting efforts to conserve supply were in divisions that had well-controlled management and effective supervision. This finding is best highlighted in the ED and inpatient settings. Feedback from clinicians and laboratory personnel indicated that ED and inpatient phlebotomists and nurses had frequently been drawing multiple sodium citrate tubes when multiple coagulation tests were ordered as well as an observation that some clinicians were ordering coagulation tests as part of “defensive medicine.” After notifying hospital leadership of the nationwide shortage, with imminent vendor-restricted order fulfillment; providing medical staff with information about minimum required tubes for coagulation assays; and retraining of phlebotomists and nurses emphasizing that all coagulation tests can be predominately completed using 1 sodium
FIGURE 2  Core laboratory assays performed (7-day moving average). The vertical dashed line represents the date of intervention.  

A, Total.  

B, Prothrombin time.  

C, Activated partial thromboplastin time.
### Table: Number of Assays Performed

| Date       | No. of Assays Performed |
|------------|-------------------------|
| 21-Apr     | 30                      |
| 23-Apr     | 35                      |
| 25-Apr     | 40                      |
| 27-Apr     | 45                      |
| 29-Apr     | 50                      |
| 1-May      | 55                      |
| 3-May      | 60                      |
| 5-May      | 65                      |
| 7-May      | 70                      |
| 9-May      | 75                      |
| 11-May     | 80                      |
| 13-May     | 85                      |
| 15-May     | 90                      |
| 17-May     | 95                      |
| 19-May     | 100                     |
| 21-May     | 105                     |
| 23-May     | 110                     |
| 25-May     | 115                     |
| 27-May     | 120                     |
| 29-May     | 125                     |
| 31-May     | 130                     |
| 2-Jun      | 135                     |
| 4-Jun      | 140                     |
| 6-Jun      | 145                     |
| 8-Jun      | 150                     |
| 10-Jun     | 155                     |
| 12-Jun     | 160                     |
| 14-Jun     | 165                     |
| 16-Jun     | 170                     |

### Figure 2 (cont)

**D.** Unfractionated heparin. **E.** Dimerized plasmin fragment D.

### Figure 3

Special testing—performed assays (7-day moving average). The vertical dashed line represents the date of intervention.
citrate tube, the resulting reduction in tube utilization and coagulation test volume was apparent and significant. Transitioning to using fewer sodium citrate tubes for multiple coagulation tests did not result in any “quantity not sufficient” sample rejections during our study interval.

Role of the Pharmacy Department
Our Pharmacy Department monitors anticoagulation therapy for more than 80% of the non-ICU patient population. This system of pharmacy supervision is widely accepted, supported by hospital and clinical leadership, and promotes better adherence to provided anticoagulation recommendations and policies. This practice ultimately resulted in a reduction in nonindicated coagulation study ordering. In addition, integration of the pharmacy into coagulation management facilitates ongoing reevaluation of patients currently on anticoagulation monitoring and therapies. For example, during the current shortage, if clinically indicated and provider approved, patients were converted to direct oral anticoagulants (DOACs). DOACs do not require ongoing anticoagulation monitoring after baseline coagulation studies have been performed. This finding supported our continuing efforts to reduce coagulation assays performed and sodium citrate tube use.

Validation and Verification of Alternative Sodium Citrate Tubes
Following the recommendations that CAP provided, we began the process of validating alternative sodium citrate tubes. We acquired 2 alternative 3.2% sodium citrate tubes that we compared with our currently validated BD Vacutainer 3.2% sodium citrate tubes. The FDA’s cleared, unmodified verification included testing 65 specimens using our current core laboratory assays (PT, aPTT, fibrinogen, heparin, and fibrin monomers) and 6 specimens using our current special coagulation assays (factor 8, VWF antigen, VWF activity, protein S function, and antithrombin III). All analysis was reviewed and the substitute tubes were deemed acceptable (below the total allowable error percentage).

The Role of the Laboratory, Lessons Learned, and Moving Forward
The Laboratory Department played a central and significant role during this critical sodium citrate tube shortage. Committee meetings, including hospital laboratory, clinical, and pharmacy leadership, formed detailed guidance on appropriate indications for coagulation testing and frequency of testing in various clinical settings. The laboratory worked diligently to secure and verify alternative sodium citrate tubes from other vendors while continually reviewing tube utilization and stock volume by department. The outcome of our efforts established more effective coagulation assay utilization, decreased overall sodium citrate tube usage, reduced unnecessary phlebotomy (potentially avoiding iatrogenic anemia), and prevented adverse consequences for our patients with active bleeding and coagulopathies. This quality improvement project highlights the laboratory’s ability to provide insight into clinical practices and identify areas of improvement. As outlined in the recently published editorial in the American Journal of Clinical Pathology, this laboratory stewardship opportunity—instigated by a national crisis during a global pandemic—demonstrates the role of the laboratory as a health care leader, with a commitment to providing equitable, appropriate, and effective patient care.

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