Clinical Biochemistry 47 (2014) 150–157

Contents lists available at ScienceDirect

Clinical Biochemistry

journal homepage: www.elsevier.com/locate/clinbiochem

Blood collection tube-related alterations in analyte concentrations in quality control material and serum specimens

Raffick A.R. Bowen [a,*], Annie Sattayapiwat [a], Verena Gounden [b], Alan T. Remaley [b]

[a] Department of Pathology, Stanford University, Stanford, CA 94305, USA
[b] Dept. of Laboratory Medicine, National Institutes of Health, Bethesda, MD 20892, USA

ARTICLE INFO

Article history:
Received 8 September 2013
Received in revised form 5 November 2013
Accepted 6 November 2013
Available online 14 November 2013

Keywords:
Blood collection tube
Quality control material
Thyroxine
Triiodothyronine

ABSTRACT

Objectives: Several previous studies have described the effects of interfering substances on clinical assay results; however, the effects of exogenous substances, particularly additives from blood collection tubes on quality control (QC) specimens and serum specimens have not been well examined. This study examines the effects of blood-collection tube additives on total triiodothyronine (TT_3), and thyroxine (TT_4), cortisol, and routine clinical chemistry tests in QC and serum specimens from apparently healthy volunteers.

Methods: QC and serum specimens were poured or collected into different blood collection tubes. TT_3 and TT_4, cortisol, and routine chemistry tests were analyzed from the different blood-collection tube types.

Results: The findings of this study demonstrate statistically and/or clinically significant blood collection tube-related alterations in the TT_3, TT_4, and cortisol concentrations of QC specimens and TT_4 concentrations from serum specimens.

Conclusions: These findings have important implications for clinical laboratories, demonstrating that QC specimens should ideally, like patients' specimens, be poured into blood collection tubes. This strategy would reveal any adverse effects caused by blood collection tubes, which otherwise would not likely be detected by most routine QC practices. The results of this study also show the importance of producing blood collection tubes that contain additives that are truly inert and do not adversely affect clinical laboratory testing.

Introduction

Blood collection and processing are two major steps in pre-analytical laboratory testing [1]. Proper blood collection and timely processing, by well-trained staff using appropriate devices, are needed to ensure test reliability. Blood collection devices have typically been regarded as inert specimen carriers; many laboratories have thus invested relatively little in evaluating new blood collection devices, and do not routinely monitor their performance. Previous studies have reported statistically and clinically significant differences in some immunoassay test results from blood collected in some types of serum evacuated blood collection tubes manufactured by Becton Dickinson (BD) because of tube additives, particularly surfactants [2–4]. To solve immunoassay problems with the BD Vacutainer serum separator (SST), SST II, and Microtainer tubes that surfaced in 2004, BD reformulated the serum tubes to reduce the amount of surfactant in them in order to eliminate assay interference [2,5]. No clinically significant differences were observed with use of the reformulated tube types; it thus appeared that the reformulated BD tubes had been successfully adjusted to reduce assay interference and yield results that were similar to those of glass and Vacuette tubes for the total triiodothyronine (TT_3), total thyroxine (TT_4), and cortisol assays tested [2,5]. However, further studies by Wang et al. [6] and Lima-Oliveira et al. [7], as well as recent TT_3, TT_4, and cortisol results from patients' specimens in the author's clinical laboratory have indicated that blood collection tube related interference in some clinical assays may not be fully resolved.

One of the central tenets of quality control (QC) and quality assurance is that a) control materials should be handled by well-trained and competent laboratory personnel, and b) these control materials should be treated in exactly the same way as patients' specimens [8]. Unfortunately, this is not always adhered to in routine practice, and previously published studies with blood collection tubes have underscored this point [8].

To the author's knowledge, only one study has investigated the impact of QC material poured into blood collection tubes on TT_3, TT_4, and cortisol concentrations; that single study examined only one tube type, SST [8]. The effects of other BD serum tube types and serum tubes from a different tube manufacturer commonly used in clinical laboratories in North America on QC material analyte concentrations are not known. There is thus little information about the potential impact of blood collection tubes on QC specimen analyte concentrations. It was hypothesized that adverse effects of additives in blood collection tubes would be apparent if the QC specimens were poured into blood

Abbreviations: BD, Becton-Dickinson; PT, proficiency testing; PRT, plain red-top; QC, quality control; RST, rapid serum tube; SCL, significant change limit; SD, standard deviation; SST, serum separator tube; TT_3, total triiodothyronine; TT_4, total thyroxine; USD, usual standard deviation.

* Corresponding author at: 300 Pasteur Drive, Room H-1507B, Stanford, CA 94305, USA. Fax: +1 650 736 1473.
E-mail address: rbowen@stanfordmed.org (R.A.R. Bowen).

0009-9120/$ – see front matter © 2013 The Canadian Society of Clinical Chemists. Published by Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.clinbiochem.2013.11.003

collection tubes and processed in the same way as patients' specimens are processed.

The purpose of this study is to evaluate the QC specimens poured into BD PRT, RST, and SST tubes and in Greiner Vacuette tubes and compare them to BD glass blood collection tubes on the Siemens Immulite™ 1000 analyzer for TT_3, TT_4, and cortisol, which are immunoassay analytes shown to be significantly affected by tube surfactant [2,3]. In addition, routine clinical chemistry assays from QC material poured in the five different blood collection tubes will be evaluated on a Siemens Dimension RxL™ analyzer.

Materials and methods

Collection tube types and QC specimens

Five types of evacuated blood collection tubes were examined in this study as shown in Table 1. Glass collection tubes are considered the control tubes in this study because this tube type has been the standard device for collecting serum samples for over five decades and these tubes contain no clot activator, internal tube coating, or separator gel [2,3]. All blood collection tubes were used before their expiration dates. QC specimens (Bio-Rad Liquichek Immunoassay Plus Control) 1 (lot 40781), 2 (lot 40782), and 3 (lot 40783) were poured (2 mL per tube) and mixed end-over-end into BD and Greiner blood collection tubes and processed as described by Kricka et al. [8].

Blood samples were drawn after written informed consent from 20 apparently healthy volunteers (ages 18 and over) by trained phlebotomists, using a butterfly connected to a vacuum tube holder. Blood samples were collected into Greiner and BD collection tubes in a randomized drawing order, and the tubes were filled to capacity. The blood collection tubes were inverted eight times after the blood was drawn to ensure proper mixing of the blood with tube additives. Serum samples from the BD glass tubes were obtained after clotting for 30 min at room temperature followed by centrifugation at 1300 *g* for 10 min. Following centrifugation, all tubes were inspected visually for complete barrier formation (except the glass and PRT tubes), fibrin, and hemolysis. All serum samples were processed within 2 h of blood collection. The serum drawn in Vacuette and BD SST and RST tubes remained on the separator gel. In contrast, the serum drawn in the BD glass and PRT tubes was transferred into 13 × 75 mm plastic test tubes in order to minimize the metabolism of the serum analytes by cellular elements in the blood tube because these two tube types have no separator gel. These samples were capped at room temperature if they were tested within 4 h. Alternatively, they were stored between testing intervals at 4 °C for up to 7 days. TT_3, TT_4, and cortisol were shown in our laboratory to be stable for 7 days at 4 °C in the different blood collection tube (data not shown). The volunteers were contacted if critical values (based on the clinical laboratory critical values list) were obtained from specimens collected from either the Greiner or the BD plastic tubes. This study was approved by an institutional review board of the National Institute of Diabetes and Digestive and Kidney Disease.

Clinical laboratory analysis

1 Determination of QC TT_3,TT_4, and cortisol concentrations.
Total thyroxine and triiodothyronine and cortisol levels in QC specimens poured into the five different types of blood collection tube were measured in random order on an Immulite™ 1000 analyzer, according to the manufacturer's instructions (n = 18) [2,3]. Multiple reagent and calibrator lots were used for the Immulite™ 1000 analyzer, but the data represent a single lot.
2 Routine chemistry analytes.
A routine chemistry panel (as shown in Supplemental Data Figs. 4–8) was performed on QC materials poured into the five tube types on a RxL™ analyzer (n = 4). The QC specimens were analyzed singly in random order and in the same analytical run.

Table 1
Sources and characteristics of the blood collection tubes examined in this study.

Tube	Catalog number	Lot number	Tube dimensions (mm)	Draw volume (mL)	Wall material	Separator gel	Surfactant	Clot activator	Stopper lubricant	Anticoagulant
Glass[a] (red-top)	366441	2219385	16 × 100	10.0	Glass (borosilicate)	None	None	None	Glycerin	None
Vacuette[b] (gold-top)	454228	B091209	13 × 75	4.0	Plastic (PET)	Olefin oligomer[b] (white-opaque)	Unknown	Silica	Silicone	None
Plain red-top[a] (red-top)	367814	2200653	13 × 100	5.0	Plastic (PET)	None	Unknown	Silica	Silicone	None
Rapid serum tube[c,d] (orange-top)	368774	120804	13 × 100	5.0	Plastic (PET)	Polymer gel[c]	Polyalkylene oxide modified poly-dimethylsiloxane[c]	Thrombin[c,d]	Unknown	None
SST[a] (gold-top)	367983	2258708	13 × 75	3.5	Plastic (PET)	Polymer gel[e,f] (yellow opaque)	Silwet L-720[g]	Silica	Silicone	None

PET, polyethylene terephthalate.
[a] From BD [11].
[b] Greiner Bio-One [23].
[c] From Dubrowny and Harrop [12].
[d] From http://www.bd.com/vacutainer/labnotes/Volume20Number1/serum_tube.asp (accessed January 23, 2013) [24].
[e] From Landt et al. [25].
[f] From Bush et al. [26].
[g] FDA enforcement report [27].