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Effect of Blood Collection Devices on Quality Blood Transmission: A Review

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A B S T R A C T

The accuracy of laboratory test findings might be negatively impacted by the improper design or use of blood collecting instruments. The shear stresses produced by vascular access devices, including catheters and needles, during blood flow predispose cells to lysis. Special tube additives may potentially change the stability of analytes. Blood collection tube components, such as stoppers, lubricants, surfactants, and separator gels, can leach into specimens and/or adsorb analytes from a specimen. Blood collection devices are a possible source of pre-analytical error in laboratory testing because of these interactions with blood specimens. Understanding the intricate relationships that exist between blood samples and collection equipment is necessary for accurate laboratory testing. The pre-analytical problems in laboratory testing must be taken into account by manufacturers, vendors, and clinical lab professionals. In this review, blood collection tube additives, their components, and methods for reducing their impact on clinical chemistry assays are identified, described, and discussed..

Keywords: Effect, blood collection, devices, blood transmission;

1. Introduction

According to the International Organization for Standardization's ISO 15189:2012 regulation, technical or quality management system non-conformities that need to be addressed as well as prospective sources of improvement must be systematically found and fixed [1]. The aforementioned standard focuses heavily on patient safety [2] while addressing requirements for quality systems (i.e., the application of quality indicators) to be used in laboratory medicine. Quality indicators are defined as objective measurements created and used to evaluate any important aspect of healthcare, such as patient safety [3, 4]. The most popular sort of biological specimens pulled and sent to laboratory medicine facilities for analysis are diagnostic blood samples obtained by phlebotomy. These samples assist compassionate doctors in patient diagnosis, follow-up, and/or therapeutic monitoring. The Phlebotomy, a relatively intrusive medical technique, is crucial for the subsequent steps carried out during either the laboratory analysis phase or the physician-led interpretation process. Poor phlebotomy quality can impair patient diagnosis, management, therapy, and eventually patient safety itself [5]. Proper blood collection and well timed processing are critical pre-analytical steps required for the integrity of laboratory results [6]. Although the influence of blood series devices on laboratory exams is of then ignored, correct pre-analytical managing is essential. However, many laboratorians do now not cautiously examine the suitability of latest gadgets or screen ongoing overall performance [7]. Blood series gadgets had been commonly appeared as inert specimen carriers [8]. However, many lab professionals do not thoroughly assess the appropriateness of new instruments or keep track of ongoing performance. In this study, we address how blood collection tools and materials, with a focus on blood collection tube (BCT) additives, can affect the outcomes of chemical tests and subsequent quality of blood transmission. Therefore, laboratories have invested little attempt to assess new blood collection gadgets and infrequently display series tool overall performance. This review seeks to underscore the significance of blood collection devices with the aid of summarizing reports of blood collection gadgets that have an impact on medical chemistry assays, and by means of describing blood collection tool components and their interactions with blood specimens for diverse analytic strategies.

2. History of blood collection devices

The initial blood collection tools were reusable glass syringes with steel hypodermic needles and a firm rubber hub [9]. The Luer-Lok syringe, which adjusted the needle tip for a more secure attachment to the syringe and insuring a more dependable and safe drug delivery, was one of the earliest improvements. Other early adjustments included a refined needle, replacing the rubber hub with glass, and refining the needle. Glass syringes were costly to produce and prone to breakage [10]; however, the numerous hepatitis outbreaks brought on by their use finally led to their replacement with sterile disposable syringes [9]. Glass syringes were able to be replaced with plastic syringes thanks to modern radiation and chemical sterilization methods. Because they automatically take a specified blood volume and rotating between tubes for additional samples lowers the danger of spillage and needlestick

injuries, evacuated BCTs have been the most widely used blood collection devices since the 1940s [11]. As a result, the development of blood collection tubes has enhanced specimen quality, workflow effectiveness, and patient and healthcare worker safety. From the 1950s until the 1990s, anticoagulant-filled glass evacuated tubes were often utilized [12]. Currently, plastic has taken the position of glass, and frequent additives include polymer gels and clot activators [13]. Despite their closeness, the materials and additives used in the evacuated tubes supplied by various manufacturers vary, which may have an impact on test results [14]. There are two major producers of evacuated tubes in the US: Greiner Bio-One (Monroe, NC, USA) and Becton Dickinson (BD) (Franklin Lakes, NJ). Many lab professionals are ignorant of the intricacy and limitations of BCTs because they typically work as intended. The widespread surfactant (SF) issue highlighted the significance of being aware of device limitations and illustrated how these devices might negatively impact laboratory test findings [15,16].

3. Effect of blood collection devices on quality blood transmission

3.1 Tubes for blood collection

BCTs are made up of tube walls, rubber stoppers, lubricants, anticoagulants, separator gels, clot activators, and SFs. Each of these components can have an impact on the accuracy and precision of laboratory testing as well as the quality of the specimens used (Figure 1).

Tube walls: BCTs that have been evacuated are typically cylindrical and range in size from 10 to 20 mm in diameter and 50 to 150 mm in length [17]. Adult clinical specimen tubes typically measure 75 to 100 mm in length, have a 13 mm diameter, and hold 2 to 10 mL of whole blood [17]. 40 to 50 mm in length and 5 to 10 mm in diameter are the dimensions of micro-collection tubes for pédiatrie specimens [18]. Initially, either soda-lime or borosilicate glass was used to make evacuated tubes, but soda-lime tubes were found to release calcium and magnesium into blood samples [19]. Glass evacuated tubes may be vacuum-preserved and have lengthy shelf life since they are produced to be airtight, watertight, and thermally resistant [20]. A non-adherent clot can be separated from blood plasma by centrifugation when blood coagulation components, such as Factor XII (Hagemann Factor), come into contact with hydrophilic glass surfaces. This activation of the clotting cascade results in the conversion of fibrinogen to fibrin. However, tests used to determine the effects of hemolysis on test results may be hampered if clots are re-suspended into plasma during handling or transport [21]. After the Occupational Safety and Health Administration (OSHA) established guidelines to improve safety and lessen exposure to blood-borne infections [21], plastic tubes recently took the place of most glass tubes. Polymers such as polyesters (such as polyethylene terephthalate [PET]), polyolefins (such as polyethylene and polypropylene [PP]), polyacrylic, polytetrafluoroethylene, polysiloxane, polyvinyl chloride, polyacrylonitrile, and polystyrene are used in the injection-molding process to create plastic tubes [17,18]. In comparison to glass, plastic has fewer biohazardous material exposure risks after fracture, is more shock resistant, can withstand faster centrifugation rates, is lighter, has superior dimensional accuracy, and can be more conveniently burned away at a cheaper cost [22]. In contrast to glass tubes, plastic has a higher gas permeability [23]. For application in chemistry [24], endocrinology [25], molecular testing [26], serology [27] and coagulation testing [17], numerous studies have compared glass and plastic tubes. None of the statistically significant variations between analyte measurements in glass and plastic tubes are thought to be clinically important. PET, a material frequently utilized to make BCTs, is unbreakable and can sustain a vacuum for a long period of time [28]. Another widely used plastic is PP, which has a lower water permeability and can maintain the volume and concentration of liquid anticoagulant [28]. Therefore, PET tubes have double walls to reduce evaporation, especially for tests based on coagulation; The inside PP layer prevents citrate solution evaporation, whilst the exterior PET layer is more transparent, making tube fill levels easier to see. The combination of PP and PET extends shelf life and increases anticoagulant volume retention [28]. Plastic tubes have a hydrophobic surface and hence do not efficiently trigger the coagulation process [29]; clots generated on plastic surfaces of tubes are gelatinous when compared to clots formed in glass tubes [29]. Furthermore, blood does not flow easily through hydrophobic plastic surfaces, which might cause platelets, fibrin, or clotted blood to stick to the tube walls [29]. This can make cleanly separating serum from blood clots by centrifugation problematic, particularly in microcollection tubes or during vacuum tube centrifugation. The hydrophilicity of plastic surfaces can be improved by introducing polar functional groups by plasma-enhanced chemical vapor deposition [30]. Interior plastic surfaces can also be coated with SFs, water-soluble polymers, or hydrophilic-hydrophobic copolymers [29], however SFs may be mixed in blood and subsequent interferes with clinical tests (8). Efforts are currently underway to insert SFs into plastic tubes to prevent exudation into blood specimens [17,18].

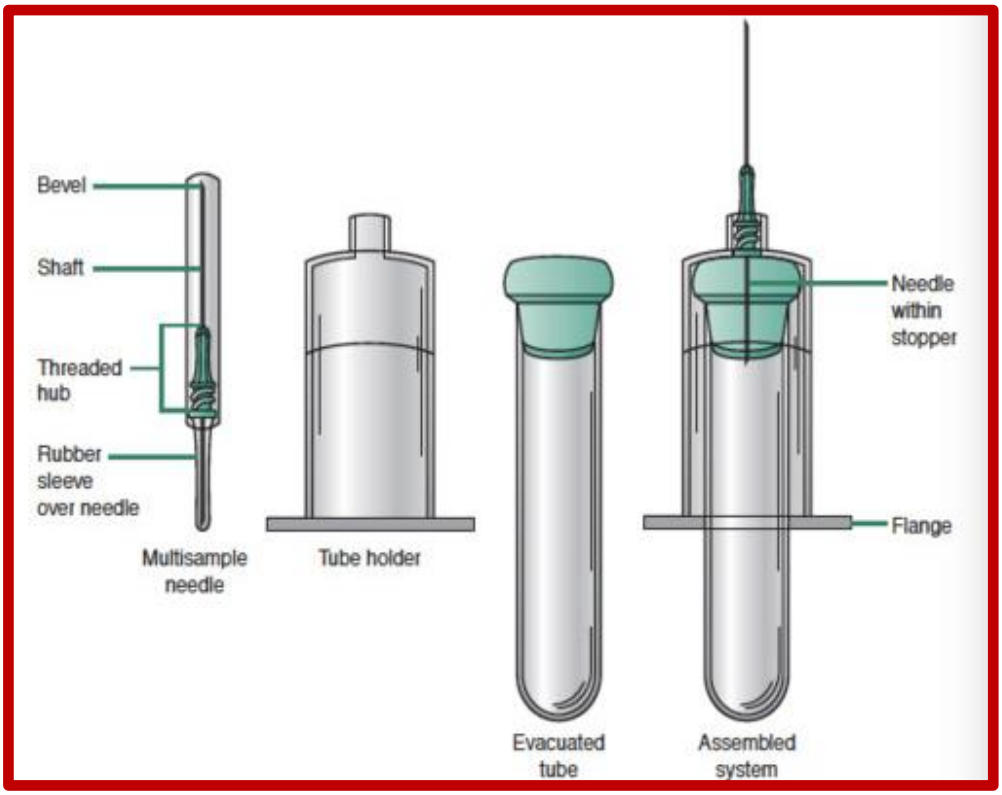

Fig.1: The components of traditional blood collection tubes(BTCs) [28].

Rubber stoppers: Rubber stoppers are frequently color-coded based on the anticoagulant's type and whether a separator gel is present. The stopper must easily allow a needle to pass through it and self-seal after the needle is removed in order to maintain the internal pressure differential [29]. Polychloroprene, silicone, styrene butadiene, isobutyleneisopropene, chlorinated ethylene-propylene copolymers, and isobutylene-isoprene rubber are among the materials that can be used [29]. As a copolymer of isobutylene and isoprene, butyl rubber has superior air and moisture impermeability, superior resistance to chemical attack and heat resistance, and good processability [29]. Halogenated butyl rubber also exhibits these qualities. A stopper shield (such as HemogardTM) is used to lessen the possibility of blood splatter when the rubber stoppers are removed from the collection tube.

The thermoplastic polymers polyethylene, polypropylene, and polyvinyl chloride can be used to create the stopper shield [14]. Blood samples were collected into tubes with rubber stoppers that contained the plasticizer tris-(2-butoxyethyl)-phosphate (TBEP), and there have been reported differences in the bioavailability and bioequivalence of tests for those samples [15]. TBEP, a substance used to soften stoppers, removes some medications from plasma-protein binding sites such the a-acid glycoprotein which increases red blood cell (RBC) absorption and falsely lowers serum or plasma levels. Tricyclic antidepressants, quinidine, propranolol, lidocaine, and numerous phenothiazine medications, such as fluphenazine and chlorpromazine, have all been linked to altered drug distribution due to TBEP. As a result, the production of rubber stoppers containing TBEP has been reduced or completely stopped by tube manufacturers [31].

Lubricants for stoppers: The insertion and removal of stoppers are made easier by lubricants including silicone oils, fluids, and glycerol [14-16]. In order to avoid serum or plasma contamination, lubricants reduce the adhesion of red blood cells and clots to stoppers [17,18]. However, if a non-glycerol blank assay is employed, glycerol should not be used to lubricate stoppers used for specimens measuring glycerol or triglycéride. Although silicone can falsely increase levels of total triiodothyronine and ionized magnesium [12], it is often favored because it is less likely to interfere with assays. Silicone can also confuse peaks during mass spectrometry (MS) analysis and peak interpretation [32] as well.

Anticoagulants: Despite the fact that serum is typically utilized for tests, plasma is a helpful option because of its quick processing time. Plasma has a higher viscosity and total protein concentration than serum because it contains fibrinogen and other clotting factors [33]. Thromboglobulins, potassium, activation peptides for coagulation factors, platelet factor 4, and platelet components generated during platelet activation are all present in higher concentrations in serum [33]. When utilizing plasma, anticoagulants that are employed to preserve analytes may interfere with other analyte results [34]. The three anticoagulants that are most frequently used are citrate, heparin, and ethylenediaminetetraacetic acid (EDTA [34-36].

Gel for separators: Plasma and cells are separated from serum in clotted whole blood using separator gels [37]. In this respect, serum separator tubes (SST) are simple to use, demand quick processing times, yield higher serum levels, prevent dangerous aerosolization, need just a single label, and only one centrifugation stage [38]. The thixotropic gel used in these tubes settles between the packed cells and the top serum layer during centrifugation. Numerous tube characteristics, including specific gravity, yield stress, viscosity, density, and tube material, influence the gel's position after centrifugation. It can also be impacted by factors related to the patient, such as heparin medication, low hematocrit, increased plasma protein, and serum/plasma specific gravity, as well as temperature, centrifugation speed, acceleration, and deceleration. Viscosity, density, and other physical qualities

are impacted by polymeric gels. Typically, fillers, tackifiers, or viscous liquids are used to create separator gels, along with gelling agents as dibenzylidene sorbitol [29].

Surfactants (SFs): Although SFs are frequently employed to reduce non-specific adsorption, they must be carefully chosen and adjusted for immunoassays because, at high concentrations, they run the risk of losing antibodies that have been passively adsorbed onto the solid support beads that are utilized in these tests. A variety of SFs are found in commercially available tubes [13-16], which enhance blood flow, disperse clot activator, and stop proteins, RBCs, and platelets from adhering to tube walls [15]. It has been demonstrated that silicone SF-coated tubes can obstruct the measurement of lithium and magnesium ions using ion-specific electrodes [13]. During the measurement of lithium and magnesium, siliconeSFs appear to interact with ion-specific electrode membranes to raise the observed voltage [13]. Separator tubes with water-soluble silicone polymer coatings can also physically conceal antibodies and change avidin-biotin binding responses in immunoradiometric tests [39]. According to research by Bowen et al. [13], the non-ionic polydimethylsiloxane-polyethylene oxide and polypropylene oxide graft copolymer SF, SilwetTM L-720 (Figure 2; OSI Specialities, Danbury, CT, USA; [40], when used in BD SSTTM tubes, falsely elevates triiodothyronine in a dose-dependent manner [13,14]. Non-competitive immunoassays (such as cancer antigen 15-3) and competitive immunoassays (such as vitamin B-j) are likewise impacted by Silwet L-720. Due to interaction with the immunoassay, BD reformulated their tubes to lower the quantities of SF [13]. Morovat et al.'s [42] analysis of immunoassay findings using these reformulated tubes revealed statistically significant but clinically negligible biases. However, in this investigation, the problematic SF was coated on the control tubes. For free triiodothyronine and free thyroxine, Wang et al. [43] reported that the reformulated tubes gave clinically significant biased results. It's interesting that Silwet L-720 and other Silwet surfactants can be employed in separator gel formulations, which could explain why the reformulated tubes yielded clinically significant biased thyroid hormone test findings [41].

Protease inhibitors: With the exception of situations when activation by surfaces or other stimuli occurs, protease inhibitors are among the most prevalent plasma protein components [44], outnumbering active proteases by a large margin. Chelating drugs, like EDTA and citrate, do not directly inhibit serine proteases, but they do limit the activation of proteases in the coagulation system by preventing inhibitors from predominating and interfering with calcium-mediated surface binding. Alternative anticoagulants include direct thrombin or coagulation factor Xa inhibitors, but due to their high price, they are not commonly used [44].

Timing of tourniquet removal: A tourniquet was applied during the collection of diagnostic blood samples in several investigations to assess the impact of venous stasis [45-47]. In a nutshell, the tourniquet-induced venous stasis encourages the outflow of water, diffusible ions, and low molecular weight compounds from the vessel, increasing the concentration of different blood analytes at the pierced site and perhaps affecting how laboratory test findings are interpreted. Additionally, endothelial cells are stimulated and may actively release a number of substances in the blood stream (for example, tissue-type plasminogen activator) when the vascular microenvironment is subjected to both hypoxia and contemporaneous stasis. Additionally, some bioproducts build up, such as protons, which may encourage adjustments to laboratory settings [48].

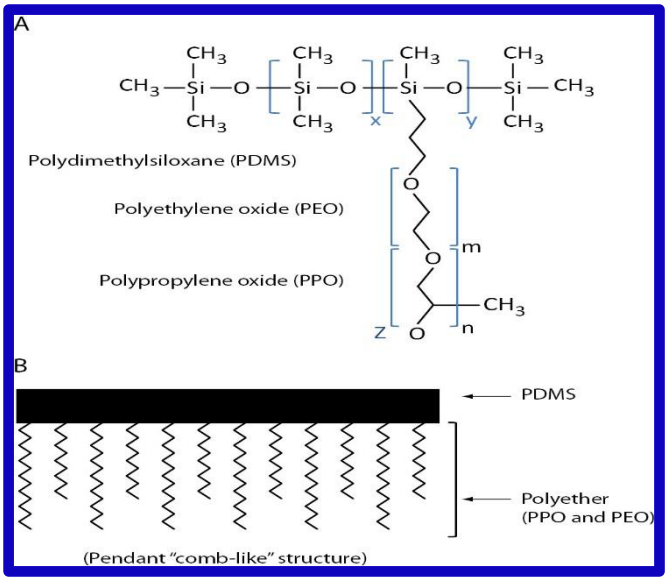

Figure 2. Siliconsurfactant; General molecular structure (A) and schematic structure (B) with polyether (polyethylene oxide and polypropylene oxide) connected to the polydimethylsiloxane backbone (through hydrosilation reaction); x, y, m, and n are numbers that are each independently higher than zero; and z can be either a hydrogen atom or an alkyl radical [41]

4.0 Recommendations

Manufacturers of tubes and assays continue to struggle with preventing pre-analytical errors caused by BCT additives, which has an impact on clinical laboratories' capacity to deliver reliable results. Ideally, each new or changed blood collection product should be extensively assessed for any potential

issues that may be produced during the processing and analysis of specimens in the downstream steps. Additionally, BCT producers ought to think about testing their goods with smaller sample sizes, longer contact periods, and long-term storage. Because manufacturers cannot predict how their tubes will perform across various assay platforms, it is crucial that they build strong working relationships with their clients and think about creating a surveillance program to spot issues as soon as they arise.

Similar to this, assay and instrument platform manufacturers should preferably test the performance of their assays on several lots of the same tube type and with a wide range of BCTs available on the market. It is advisable to repeat reference interval tests that were conducted using outdated equipment and tubes with materials and circumstances that are compatible with current usage.

Since regular quality control (OC) practice often does not evaluate all parts of laboratory testing from blood collection, including specimen processing, analytical testing, and test reporting, blood collection device issues may go unnoticed by laboratory personnel. Programs for proficiency assessment that do not involve blood collection also fall short in identifying issues with blood collection devices [12,13].

5.0 Conclusions

Despite the fact that modern BCTs largely function as intended and are thus frequently taken for granted, it is crucial that lab professionals become aware of the possible issues that they can cause when analyzing specimens. BCTs are medical devices, and as such, they come with some built-in restrictions. BCT-related interferences in test findings can have a negative impact on patient outcomes, reduce laboratory productivity, delay test results, and raise the cost per test due to recollection and retesting when used inappropriately or due to issues with its manufacturing. As a result, BCT standardization and optimization are essential for valid test analysis. Tube makers, in vitro diagnostic businesses, and lab technicians should all be attentive in preventing the negative consequences of BCT because the quality of laboratory test results ultimately depends on specimen integrity.

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