

RAPID COMMUNICATION

CARBOHYDRATE-DEFICIENT TRANSFERRIN IS NOT AFFECTED BY SERUM SEPARATORS

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Abstract — We studied the possible effects on serum carbohydrate-deficient transferrin (CDT) determination by a CDTECT (Pharmacia) method of serum isolation in four different types of blood-collection tubes, namely: (1) glass tubes (glass Vacutainer tubes with no additive); (2) S-Monovette Neutral tubes (plastic tubes with no additive); (3) S-Monovette Serum tubes (plastic tubes with kaolin-coated plastic granulate coagulation accelerator); and (4) S-Monovette Serum/Gel tubes (plastic tubes with kaolin-coated plastic granulate and a polymerized acrylamide resin). Using Passing and Bablok regression analysis, we did not observe significant differences in CDT concentrations determined in 58 serum samples using any of these four blood-collection systems.

INTRODUCTION

Carbohydrate-deficient transferrin (CDT), the most specific laboratory marker for chronic alcohol abuse so far, is measured in serum. Serum is usually obtained after clotting of the blood sample at room temperature followed by centrifugation. A coagulation accelerator (e.g. kaolin) and/or a separating gel (e.g. a polymerized acrylamide resin) are well-established tools to speed up and improve the separation of cells and blood clot from serum. During centrifugation, the serum separator moves, because of its well-defined density, between the packed cell layer and serum, inhibiting redistribution between blood clot and serum. However, the effects of serum separators on analyte concentrations are known. Thus, in serum samples stored in contact with the blood clot, Dasgupta *et al.* (1994, 1996) found significantly decreased concentrations of com-

monly monitored therapeutic drugs, e.g. phenytoin, phenobarbital, lidocaine, chinidine, and carbamazepine. As they showed by chemical extraction of the barrier gels, these decreases were due to adsorption of the analytes to the gel. Losses of tricyclic antidepressants (e.g. amitriptyline, imipramine, and clomipramine and their monodemethylated metabolites) in serum samples obtained from blood tubes containing a serum separator have also been demonstrated, e.g. by Nyberg and Martensson (1986) and Levy *et al.* (1987). In some cases, these losses were greater than 40% (Nyberg and Martensson, 1986). Variations in serum potassium concentrations after repeated centrifugation of stored tubes (Hue *et al.*, 1991), after mail transport (Sandberg *et al.*, 1988) or owing to an incomplete separating gel (Eichhorn *et al.*, 1997) have been described. Altered concentrations of some organic solvents, e.g. ethylbenzene and xylene (Streete and Flanagan, 1993) or organochlorines (Longnecker *et al.*, 1996) have also been reported.

We have often been asked by colleagues

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Table 1. Comparison of carbohydrate-deficient transferrin (CDT) values obtained from different blood-collection tubes according to the method of Passing and Bablok (1983)

Tube types	Regression function			
	Slope (U/l)	95% CI	Intercept (U/l)	95% CI
Glass vs plastic ^a	1.045	1.000–1.231	–0.818	–4.115–0.000
Glass vs plastic/kaolin	1.000	0.933–1.200	–1.000	–4.100–0.433
Glass vs plastic/kaolin/gel	1.000	0.833–1.030	–1.000	–1.500–1.833
Plastic vs plastic/kaolin	1.000	0.900–1.050	–1.000	–1.500–1.200
Plastic vs plastic/kaolin/gel	0.857	0.750–1.000	1.786	–1.000–4.000
Plastic/kaolin vs plastic/kaolin/gel	0.870	0.750–1.000	2.326	0.000–4.500

^a Glass: Vacutainer No Additives; plastic: S-Monovette Neutral; plastic/kaolin: S-Monovette Serum; plastic/kaolin/gel: S-Monovette Serum/Gel.

Since all 95% confidence intervals (CI) included the values 1 (slope) and 0 (intercept), the equality of CDT values in the serum obtained from the blood-collection tubes studied is demonstrated.

whether similar effects have been studied for measurement of CDT. To our knowledge, there is no appropriate information available so far. We have therefore studied in the present paper the effects on CDT of four widely distributed blood-collection tubes.

MATERIALS AND METHODS

The four widely used blood-collection tubes used in the present work were: (1) S-Monovette Neutral (a plastic tube without additives); (2) S-Monovette Serum (a plastic tube with kaolin-coated plastic granulate as a coagulation accelerator); (3) S-Monovette Serum/Gel (a plastic tube with kaolin-coated plastic granulate and a polymerized acrylamide resin); and (4) Vacutainer No Additive tube (a glass blood tube). The first three of these tube types were supplied by Sarstedt (Nümbrecht, Germany), the Vacutainer tube was provided by Becton-Dickinson (Heidelberg, Germany).

Blood was taken from 58 healthy persons by venipuncture using Multifly Sets (Sarstedt, Nümbrecht, Germany). The tubes were filled in a randomized order. Serum was obtained after clotting for 30–45 min at room temperature followed by centrifugation at 2000 g for 10 min. CDT was determined by the CDTEct-EIA assay in accordance with the instructions of the manufacturer. For statistical analysis, we used the method of Passing and Bablok (1983), which is independ-

ent of the assignment of the tubes to the X- and Y-axes. Statistical calculations could therefore be reduced from 12 to six possible blood-tube combinations.

RESULTS AND DISCUSSION

The means (and ranges) of the CDT concentrations measured in 58 serum samples obtained from each type of blood-collection tube were (in U/l) as follows: 19.6 (7–51) for Vacutainer No Additive (a glass blood tube), 19.5 (8–48) for S-Monovette Neutral (plastic tube with no additive), 19.1 (7–62) for S-Monovette Serum (plastic tube with kaolin-coated plastic granulate as a coagulation accelerator), and 18.6 (8–48) for S-Monovette Serum/Gel (plastic tube with kaolin-coated plastic granulate and a polymerized acrylamide resin). The differences in means are clearly below the upper limits for the within-day and pure between-day coefficients of variation of the CDTEct-EIA assay of <9.2% and <14% respectively (Arndt *et al.*, 1998b).

Table 1 shows the correlation functions and the corresponding 95% confidence intervals (CI) of the slopes and intercepts of these six tube combinations. Figure 1 illustrates the correlation of CDT values measured in serum samples which were obtained from the Vacutainer No Additive (glass) tube and the S-Monovette Serum/Gel (plastic, kaolin and gel) tube as the blood-collection tubes which differed most in our

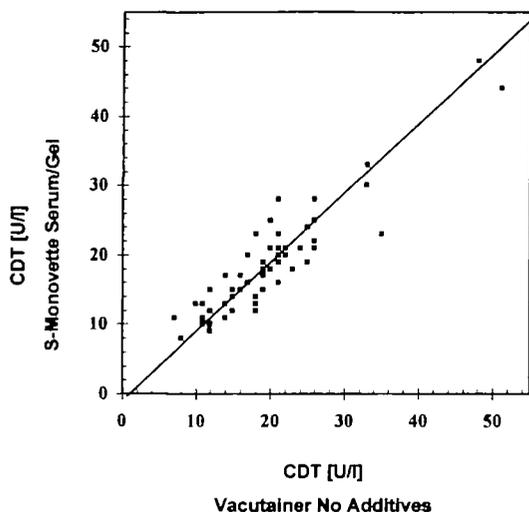


Fig. 1. Comparison of carbohydrate-deficient transferrin (CDT) values obtained in serum from a glass blood-collection tube without coagulation accelerator or serum separator (Vacutainer No Additives) and a plastic tube with kaolin-coated plastic granulate and polymerized acrylamide resin as a serum separator (S-Monovette Serum/Gel).

The Passing and Bablok (1983) regression function is $Y = X - 1$ ($n = 58$). The 95% confidence intervals of the slope and intercept are given in Table 1.

study. All 95% CI for the slopes and the intercepts of the Passing and Bablok correlation functions included the values 1 (for the slopes) and 0 (for the intercepts). Thus, the CDT values obtained from the blood tubes examined in our study are proven not to differ. From this, we conclude that neither the blood tube material (glass vs plastic) nor kaolin and/or polymerized acrylamide resin additives had significant effects on the serum CDT values. From Fig. 1, it follows that CDT is not (significantly) adsorbed to the polymerized acrylamide resin used as a serum separator in the S-Monovette Serum/Gel tube.

A great number of studies have been published on the analytical phase of analysis of CDT, e.g. descriptions of new CDT analysis procedures, evaluations or comparisons of non-commercial and commercially available CDT analysis methods; (for literature, see, e.g., Stowell *et al.*, 1997; Arndt *et al.*, 1998a) and the post-analytical phase, e.g. the diagnostic sensitivity and specificity of CDT as a laboratory marker of chronic alcohol abuse in different clinical settings and among different

populations (for literature, see e.g., Morgan and Major, 1996; Helander and Tabakoff, 1997). In contrast, little information regarding the pre-analytical phase (e.g. effects of patient pre-treatment, blood sampling, blood processing, sample storage, and transportation) is available. As with any analyte, an adequate pre-analysis forms the basis of correct quantification of the analyte and reliable interpretation of the analysis result. Because of this, the pre-analytical phase of CDT determination requires more investigation. With the present paper, we hope to have provided useful information for both the physician and the clinical chemist (who have a wide choice of blood-collection tubes) and to initiate further studies concerning the pre-analytical phase of CDT analysis.

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