



Test results comparison : is the S-Monovette[®] Lithium-Heparin Gel+ a suitable replacement for the S-Monovette[®] Lithium-Heparin Gel on Alinity Abbott[®]?

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1 Test results comparison : is the S-Monovette[®] Lithium-Heparin Gel+ a suitable replacement for the S-Monovette[®] Lithium-Heparin Gel on Alinity Abbott[®]?

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15 S-Monovette; Gel+; Turn-around-time, Emergency
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For Review Only

INTRODUCTION

Centrifugation time is a limiting step in reducing the Turn-Around-Time (TAT). Reducing TAT is of capital importance in the clinical course, especially in emergency department (ED) since the time gained allows to shorten the therapeutic decisions^{1, 4}. Thus development of methods able to reduce centrifugation time is a great deal of interest. The implementation of the new tubes S-Monovette® Lithium-Heparin Gel+ (LH Gel+, Sarstedt AG&Co, Nümbrecht, Germany) could be a solution as these require half the centrifugation time than previous LH Gel (Sarstedt AG&Co, Nümbrecht, Germany). This is achieved by modifying the rheological properties of the previously used polyacrylate beads.

The aim of the study is to demonstrate the clinical equivalence between both of these tubes. To carry out this study, we compared the results of 64 frequently requested clinical, chemical and immunological parameters in plasma LH Gel and LH GEL + using the Alinity Abbott® (Abbott Park, IL) analyzers.

METHODS

SUBJECT

Venipuncture using the aspiration technique was performed by nurse collector under the supervision of the clinical chemistry department. To assess equivalence at a patient matrix level, 42 patients coming from different departments were selected: 7 patients from ED, intensive care unit (ICU), dialysis, oncology, 7 pregnant women and 7 healthy individuals (HI) were included. Such a selection of patients permitted to meet as closely as possible the conditions of routine work and an adequate sample size to obtain results covering the majority of the assay range.

BLOOD SAMPLING

For each individual, 4 blood sample tubes were drawn: 2 tubes LH Gel+ 4.9 mL (REF 04.1954) and 2 tubes LH Gel (REF 04.1940), in order to get enough sample volume. The pre-analytical conditions were as similar as possible in order to minimize eventual influences. All the samples were immediately transported to the laboratory. Blood samples were centrifuged according to the manufacturer recommendation. The LH Gel tubes were centrifuged in the "Centrifuge 5810" (Eppendorf) for 10 minutes at 3000g and at the same moment, the LH Gel+ tubes were centrifuged in the "Dash Apex Series" (Drucker Diagnostics) for 5 minutes at 3000g. The study was approved by the Ethics Committee and lab tests were performed in accordance with the recommendations provided by the manufacturer.

TEST MEASUREMENT

All measurements were carried out on each tube, at the same time of the day, in the same run. Alinity CI series Abbott® (Abbott Park, IL) analyzers were used in this study. The analyses were performed in duplicate in order to be able to use the Deming regression. A panel of 64 parameters, which includes the most frequently requested analyses in clinical practice and more particularly in the emergency department, was selected. They include chemical analyses (potentiometry, enzymatic reaction) and immunoanalyses.

STATISTICAL ANALYSIS

The data were analyzed by EP Evaluator® (11.03.0.23) for Windows and were plotted against each other and Passing-Bablok regressions were calculated. For between-tube comparison, the parameters which results displayed proportional and/or systematic errors, a mean difference was calculated according to the formula: [(comparison tube result - reference tube result) / reference tube result] x 100, where LH Gel represents the reference tube and LH Gel+ the comparison tube. The mean difference calculated was compared to the acceptable change limit (ACL) and the total change limit (TCL) according respectively to the formula $ACL = 2.77 CVa$, $TCL = \sqrt{(2.77 CVa)^2 + (0.5 CVb)^2}$ where CVa stands for analytical coefficient variation and CVb for the within-subject biologic variation. The CVa was taken from the data provided by the laboratory's computer software using the internal quality controls whether the CVb is either taken from European Federation of Clinical Chemistry and Laboratory Medicine (EFLM) Biological Variation Database² when available or, from the Westgard's database³ if the information was not provided.

RESULTS

Some observed results were either below the LoD (Limit of detection) or beyond the LoQ (Limit of quantification), these results were excluded. In all patient groups and among all parameters, 43 parameters did not show any statistically significant difference since the confidence interval 95% (CI95) of the slope included value 1 and CI95 of intercept included value 0. Although 21 analytes showed a statistically significant difference between tested tubes (Table 1), only two of them (CK and insulin) exceeded the ACL. However, none of the mean differences exceeded the TCL (Table 2). Thus, the measurement differences between LH Gel+ and LH Gel for all parameters among all patients groups are within the acceptance range.

DISCUSSION

Through the improvement of the rheological properties of the polyacrylate gel, the company Sarstedt announces to be able to reduce the centrifugation time by half while keeping an optimal quality of the results⁴. Therefore, clinical studies are needed to prove the applicability

of these tubes in routine practice. Thus, we were able to demonstrate in our study that for the 64 parameters there is no clinical difference between the tubes. Nevertheless, our study has some limitations. Insufficient sample size for beta-hCG (n=14), oestradiol (n=17), and Free PSA (n=23) due to the restriction of the selection of patients in specific different departments is one of those limitations. Moreover a study on the stability could be envisaged as it was already carried out in another study but with another device.⁵

CONCLUSION

Reducing TAT is of paramount importance in clinical practice as it can lead to faster medical decisions and even life-saving outcomes. The LH Gel+ with a short centrifugation time of 5 minutes is suitable for a medical use as it showed clinical equivalence with the LH Gel; especially for the ED.

BIBLIOGRAPHY

- Hawkins RC. Laboratory turnaround time. *Clin Biochem Rev.* **28(4)**, 179–94 (2007).
- EFLM Biological Variation Database: European Federation of Clinical Chemistry and Laboratory Medicine. <https://biologicalvariation.eu/>.
- Biological variation database, and quality specifications for imprecision, bias and total error (desirable and minimum). The 2014 update. <https://www.westgard.com/biodatabase-2014-update.htm>. <https://www.westgard.com/biodatabase1.htm> (2014).
- S-Monovette® Lithium-Heparin Gel +. https://dafxb5xjcds.cloudfront.net/fileadmin/user_upload/99_Broschueren/NEU/817/20_817_0000_200_LH-gel-plus_1118.pdf.
- Scheer, F., Schuster, R. & Flach, D. S-Monovette® Lithium-Heparin Gel + Clinical Equivalence on Roche cobas® Analysers. (2018).

Blood parameter	Slope (IC95)	Intercept (IC95)	Blood parameter	Slope (IC95)	Intercept (IC95)	Blood parameter	Slope (IC95)	Intercept (IC95)
Uric acid	0,999 (0,994 à 1,004)	0,003 (-0,024 à 0,029)	Creatinine	0,999 (0,997 à 1,001)	0,001 (-0,004 à 0,006)	Myoglobin	0,994 (0,991 à 0,997)	-0,37 (-3,77 à 3,03)
Alpha-fetoprotein (AFP)	1,001 (0,996 à 1,006)	0,003 (-0,435 à 0,442)	Dehydroepiandrosterone	1,000 (0,991 à 1,009)	-0,005 (-0,049 à 0,038)	NT-Pro BNP	1,020 (1,012 à 1,028)	-23,279 (-60,628 à 14,071)
Albumin	0,997 (0,980 à 1,014)	0,007 (-0,641 à 0,656)	Iron	0,995 (0,988 à 1,001)	0,008 (-0,089 à 0,104)	Oestradiol	0,960 (0,988 à 1,022)	4,117 (0,394 à 7,901)
Amylase	0,998 (0,992 à 1,005)	-0,398 (-1,015 à 0,220)	Ferritin	0,984 (0,979 à 0,988)	7,590 (-0,971 à 16,150)	Alkaline phosphatase	0,994 (0,990 à 0,998)	1,141 (0,392 à 1,890)
Anti-Thyroglobulin	0,981 (0,971 à 0,990)	0,102 (-0,159 à 0,362)	Folic acid	0,989 (0,960 à 1,019)	0,108 (-0,138 à 0,354)	Phosphorus	0,996 (0,984 à 1,009)	0,004 (-0,010 à 0,017)
Beta-Human chorionic gonadotropin	1,014 (1,001 à 1,027)	-43,491 (-207,249 à 120,266)	Free PSA	0,984 (0,977 à 0,991)	0,0018 (-0,0093 à 0,0128)	Potassium	0,987 (0,952 à 1,021)	0,049 (-0,090 à 0,188)
Bicarbonate	1,028 (0,994 à 1,062)	-0,612 (-1,494 à 0,271)	Free T3	1,015 (0,969 à 1,062)	-0,071 (-0,248 à 0,107)	Procalcitonin	0,996 (0,993 à 0,999)	0,004 (-0,006 à 0,015)
Direct bilirubin	1,009 (1,007 à 1,010)	-0,002 (-0,008 à 0,004)	Free T4	0,981 (0,950 à 1,012)	0,106 (-0,284 à 0,495)	Progesterone	0,994 (0,985 à 1,002)	0,054 (-0,324 à 0,433)
Total bilirubin	1,001 (0,999 à 1,003)	-0,002 (-0,009 à 0,006)	Follicle stimulating hormone	0,984 (0,974 à 0,993)	0,142 (-0,083 à 0,367)	Prolactin	0,985 (0,975 à 0,995)	0,206 (-0,668 à 1,080)
C-peptide	0,974 (0,958 à 0,989)	3,335 (-35,230 à 41,899)	Gamma-glutamyl transpeptidase	0,997 (0,995 à 0,999)	0,207 (-0,211 à 0,626)	Total protein	0,996 (0,969 à 1,023)	0,038 (-1,772 à 1,848)
Cancer antigen 15-3	1,006 (0,998 à 1,014)	-0,081 (-0,296 à 0,133)	High density lipoprotein cholesterol	1,007 (0,998 à 1,016)	-0,250 (-0,705 à 0,205)	Sex hormone-binding globulin	0,984 (0,972 à 0,995)	0,877 (-1,960 à 3,714)
CA 19-9	0,997 (0,964 à 1,029)	0,139 (-0,489 à 0,768)	High sensitivity cardiac troponin I	1,063 (1,055 à 1,072)	-1,687 (-3,869 à 0,496)	Sodium	0,988 (0,958 à 1,019)	1,501 (-2,796 à 5,799)
Calcium	1,004 (0,966 à 1,043)	-0,007 (-0,093 à 0,079)	IgA	0,995 (0,989 à 1,000)	0,009 (-0,011 à 0,030)	Testosterone	1,005 (0,986 à 1,024)	-0,012 (-0,148 à 0,124)
Carcinoembryonic antigen	0,997 (0,985 à 1,010)	-0,021 (-0,115 à 0,074)	IgG	0,998 (0,987 à 1,008)	-0,024 (-0,125 à 0,078)	Aspartate aminotransferase (AST)	1,000 (0,995 à 1,006)	-0,208 (-0,520 à 0,104)
Chloride	0,993 (0,975 à 1,012)	0,666 (-1,280 à 2,612)	IgM	1,003 (0,997 à 1,009)	-0,001 (-0,010 à 0,007)	Alanine taminotransferase (ALT)	1,003 (0,998 à 1,007)	0,242 (-0,101 à 0,585)
Cholesterol	0,996 (0,987 à 1,005)	0,373 (-1,287 à 2,033)	Insulin	1,075 (1,056 à 1,095)	-5,424 (-8,604 à -2,245)	Total PSA	0,976 (0,968 à 0,985)	0,0135 (-0,0127 à 0,0396)
Cholinesterase	0,994 (0,988 à 1,000)	9,6 (-37,6 à 56,8)	Lactate dehydrogenase	1,036 (1,014 à 1,059)	-10,973 (-17,531 à -4,414)	Transferrin	1,004 (0,994 à 1,014)	-0,011 (-0,036 à 0,015)
CK-MB	0,982 (0,979 à 0,986)	0,01 (-0,02 à 0,04)	LDL-cholesterol	0,995 (0,990 à 1,001)	0,116 (-0,608 à 0,840)	Triglyceride	0,993 (0,984 à 1,002)	0,882 (-0,557 à 2,321)
Cortisol	1,004 (0,993 à 1,016)	-2,914 (-8,223 à 2,394)	Luteinizing hormone (LH)	1,005 (0,998 à 1,011)	-0,007 (-0,075 à 0,061)	Thyroid stimulin hormone	0,999 (0,993 à 1,005)	-0,01178 (-0,02647 à 0,00291)
C-reactive protein	0,999 (0,996 à 1,002)	-0,045 (-0,276 à 0,185)	Lipase	1,004 (1,000 à 1,007)	-0,15 (-0,36 à 0,06)	Urea	1,006 (1,001 à 1,010)	-0,095 (-0,379 à 0,190)
CK	0,991 (0,990 à 0,993)	0,700 (0,230 à 1,170)	Magnesium	1,035 (0,998 à 1,072)	-0,028 (-0,060 à 0,004)	Cyanocobalamin	1,008 (0,999 à 1,017)	-4,847 (-16,648 à 6,955)

Table 1. Slope and intercept of 63 blood parameters

	Mean difference (%)	Acceptable change limit (ACL) %	Total change limit (TCL) %
Beta-Human chorionic gonadotropin (B-HCG)	2,018	3,3	X
Direct bilirubin	3,56	11,4	21,7
Lactate dehydrogenase	5,2	6,7	8,0
Anti-Thyroglobulin	12,79	18,6	19,4
C-peptide	4,58	7,4	11,1
CK-MB	2,75	19,7	21,7
CK	6,46	4,1	12,1
Ferritin	2,93	12,0	14,0
Free prostatic specific antigen (PSA)	3,13	12,3	12,8
Follicle-stimulating hormone (FSH)	1,96	7,2	9,0
Gammaglutamyl transpeptidase (GGT)	3,9	7,0	9,7
High sensitivity cardiac troponin I	4,77	18,4	19,7
Insulin	7,13	5,9	12,1
Myoglobin	2,35	8,8	11,2
N-terminal Pro Brain natriuretic peptide (NT-Pro BNP)	4,96	14,8	15,7
Oestradiol	9,27	14,7	18,5
Alkaline phosphatase (PAL)	1,93	6,8	7,5
Procalcitonin	1,93	28,3	X
Prolactin	2,75	11,1	16,0
Sex hormone-binding globulin (SHBG)	3,4	13,0	14,5
Total PSA	2,46	11,8	14,9

Table 2. Mean difference, ACL and TCL of the 21 analytes with systematic and/or proportional bias.

Comité d'Ethique Hospitalo-Facultaire Universitaire de Liège (707)

Sart Tilman, le 9 mai 2012

Monsieur le **Prof. J. P. CHAPELLE**
Service de **CHIMIE MEDICALE**
CHU B35

Concerne: Votre demande d'avis au Comité d'Ethique
Nr belge : B70720095522; Notre réf: 2008/55

CH. MEI
18 MAI 2012

Cher Collègue,

J'ai le plaisir de vous informer que le Comité d'Ethique renouvelle son approbation au projet intitulé :

"Utilisation à des fins de sérothèque de surplus d'échantillons de plasma et/ou de sérum sanguins"

Vous trouverez, sous ce pli, la composition du Comité d'Ethique.

Je vous prie d'agréer, Cher Collègue, l'expression de mes sentiments les meilleurs,

Prof. G. RORIVE
Vice-Président du Comité d'Ethique

C.H.U. Sart Tilman, Domaine Universitaire du Sart Tilman – B35, 4000 LIEGE 1

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