Procjena analitičkih značajki reagensa *Randox Full Range* za određivanje koncentracije C-reaktivnog proteina u nedonoščadi i novorođenčadi

Assessment of analytical properties of the Randox full range assay for determination of C-reactive protein concentration in preterm infants and newborns

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Sažetak

Uvod: C-reaktivni protein (CRP) je u zdravih osoba prisutan u niskim koncentracijama, a rutinski se određuje kao pokazatelj sistemske upalne reakcije. Međutim, klinički značaj vrlo niskih koncentracija potaknuo je proizvođače na razvoj osjetljivih metoda koje omogućavaju određivanje koncentracije CRP u širokom rasponu od vrlo niskih do visokih koncentracija. Ovaj je pristup od iznimne važnosti u dijagnozi i praćenju infekcije u nedonoščadi i novorođenčadi, jer u njih sepsa započinje nespecifičnim simptomima i dijagnosticira se tek na osnovu laboratorijskih nalaza.

Cilj rada: Učiniti analitičku procjenu novoga kombiniranog reagensa Randox *Full Range* za određivanje koncentracije CRP u usporedbi s reagensima tvrtke Olympus kao referentnim reagensima. Novi reagens ima mjerno područje 0,1-160,0 mg/L, što bi trebala biti prednost nad reagensima tvrtke *Olympus* koji za to mjerno područje trebaju dva reagensa i tri aplikacije.

Materijali i metode: Analitička procjena obuhvatila je nepreciznost u seriji, nepreciznost iz dana u dan, netočnost i usporedna određivanja koncentracije CRP u uzorcima bolesnika. Ispitivanja su provedena u skladu s preporukama ECCLS na aparatu *Olympus AU 640*.

Rezultati: Dobiveni su zadovoljavajući rezultati za analitičku nepreciznost u seriji (KV ≤ 2,18%), nepreciznost iz dana u dan (KV ≤ 1,64%) i netočnost (R ≤ 3,67%). Rezultati usporednih određivanja koncentracije CRP u uzorcima bolesnika s reagensima dvaju proizvođača pokazala su visok stupanj korelacije (r ≥ 0,993).

Zaključak: Na temelju dobivenih rezultata može se zaključiti da je novi reagens *Full Range* tvrtke *Randox* osjetljiv i repr oducibilan reagens za određivanje koncentracije CRP.

Ključne riječi: C-reaktivni protein, sepsa, nedonoščad, novorođenčad

Abstract

Introduction: C-reactive protein (CRP) is present in healthy individuals in low concentrations and is routinely determined as an indicator of systemic inflammatory reaction. However, clinical significance of the very low concentrations of CRP encouraged manufacturers to develop sensitive methods that allow CRP determination in a wide range from very low to high concentrations. Such approach is of extraordinary importance in the diagnosis and follow-up of infection in preterm infants and newborns because the onset of sepsis in these patients is characterized by unspecific symptoms and is diagnosed only on the basis of laboratory results.

Aim: Analytical assessment of a new combined Randox Full Range assay for determination of CRP concentration in comparison with Olympus reagents as reference reagents. The measuring range of the new reagent is 0.1-160.0 mg/L, which should be an advantage over Olympus reagents as they require two reagents and three applications for this measuring range.

Materials and methods: Analytical assessment comprised within-run imprecision, between-run imprecision, inaccuracy and comparative determinations of CRP concentration in patient samples. The examinations were performed in accordance with ECCLS recommendations on Olympus AU 640 instrument.

Results: Satisfactory results were obtained for analytical within-run imprecision (CV ≤ 2.18%), between-run imprecision (CV ≤ 1.64%) and inaccuracy (R ≤ 3.67%). Results of comparative determinations of CRP concentrations in patient samples using reagents by two manufacturers showed a high degree of correlation (r ≤ 0.993).

Conclusion: Based on the obtained results, we may conclude that the Randox Full Range assay is a sensitive and reproducible reagent for determination of CRP concentration.

Keywords: C-reactive protein, sepsis, preterm infants, newborns

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Uvod

C-reaktivni protein (CRP) je reaktant akutne faze koji je u zdravih osoba prisutan u niskim koncentracijama. Patološka stanja kao što su bakterijske infekcije, upale ili razaranje tkiva praćena su povećanjem koncentracije CRP zbog otpuštanja proupalnih citokina (1). Bakterijski endotoksini su najjači stimulatori reakcije akutne faze upale (2). Najviše koncentracije CRP uzrokovane su infekcijama Gram-negativnim bakterijama (3).

Određivanje koncentracije C-reaktivnog proteina od iznimne je važnosti u dijagnozi i praćenju infekcije u nedonoščadi i novorođenčadi (1). U novorođenčadi sepsa može početi nespecifičnim simptomima i dijagnosticira se tek na osnovu laboratorijskih nalaza. Nepravovremena dijagnoza bakterijske sepse jedan je od glavnih uzroka pobola i smrtnosti u nedonoščadi i novorođenčadi (2,3,4,6,7).

Značajan je broj publikacija o uzrocima, poteškoćama u postavljanju pravovremene dijagnoze, dijagnostičkom značaju pojedinih medijatora upale u stanju sepse i liječenju neonatalne sepse (kriteriji za početak i završetak terapije) (2–6, 8–12).

Postoje preporuke pojedinih ustanova da CRP, iako nespecifičan, ima najbolju dijagnostičku vrijednost kao pojedinačna pretraga, važan je pokazatelj u započinjanju i kontroli terapije, a može se koristiti i kao pokazatelj identifikacije vremena kad se sigurno može prekinuti terapija antibioticima (1,2,6,10,11).

Klinički značaj povišenja koncentracije CRP unutar granica referentnog intervala potaknuo je mnoge proizvođače da razviju testove za određivanje CRP posebno namijenjene mjerenju vrlo niskih koncentracija. Proizvođači i nefelometrijskih i turbidimetrijskih reagensa okrenuli su se lateks-mikropolimerima da bi postigli odgovarajuću osjetljivost, pa tako laboratoriji imaju na raspolaganju nekoliko vrsta reagensa za određivanje CRP: visoko linearni za uzorke koji se analiziraju na opću upalu i infekciju; te osjetljivi (SCRP) i visoko osjetljivi (HSCRP) koji nalaze primjenu u neonatalogiji, procjeni rizika za kardio- i cerebrovaskularne bolesti.

Tvrtka *Randox* proizvela je novi kombinirani reagens za CRP *Full Range*. Karakteristika novog reagensa je mjerno područje 0,1-160,0 mg/L. Za to mjerno područje kod rada s reagensima tvrtke *Olympus* koristimo dva reagensa i tri aplikacije. S obzirom na važnost ranog otkrivanja sepse u nedonoščadi i novorođenčadi, novi smo reagens ispitali na uzorcima te populacije. Prednost ispitivanog reagensa je u tome što bi rad s jednim reagensom u usporedbi s dosadašnjim načinom rada, tj. kombinacijom dva reagensa i tri aplikacije, pridonio bržoj dijagnostici sepse u tako osjetljivoj populaciji i smanjio troškove određivanja.

Cilj

Učiniti analitičku procjenu novoga kombiniranog reagensa *Randox Full Range* za određivanje koncentracije CRP u

Introduction

C-reactive protein (CRP) is an acute phase reactant present in healthy individuals in low concentrations. Pathologic conditions like bacterial infections, inflammations or tissue destruction are followed by CRP concentration increase due to the release of proinflammatory cytokines (1). Bacterial endotoxins are the strongest stimulators of inflammatory acute phase reaction (2). The highest CRP concentrations are caused by infections by Gram-negative bacteria (3).

The measurement of C-reactive protein concentration is of extraordinary importance in the diagnosis and follow-up of infection in preterm infants and newborns (1). The onset of sepsis in the newborns may manifest by unspecific symptoms and is diagnosed only on the basis of laboratory findings. Untimely diagnosis of bacterial sepsis is one of the major causes of morbidity and mortality in preterm infants and newborns (2,3,4,6,7).

There is a considerable number of publications about causes, difficulties in making timely diagnosis, diagnostic significance of certain mediators of inflammation in sepsis and treatment, of neonatal sepsis (criteria for instituting and discontinuing therapy (2–6, 8–12).

Recommendations of some institutions are that CRP, though unspecific, has the best diagnostic value as an individual test, is an indicator in therapy onset and monitoring, and may also be used as an indicator to identify the time-point when antibiotic therapy may be safely discontinued (1,2,6,10,11).

Clinical significance of CRP concentration increase within the reference interval induced many manufacturers to develop tests for CRP determination particularly designed to measure very low concentrations. Manufacturers of both nephelometric and turbidimetric reagents turned to latex micro-polymers to achieve the necessary sensitivity so that laboratories have at their disposal several reagent types for CRP determination: highly linear for samples analyzed for general inflammation and infection, and sensitive (SCRP) and highly sensitive (HSCRP) that are employed in neonatology and assessment of the risk of cardio- and cerebrovascular diseases.

The Randox company produced a new combined Full Range CRP assay, characterized by the measuring range of 0.1-160.0 mg/L. When applying Olympus reagents for the same measuring range, we use two reagents and three applications. Considering the importance of early detection of sepsis in preterm infants and newborns, we examined the new reagent on samples from this population. In comparison to the previously applied analytic procedure, expected advantage of the examined reagent was that the use of one reagent instead of a combination of two reagents and three applications should contribute to faster diagnosis of sepsis in such a sensitive population and also to reduced measurement costs.

Aim

Analytical assessment of a new combined Randox Full Range assay for determination of CRP concentration in

usporedbi s reagensima tvrtke *Olympus* kao referentnim reagensima.

Materijali i metode

Koncentracija CRP u serumu određivana je kombiniranim reagensom za CRP *Full Range* tvrtke *Randox* (CP3847) i uspoređivana s dva reagensa tvrtke *Olympus* (OSR6147 i OSR6185) koji se rutinski koriste u Kliničkom zavodu za kemiju KB "Sestre milosrdnice".

Reagens *Full Range* tvrtke *Randox* koristi lateksovim mikropolimerom pojačanu imunoturbidimetrijsku pretragu koja omogućava određivanje koncentracije CRP u serumu/plazmi u rasponu od 0,1–160,0 mg/L. Reagens je primijenjen na uređaju *Olympus AU640* uz preporučenu aplikaciju tvrtke *Randox*. Korišteni su originalni kalibrator tvrtke *Randox* (CP2499), te kontrolni uzorci *High Sensitivity CRP Control 2* (CP 2477) i *CRP Control 3* (CP 2481).

Reagensi tvrtke *Olympus* s kojima je uspoređivan reagens za CRP *Full Range* tvrtke *Randox* su:

1. *Olympus CRP reagent* (OSR 6147), imunoturbidimetrijski reagens za koncentracijsko područje 5,0–300,0 mg/L.

   Za kalibraciju su korišteni originalni kalibratori tvrtke *Olympus* (ODR3021 Serum Protein Multi-Calibrator), a za kontrolu kvalitete rada originalni kontrolni uzorci tvrtke *Olympus*: *ITA Control Sera Level 1* (ODC0014), *ITA Control Sera Level 2* (ODC0015) i *ITA Control Sera Level 3* (ODC0016).
2. *Olympus CRP Latex reagent* (OSR6185), imunoturbidimetrijski reagens namijenjen ranoj dijagnozi infekcije u nedonoščadi i novorođenčadi. Za ovaj reagens postoje dvije aplikacije:
   - osjetljiva – za koncentracijsko područje 0,5–20,0 mg/L (SCRP)
   - visoko osjetljiva – za koncentracijsko područje 0,05–2,00 mg/L (HSCRP)

   Za kalibraciju su korišteni originalni kalibratori tvrtke *Olympus* (ODR3031 – sadrži pet kalibracijskih otopina, kalibracijske otopine 3, 4 i 5 koriste se za osjetljivu aplikaciju, a kalibracijske otopine 1 i 2 za visoko osjetljivu aplikaciju). Za kontrolu kvalitete rada korišten je *Olympus CRP (Latex) Control Sera* (ODC0013 – Control 1 i Control 2).

Analitička procjena obuhvatila je nepreciznost u seriji, nepreciznost iz dana u dan, netočnost i usporedna određivanja koncentracije CRP u uzorcima novorođenčadi i nedonoščadi. Ovo istraživanje nije zahtijevalo vađenje dodatnih uzoraka krvi, već su korišteni uzorci poslani za rutinsku analizu.

Nepreciznost

Nepreciznost unutar serije određena je višekratnim (20 x) mjerenjem koncentracije CRP u uzorcima seruma A i B i izražena kao koeficijent varijacije (KV %).

comparison to Olympus reagents as reference reagents.

Materials and methods

Serum CRP concentration was determined by the combined Full Range CRP assay produced by the Randox company (CP3847) and compared with two reagents produced by the Olympus company (OSR6147 and OSR6185) that are routinely used in the Clinical Institute of Chemistry, Sestre milosrdnice Clinical Hospital.

The Randox Full Range assay uses latex micropolymer-enhanced immunoturbidimetric test which allows determination of CRP concentration in the serum/plasma in the 0.1-160.0 mg/L range. The reagent was applied on the Olympus AU 640 using the application recommended by the Randox company. The original calibrator by the Randox company (CP2499) was used, as well as High Sensitivity CRP Control 2 (CP2477) and CRP Control samples.

The Olympus reagents used for comparison to the Randox Full Range CRP assay were:

1) Olympus System reagent for CRP (OSR 6147), an immunoturbidimetric reagent for the 5.0-300.0 mg/L concentration range.

   The original calibrator by the Olympus company was employed for calibration (ODR3021 Serum Protein Multi-Calibrator), and original control samples by the Olympus company for quality control: ITA Control Sera Level 1 (ODC0014), ITA Control Sera Level 2 (ODC0015) and ITA Control Sera level 3 (ODC0016).
2) Olympus CRP Latex reagent (OSR6185), an immunoturbidimetric reagent intended for early diagnosis of infection in preterm infants and newborns. Two applications are available for this reagent:
   - sensitive - for the 0.5-20.0 mg/L concentration range (SCRP)
   - highly sensitive - for the 0.05-2.00 mg/L concentration range (HSCRP).

   Original calibrators by the Olympus company were used for calibration (ODR3031 – contains five calibration solutions, calibration solutions 3, 4 and 5 are used for sensitive application, while calibration solutions 1 and 2 for highly sensitive application). For quality control, Olympus CRP (Latex) Control Sera (ODC0013 - Control 1 and Control 2) were used.

Analytical evaluation included within-run imprecision, between-run imprecision, inaccuracy and comparative determinations of CRP concentration in the samples of newborns and preterm infants. This study did not require collection of additional blood samples; it involved the use of routine analytical samples.

Imprecision

Within-run imprecision was determined by multiple (20 x) measurements of serum sample A and serum sample B and expressed as a coefficient of variation (CV %).

Nepreciznost iz dana u dan određena je mjerenjem koncentracije CRP u uzorku seruma C u tri primjera tijekom 10 dana i izražena kao koeficijent varijacije (KV %).

Netočnost

Ispitivanje netočnosti provedeno je određivanjem koncentracije CRP u uzorcima pet različitih komercijalnih kontrolnih seruma u triplikatu: *Olympus Latex Control* 1 (ODC 0013), *Olympus ITA Control Sera Level 1* (ODC0014), *Olympus ITA Control Sera Level 2* (ODC0015), *Olympus ITA Control Sera level 3* (ODC0016) i *Randox Control Level 3* (CP2481). Netočnost je izražena kao postotak odstupanja (R%) srednje izmjerene vrijednosti od srednje deklarirane vrijednosti.

Usporedna određivanja

Ukupno 139 uzoraka seruma nedonoščadi i novorođenčadi podijeljeno je u 3 skupine. Skupina 1, n=35, s koncentracijom CRP manjom od 2,00 mg/L; skupina 2, n=63, s koncentracijom CRP 2,0–20,0 mg/L; skupina 3, n=41, s koncentracijom CRP 5,0-300,0 mg/L. Skupina 1 analizirana je pomoću reagensa *Olympus Latex* (OSR 6185) - visoko osjetljiva aplikacija (HSCRP, mjerno područje 0,05-2,00 mg/L) i reagensa za CRP *Randox Full Range* (CP 3847), skupina 2 pomoću reagensa *Olympus Latex* (OSR 6185) - osjetljiva aplikacija (SCRP, mjerno područje 0,5-20,0 mg/L) i reagensa za CRP *Randox Full Range* (CP 3847), a skupina 3 pomoću reagensa za CRP tvrtke *Olympus* (OSR 6147, mjerno područje 5,0-300,0 mg/L) i reagensa za CRP *Full Range* tvrtke *Randox* (CP 3847).

Statistička obrada rezultata

Rezultati su obrađeni pomoću statističkog programa MedCalc (Ver. 9.0.1.0.; Franck Schoonjans, Belgium). Statistička značajnost razlika ispitana je korištenjem studentovog t-testa. Izračunati su koeficijenti korelacije (Pearsonov i koeficijent sukladnosti) i linearna regresijska analiza po Passing-Babloku. Statistički značajnom promjenom smatrana je promjena za koju je $p < 0,05$.

Rezultati

Rezultati ispitivanja nepreciznosti i netočnosti (srednja vrijednost, standardna devijacija, koeficijent varijacije, % odstupanja) prikazani su u tablicama 1-3.

Between-run imprecision was determined by measuring serum sample C in triplicate during 10 days and expressed as a coefficient of variation (CV %).

Inaccuracy

Examination of inaccuracy was performed by measuring CRP concentration in the samples of five different commercial control sera in triplicate: Olympus Latex Control 1 (ODC 0013), Olympus ITA Control Sera Level 1 (ODC0014), Olympus ITA Control Sera Level 2 (ODC0015), Olympus ITA Control Sera level 3 (ODC0016), and Randox Control Level 3 (CP2481). Inaccuracy was expressed as a percentage of bias (R%) of the determined mean value from the declared mean value.

Comparative measurements

A total of 139 samples from preterm infants and newborns were divided in three groups: group 1, n=35, with CRP concentration lower than 2.00 mg/L; group 2, n=63, CRP concentration between 2,0–20,0 mg/L; group 3, n=41, CRP concentration in the 5.0-300.0 mg/L range. Group 1 was analyzed using Olympus Latex reagent (OSR6185), a highly sensitive application (HSCRP, 0.05-2.00 mg/L measuring range), and the Randox Full Range CRP assay (CP 3847); group 2 was examined using Olympus Latex reagent (OSR 6185), a sensitive application (SCRP, 0.5-20.0 mg/L measuring range) and the Randox Full Range CRP assay (CP 3847); and group 3 using Olympus CRP reagent (OSR 6147, 5.0-300.0 mg/L measuring range) and the Randox Full Range CRP assay (CP 3847).

Statistical processing of results

Results were processed using the statistical program MedCalc (Ver. 9.0.1.0.; Franck Schoonjans, Belgium). Statistical significance of differences was examined by Student T-test. Coefficients of correlation (Pearson's and coefficient of concordance) were calculated, and linear regression analysis performed according to Passing-Bablok. A change was considered statistically significant if $p<0.05$.

Results

Results of examining imprecision and inaccuracy (mean value, standard deviation, coefficient of variation, % of bias) are presented in Tables 1-3.

Tablica 1. Rezultati ispitivanja nepreciznosti u seriji

Table 1. Results of within-run imprecision analysis

Sample N = 20	CRP (mg/L) mean value ± SD	CV (%)
Serum A	1.932 ± 0.042	2.18
Serum B	20.990 ± 0.371	1.77

Tablica 2. Rezultati ispitivanja nepreciznosti iz dana u dan

Table 2. Results of between-run imprecision analysis

Sample N = 30	CRP (mg/L) mean value ± SD	CV (%)
Serum C	21.119 ± 0.350	1.64

Tablica 3. Rezultati ispitivanja netočnosti

Table 3. Results of imprecision analysis

Control sample N = 3	CRP (mg/L) declared mean concentration	CRP (mg/L) determined mean concentration	R (%)
Olympus Latex Control 1	0.94	0.917	-2.45
Randox Control Level 2	3.80	3.850	1.32
Olympus ITA Control Level 1	16.20	16.567	3.67
Olympus ITA Control Level 3	58.70	58.073	1.07
Randox Control Level 3	156.00	156.080	0.05

R, % bias

Rezultati statističke obrade rezultata usporednih određivanja koncentracije CRP u uzorcima bolesnika (srednja vrijednost, standardna devijacija, statistička značajnost razlika, koeficijenti korelacije, linearna regresijska analiza po Passing-Babloku) prikazani su u tablicama 4 i 5.

Results of the statistical processing of results of comparative determinations of CRP levels in patient samples (mean value, standard deviation, statistical significance of differences, coefficients of correlation, linear regression analysis according to Passing-Bablok) are presented in Tables 4-5.

Tablica 4. Statistička značajnost razlika i koeficijenti korelacije dobiveni usporednim određivanjem koncentracije CRP u tri skupine ispitanika s reagensima dva različita proizvođača

Table 4. Statistical significance of differences and coefficients of correlation obtained by comparative determination of CRP concentration in three subject groups using reagents by two different manufacturers

Group N	Olympus CRP (mg/L) mean value ± SD	Randox, CRP (mg/L) mean value ± SD	p	Coefficients of correlation	
				r, Pearson's 95% CI	ρc, compatibility 95% CI
1. n =35	0.817 ± 0.525 *	0.821 ± 0.527	0.681	0.994 0.988 - 0.997	0.994 0.988 - 0.997
2. n =63	4.850 ± 4.861 **	4.743 ± 4.836	0.129	0.994 0.989 - 0.996	0.993 0.989 - 0.996
3. n =41	29.050 ± 32.320 ***	28.905 ± 31.854	0.570	0.999 0.998 - 0.999	0.999 0.998 - 0.999

*HSCRP, for 0.05 –2.00 mg/L CRP concentration range, ** SCRP; for 0.5-20.0 mg/L CRP concentration range, *** CRP for 5.0-300.0 mg/L CRP concentration range; CI – confidence interval

Tablica 5. Regresijska analiza po Passing-Babloku

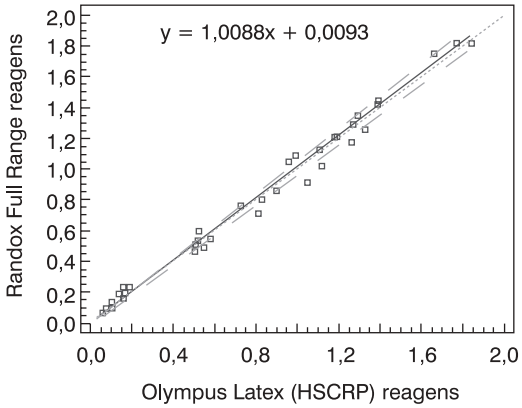
Tablica 5. Regression analysis according to Passing-Bablok

Reagent	Regression equation	95% CI	
		Slope, b	Intercept, a
Randox Full Range and Olympus Latex (HSCRP)	y = 1.0088 x + 0.0093	0.9773 - 1.0359	- 0.0124 - 0.0218
Randox Full Range and Olympus Latex (SCRP)	y = 0.9789 x - 0.0429	0.9647 - 0.9904	- 0.0664 – (-0.0203)
Randox Full Range and Olympus CRP	y = 1.0114 x - 0.2920	0.9759 - 1.0354	- 0.5574 - 0.0901

CI – confidence interval

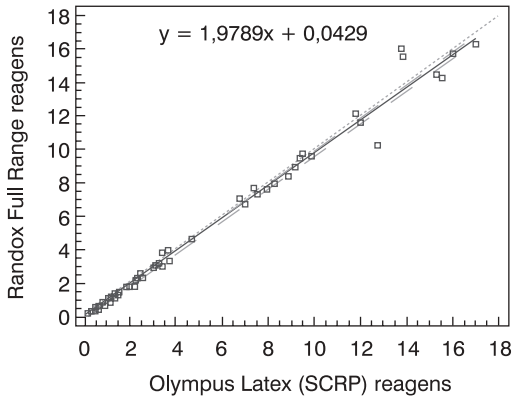
Grafički prikaz linearne regresijske analize po Passing-Babloku prikazan je na slikama 1-3.

Schematic presentation of linear regression analysis according to Passing-Bablok is laid down in Figures 1-3.



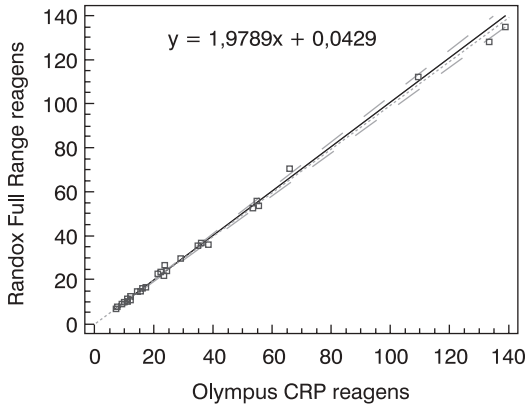
Slika 1. Grafički prikaz usporednih određivanja koncentracije CRP s reagensom *Randox Full Range* i reagensom *Olympus Latex* (HSCRP) u skupini 1

Figure 1. Schematic presentation of comparative determinations of CRP concentration by using the Randox Full Range assay and Olympus Latex (HSCRP) reagent in group 1



Slika 2. Grafički prikaz usporednih određivanja koncentracije CRP s reagensom Randox Full Range i reagensom Olympus Latex (SCRP) u skupini 2

Figure 2. Schematic presentation of comparative determinations of CRP concentration by using the Randox Full Range assay and Olympus Latex (SCRP) reagent in group 2



Slika 3. Grafički prikaz usporednih određivanja koncentracije CRP s reagensom Randox Full Range i reagensom za CRP tvrtke Olympus u skupini 3

Figure 3. Schematic presentation of comparative determinations of CRP concentration by using the Randox Full Range assay and Olympus CRP reagent in group 3

Rasprava

Rezultati dobiveni ispitivanjem reagensa *Randox Full Range* za određivanje koncentracije CRP pokazuju zadovoljavajuću nepreciznost kako unutar serije (KV ≤ 2,18%) tako i nepreciznost iz dana u dan (KV ≤ 1,64%). Također su dobiveni zadovoljavajući rezultati prilikom ispitivanja netočnosti (R ≤ 3,67%).

Uspoređivali smo dva reagensa različitih proizvođača u tri skupine ispitanika (tri različita koncentracijska područja). Usporedni rezultati linearne regresijske analize po Passing-Babloku pokazali su vrlo dobru podudarnost dviju metoda, jer je nagib pravca vrlo blizu 1,0 i podjednak u sve 3 skupine, a odsječak na osi y malen. U skupini 2 kojom je obuhvaćeno mjerno područje koncentracijskog raspona CRP od 0,5-20,0 mg/L, rezultati dobiveni reagensom *Randox Full Range* razlikuju se za vrlo malenu konstantu (unutar CI za odsječak, a nije sadržana 0, a = -0,0429). Izračunati koeficijenti korelacije za svaku skupinu ispitanika pokazuju visok stupanj korelacije reagensa *Randox Full Range* s reagensima tvrtke *Olympus*. Osim toga, sukladni koeficijent korelacije se ne razlikuje od Pearsonovog, pa zaključujemo da postoji skoro idealna korelacija između koncentracija CRP dobivenih korištenjem ovih dvaju reagensa. Sukladni koeficijent korelacije (ρ_c) je mjera preciznosti i točnosti. Sadrži Pearsonov koeficijent korelacije (r) i korekcijski faktor (Cb) koji je mjera odstupanja od najbolje korelacijske krivulje koja leži pod kutom od 45^0 ($\rho_c = r \times C_b$).

Stoga možemo zaključiti da bi reagens *Randox Full Range* mogao zamijeniti reagense tvrtke *Olympus* koji su u ovom ispitivanju bili referentni reagensi jer je njihova analitička pouzdanost dokazana dugogodišnjim korištenjem.

Discussion

The results obtained by examining the Randox Full Range assay for measuring CRP concentration demonstrated satisfactory imprecision, both within-run- (CV ≤ 2.18%) and between-run imprecision (CV ≤ 1.64%). Satisfactory results were also achieved during examination of inaccuracy (R ≤ 3.67%).

We compared two reagents by different manufacturers in three subject groups (three different concentration ranges). Comparative results of linear regression analysis according to Passing-Bablok showed very good agreement of the two methods as the slope was close to 1.0 and almost equal in all three groups, while the intercept was low. In group 2 which involved 0.5-20.0 mg/L CRP concentration as the measuring range, the results obtained by the Randox Full Range assay differed by a slight constant (within confidence interval for intercept, 0 not included, a= -0.0429). The coefficients of correlation calculated for each subject group showed a high degree of correlation between the Randox Full Range assay and Olympus reagents. Besides, the coefficient of concordance did not differ from the Pearson's coefficient, allowing us to conclude on the actual, almost ideal correlation between CRP concentrations obtained by using the foregoing two reagents. The coefficient of concordance (ρ_c) is a measure of precision and accuracy. It comprises the Pearson's coefficient of correlation (r) and a correction factor (Cb) which is a measure of the bias from the best correlation curve at a slope of 45^0 ($\rho_c = r \times C_b$).

Therefore, we may conclude that the Randox Full Range assay could replace Olympus reagents which were used

Dobiveni rezultati u skladu su s rezultatima drugih autora koji su uspoređivali iste reagense (nepreciznost u seriji: KV ≤ 3,3%; nepreciznost iz dana u dan: KV ≤ 3,7%; rezultati regresijske analize usporednih određivanja koncentracije CRP u uzorcima bolesnika: $r^2 \geq 0,9956$) (13).

Naši rezultati pokazuju da je određivanje koncentracije CRP jednako pouzdano i reproducibilno s oba reagensa. Prednost reagensa *Full Range* tvrtke *Randox* je u tome što jedan reagens pokriva raspon koncentracija od 0,1-160,0 mg/L, što je od osobite važnosti za pedijatrijske uzorke jer omogućuje brže dobivanje nalaza, dok tvrtka *Olympus* za to područje koristi dva reagensa i tri aplikacije. Prednost reagensa za CRP tvrtke *Olympus* je njegovo vrlo široko mjerno područje 5,0-300,0 mg/L, što je vrlo pogodno za bolesnike drugih odjela i klinika (Kirurške klinike i intenzivnih jedinica).

as reference reagents in this study since their analytical reliability has been confirmed by long-term use.

The results obtained are in consistence with results by other authors who compared the same reagents (within-run imprecision: CV ≤ 3.3%; between-run imprecision: CV ≤ 3.7%; results of regression analysis of comparative determinations of CRP concentration in patient samples: $r^2 \geq 0.9956$) (13).

Our results showed that determination of CRP concentration was equally reliable and reproducible with both reagents. The advantage of the Randox Full Range CRP assay is that a single reagent covers the concentration range from 0.1 to 160.0 mg/L, the fact that is of particular importance for pediatric samples as it allows faster availability of results, whereas the Olympus company employs two reagents and three applications for the same range. The advantage of the Olympus CRP reagent is its very broad measuring range, i.e. 5.0-300.0 mg/L which is very suitable for patients from other departments and wards (department of surgery and intensive care units).

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