

C-reaktivni protein u djece s astmom i alergijskim rinitisom

C-reactive protein in children with asthma and allergic rhinitis

Daniela Galez, Slavica Dodig, Miljenko Raos, Boro Nogalo

Dječja bolnica Srebrnjak, Referentni centar Ministarstva zdravstva za kliničku alergologiju djece, Zagreb

Srebrnjak Children's Hospital, Reference Center for Clinical Pediatric Allergology of the Ministry of Health and Social Welfare, Zagreb, Croatia

Sažetak

Uvod: Jedno od glavnih obilježja astme i alergijskog rinitisa je kronična upala dišnih putova. Cilj ovoga istraživanja bio je ispitati može li se određivanje koncentracije C-reaktivnog proteina (CRP) primijeniti kao biljeg upale u djece s astmom odnosno alergijskim rinitisom.

Materijali i metode: Ispitano je 42 zdrave djece prosječne dobi 9 ± 5 godina i 70 bolesnika s respiracijskim alergijskim bolestima u tijeku redovite kontrole: s astmom ($n=47$) i rinitisom ($n=23$) prosječne dobi 7 ± 4 godina. Koncentracija visoko osjetljivog CRP (hsCRP) određivana je imunoturbidimetrijskom metodom na lateks česticama. Koncentracije C3 i C4 te alfa-1-antitripsina određivane su imunoturbidimetrijskom metodom na biokemijskom analizatoru Olympus AU 400, a broj leukocita i trombocita na hematološkom brojaču Sysmex XT-1800i.

Rezultati: Koncentracija hsCRP bila je statistički značajno veća u bolesnika s astmom i rinitisom nego u zdrave djece. Bolesnici su također imali statistički značajno veće vrijednosti C3, C4, A1-AT i broja leukocita nego zdrava djeca. Broj trombocita bio je značajno veći u bolesnika s astmom (ali ne i u bolesnika s rinitisom) nego u zdravih ispitanika.

Zaključak: Rezultati ovoga istraživanja pokazali su da djeca s alergijskim bolestima dišnih putova imaju veću koncentraciju hsCRP u serumu nego klinički zdrava djeca.

Ključne riječi: CRP, upala, astma, alergijski rinitis

Abstract

Introduction: Chronic inflammation of airways is one of the major characteristics of asthma and allergic rhinitis. The aim of the study was to estimate whether determination of C-reactive protein (CRP) concentration could be used as an inflammation marker in children with asthma and allergic rhinitis.

Materials and methods: The study included 42 healthy children (mean age 9 ± 5 years) and 70 pediatric patients during regular control of respiratory allergic diseases, asthma ($n=47$) and rhinitis ($n=23$), mean age 7 ± 4 years. High sensitive CRP (hsCRP) concentration was determined by immunoturbidimetric method on latex particles. The concentrations of C3, C4 and alpha1-antitrypsin were determined by immunoturbidimetric method on an Olympus AU 400 biochemistry analyzer, whereas leukocyte and platelet counts were determined on a Sysmex XT-1800i counter.

Results: The concentration of hsCRP was statistically significantly higher in patients with asthma and allergic rhinitis than in healthy children. These patients also had statistically significantly higher levels of C3, C4, alpha1-antitrypsin and leukocyte count as compared with healthy subjects. Platelet count was significantly greater in asthma (but not rhinitis) patients as compared with the group of healthy children.

Conclusion: Study results demonstrated that children with respiratory allergic diseases had greater concentrations of hsCRP in serum compared with healthy children.

Key words: C-reactive protein, asthma, allergic rhinitis

Pristiglo: 28. srpnja 2006.

Prihvaćeno: 1. studenog 2006.

Received: July 28, 2006

Accepted: November 1, 2006

Uvod

Alergijske respiracijske bolesti koje su jedne od najčešćih kroničnih bolesti u djece (1,2) mogu se očitovati simptomima na gornjim (alergijski rinitis i sinusitis) i donjim (alergijska astma) dišnim putovima. Budući da gornji i donji dišni putovi imaju jedinstvena histologiju, jedinstvenu epidemiologiju alergijskih bolesti, mehanizme upale, je-

Introduction

Allergic respiratory diseases, which are among the most common chronic diseases in children (1,2), may manifest with symptoms in the upper (allergic rhinitis and sinusitis) and lower (allergic asthma) airways. As the histology, allergic disease epidemiology, mechanisms of inflammation, triggers for allergic disease clinical manifestations, diag-

dinstvene pokretače kliničkog očitovanja alergijskih bolesti, dijagnostičke postupke i liječenje, može se govoriti o jedinstvenom dišnom sustavu (3). Prema tome, astma i rinitis mogli bi se smatrati očitovanjima jednoga kroničnog alergijskog respiracijskog sindroma (4).

Jedno od glavnih obilježja astme i alergijskog rinitisa je kronična upala dišnih putova u kojoj sudjeluju mnoge stanice, a najvažnije su mastociti, eozinofilni granulociti i T-limfociti. U preosjetljivih osoba upala potaknuta alergenima iz okoliša dovodi do pojave simptoma astme (bronhokonstrikcija, kašalj i pritisak u prsima, često noću ili pred jutro) (5,6), odnosno rinitisa (začepljenost nosa, rinoreja, kihanje, svrbež nosa) (7). Smetnje su često reverzibilne te prođu spontano ili uz terapiju.

C-reaktivni protein (CRP) je dobro poznati upalni biljeg koncentracija kojega se u serumu često određuje kako bi se procijenila sistemska upala (8), primjerice pneumonija, reumatske bolesti, crijevne bolesti (9,10). U zadnje vrijeme uočeno je da CRP, čak i u referentnom intervalu (određivanje visoko osjetljivog CRP – hsCRP, od engl. *high sensitive CRP*), može biti važan upalni prognostički biljeg u bolesnika s kardiovaskularnim bolestima (11) ili šećernom bolešću (12). Određivanje koncentracije hsCRP podrazumijeva određivanje koncentracije CRP uobičajenom turbidimetrijskom metodom na lateks česticama, ali prilagođenom u niskom mjernom području. Primjenjujući hsCRP moguće je procijeniti upalu i u bolesnika s astmom (13).

Budući da je upala jedno od glavnih obilježja respiracijskih alergijskih bolesti, ovim smo radom željeli ispitati može li se određivanje koncentracije CRP primijeniti kao biljeg upale u djece s astmom odnosno alergijskim rinitisom.

Materijali i metode

Ispitanici

Ispitivanja su učinjena kod ukupno 42 zdrave djece (kontrolna skupina) srednje dobi od 9 godina ($\bar{x} \pm SD = 9 \pm 5$ godina) i 70 bolesnika s respiracijskim alergijskim bolestima u tijeku redovite kontrole: astmom ($n=47$) i rinitisom ($n=23$) srednje dobi od 7 godina ($\bar{x} \pm SD = 7 \pm 4$ godina). U kontrolnu skupinu bila su uključena klinički zdrava djeca bez podataka o atopiji koja su bila upućena na sistematski pregled u Dječju bolnicu Srebrnjak. Dijagnoza alergijskih bolesti postavljena je temeljem kliničkih kriterija (osobna i obiteljska anamneza, fizikalni pregled bolesnika, mjerenje plućne funkcije, provokacijskih testova u koži) i laboratorijskih pretraga (povećana koncentracija ukupnih i specifičnih protutijela IgE, broj eozinofilnih granulocita u krvi i obrisku nosa). U ispitivanim skupinama nijedno dijete nije imalo šećernu bolest. Obje skupine ispitanika bile su ujednačene po indeksu tjelesne mase (između 5. i 85. centilnih vrijednosti za dob). Djeca s akutnom virusnom ili bakterijskom infekcijom dišnoga sustava bila su isključena. Ispitanici su u razdoblju od siječnja do lipnja 2006. godine iz primarne zdravstvene zaštite bili upućeni u Dječju

nostic procedures and treatment are common to both upper and lower airways, they can be referred to as an integral respiratory system (3). Accordingly, asthma and rhinitis can be considered as manifestations of a single chronic allergic respiratory syndrome (4).

Chronic airway inflammation as one of the major features of asthma and allergic rhinitis involves many cell types, of which mastocytes, eosinophilic granulocytes and T-lymphocytes play most important roles. In sensitive individuals, the inflammation induced by environmental allergens leads to the symptoms of asthma (bronchoconstriction, cough and chest tightness, frequently overnight or at dawn) (5,6) and rhinitis (nasal congestion, rhinorrhea, sneezing, nose itching) (7). The discomforts are usually reversible and resolve spontaneously or with therapy.

C-reactive protein (CRP) is a well known inflammation marker. Serum concentration of CRP is generally determined to assess a systemic inflammation (8), e.g., pneumonia, rheumatic disease, intestinal disease, etc. (9,10). It has recently been observed that CRP, even in the reference interval, i.e. determination of high sensitive CRP (hsCRP), can serve as a relevant prognostic marker in patients with cardiovascular disease (11) or diabetes mellitus (12). Determination of hsCRP concentration implies determination of CRP concentration by the established turbidimetric method on latex particles but adjusted to the low measurement area. So, hsCRP can also be used to assess the grade of inflammation in asthma patients (13).

As inflammation is one of the major characteristics of respiratory allergic diseases, the aim of this study was to estimate whether determination of CRP concentration would be of use as a marker of inflammation in children with asthma and allergic rhinitis.

Materials and methods

Subjects

The study included 42 healthy children (control group), mean ($\bar{x} \pm SD$) age 9 ± 5 years, and 70 pediatric patients during regular control of respiratory diseases, asthma ($n=47$) and rhinitis ($n=23$), mean ($\bar{x} \pm SD$) age 7 ± 4 years. Control group consisted of clinically healthy children without information of atopic status referred for systematic medical check-up at Srebrnjak Children's Hospital. The diagnosis of allergic disease was based on clinical criteria (personal and family history, physical examination, pulmonary function measurement, provocation skin tests) and laboratory testing (increased concentration of total and specific IgE antibodies, blood and nasal swab eosinophilic granulocyte count). The study groups included children without diabetes mellitus. Body mass index was uniform in both study groups (between 5th and 85th centile values for age). Children with acute viral or bacterial infection of the airways were excluded. All patients were referred from primary health care offices to Srebrnjak Children's

bolnicu Srebrnjak, Zagreb. Kod svih je ispitanika dijagnostički postupak proveden prema standardiziranom postupku, a u skladu s etičkim načelima (uz odobrenje Etičkog povjerenstva Bolnice) i Deklaracijom o ljudskim pravima iz Helsinkija 1975. i izmjenama iz Tokija 2004. godine (14). Krv za analizu uzimana je nakon kliničkog pregleda djeteta u alergološkoj i pulmološkoj ambulanti u vremenu od 8 do 15 sati.

Metode

Koncentracija CRP određivana je imunoturbidimetrijskom metodom na lateks česticama (15), na biokemijskom analizatoru Olympus AU 400 i s reagensima istoga proizvođača. Koncentracija CRP određena je na dva načina: a) postupkom kod kojeg je linearnost od 0,2 do 480 mg/L i b) postupkom u niskom mjernom području (linearnost od 0,08 do 160 mg/L; hsCRP).

Koncentracije komponenata komplemента C3 i C4 te alfa-1-antitripsina (AAT) određivane su imunoturbidimetrijskom metodom na biokemijskom analizatoru Olympus AU 400 i uz primjenu reagensa istoga proizvođača. Broj leukocita i trombocita izmjeren je na hematološkom brojaču Sysmex XT-1800i.

Statističke metode

Pohrana i priprema podataka za statističku analizu učinjena je u programu Excel 2000 programskoga paketa Microsoft Office (Microsoft, SAD). Podaci s normalnom raspodjelom prikazani su aritmetičkom sredinom i standardnom devijacijom, a podaci s asimetričnom raspodjelom medijanom i rasponom. Raspodjela podataka testirana je χ^2 -testom, a $p > 0,05$ dokaz je normalne raspodjele. Značajnost razlika među skupinama testirana je testom ANOVA (za normalnu raspodjelu) ili Kruskal-Wallisovim testom (za asimetričnu raspodjelu), a pojedinačni odnosi između pojedinih skupina testirani su Studentovim testom (za normalnu raspodjelu) ili Wilcoxonovim testom (za asimetričnu raspodjelu). Vrijednosti $p < 0,05$ smatrane su statistički značajnima (16). Rabili smo statistički program MedCalc, verzija 4.10, Windows 95 (17).

Rezultati

Djeca s alergijskim bolestima prikazana su na dva načina: skupno, bez obzira na dijagnozu i svrstana prema dijagnozi (astma i alergijski rinitis), kako bi se mogla učiniti statistička analiza svih bolesnika, ali i svake skupine bolesnika zasebno. Rezultati ispitivanja koncentracije hsCRP, CRP, C3, C4, AAT, broja trombocita i leukocita u zdravih ispitanika i bolesnika s respiracijskim alergijskim bolestima, astmom i rinitisom, prikazani su u tablici 1.

Kako su razlike između skupina bile statistički značajne za C3, C4, AAT, broj leukocita, te granične za CRP, hsCRP i broj trombocita, izvedeno je testiranje i između pojedinih skupina. Koncentracija CRP, bez obzira na metodu mjere-

Hospital in Zagreb between January and June 2006. Diagnostic work-up was performed according to standardized procedure, and in line with ethical principles (approved by the Hospital Ethics Board) and Declaration on Human Rights from Helsinki 1975 and Tokyo amendments 2004 (14). Blood sampling was done upon clinical examination at outpatient clinics of allergology and pulmonology, between 8.00 a.m. and 3.00 p.m.

Methods

CRP concentration was determined by immunoturbidimetric method on latex particles (15), on an Olympus AU 400 biochemistry analyzer, using reagents from the same manufacturer. CRP concentration was determined in two ways: (a) a method with linearity of 0.2 to 480 mg/L, and (b) a method in low measurement area (linearity of 0.08 to 160 mg/L; hsCRP). The concentrations of complement components C3 and C4 and of alpha1-antitrypsin (AAT) were determined by immunoturbidimetric method on an Olympus AU 400 biochemistry analyzer, using reagents from the same manufacturer. Leukocyte and platelet counts were measured on a Sysmex XT-1800i blood counter.

Statistics

Data storage and processing for statistical analysis were performed by use of Excel 2000 Microsoft Office software (Microsoft, USA). Data with normal distribution were described by arithmetic mean (\bar{x}) and standard deviation (SD), and data with asymmetric distribution were described by median (M) and interval. Data distribution was assessed by χ^2 -test, with $p > 0.05$ as evidence of normal distribution. Statistical significance of between-group differences was assessed by ANOVA test (for normal distribution) or Kruskal-Wallis test (for asymmetric distribution); between-group relation was assessed by Student's t-test (for normal distribution) or Wilcoxon test (for asymmetric distribution). Statistical significance was set at $p < 0.05$ (16). The MedCalc® statistical package, version 4.10-Windows 95, was employed (17).

Results

The group of children with allergic diseases were presented in two modes: in total, irrespective of diagnosis, and in subgroups according to diagnosis (asthma and allergic rhinitis), for statistical analysis to be performed for the group as a whole and for each subgroup in separate. Results obtained on the concentrations of hsCRP, CRP, C3, C4, AAT, leukocyte count and platelet count in the control group of healthy children and the group of children with respiratory allergic diseases (asthma and rhinitis) are presented in Table 1. As between-group differences were statistically significant for C3, C4, AAT and leukocyte count, and borderline for hsCRP, CRP and platelet count,

TABLICA 1. Koncentracije hsCRP, CRP, C3, C4, A1-AT, te broj trombocita i leukocita u zdravih ispitanika i bolesnika s respiracijskim alergijskim bolestima, astmom i rinitisom**TABLE 1.** HsCRP, CRP, C3, C4, A1-AT concentrations, and platelet and leukocyte counts in healthy subjects and patients with respiratory allergic diseases asthma and rhinitis

		hsCRP (mg/L)	CRP (mg/L)	C3 (g/L)	C4 (g/L)	AAT (g/L)	PLT ($\times 10^9/L$)	LKC ($\times 10^9/L$)
Control N=42	Range	0.08 - 0.79		0.90 - 1.30				
	M	0.23		1.10				
	X \pm SD		0.4 \pm 0.2		0.22 \pm 0.05	1.30 \pm 0.27	299 \pm 57	7.0 \pm 1.6
	p	0.064 (5)	0.074 (5)	<0.001 (5)	0.011 (5)	0.020 (5)	0.054 (5)	0.006 (5)
Asthma/ Rihinitis N=70	Range	0.10 - 2.75	0.2 - 3.4					
	M	0.50	0.7					
	X \pm SD			1.64 \pm 0.25	0.32 \pm 0.09	1.79 \pm 0.30	326 \pm 91	8.3 \pm 1.9
	p	<0.001(1)	<0.001 (1)	<0.001 (1)	<0.001 (1)	<0.001 (1)		<0.001 (1)
Asthma N=47	Range	0.13 - 2.75	0.3 - 3.4					
	M	0.55	0.7					
	X \pm SD			1.67 \pm 0.23	0.33 \pm 0.08	1.83 \pm 0.33	338 \pm 103	8.4 \pm 2.1
	p	<0.001(2)	<0.001 (2)	<0.001 (2)	<0.001 (2)	<0.001 (2)	0.042 (2)	<0.001 (2)
Rihinitis N=23	X \pm SD	0.53 \pm 0.50	0.7 \pm 0.6	1.56 \pm 0.28	0.29 \pm 0.09	1.69 \pm 0.20	298 \pm 47	8.1 \pm 1.5
			0.0048 (3)					
	p	0.003(3)	0.045 (4)	<0.001 (3)	<0.001 (3)	<0.001 (3)	0.479 (6)	0.017(3)

(1) Asthma/rhinitis vs. control; (2) Asthma vs. control; (3) Rhinitis vs. control; (4) Rhinitis vs. asthma; (5) ANOVA or Kruskal-Wallis for asthma, rhinitis and control.

nja, bila je statistički značajno veća u bolesnika s astmom i rinitisom nego u ispitanika kontrolne skupine. Bolesnici su također imali statistički značajno veće vrijednosti C3, C4, AAT i broja leukocita nego zdrava djeca, bez obzira jesu li prikazani skupno ili prema dijagnozi. Broj trombocita bio je značajno veći u bolesnika s astmom (ali ne i u bolesnika s rinitisom) nego u zdravih ispitanika.

Prosječna koncentracija hsCRP u djece s alergijskim bolestima (0,65 \pm 0,55 mg/L) bila je statistički značajno veća nego u djece iz kontrolne skupine (0,28 \pm 0,16 mg/L). Bolesnici s astmom imali su veću vrijednost gornje granice raspona hsCRP (2,75 mg/L) nego bolesnici s alergijskim rinitisom (1,57 mg/L).

between group analysis was performed. The concentration of CRP was statistically significantly higher in patients with asthma and rhinitis than in the control group, irrespective of the method of determination. The levels of C3, C4, AAT and leukocyte count were also statistically significantly higher in the patient group, either in total or in groups according to diagnosis. Platelet count was statistically significantly higher in asthma patients but not in rhinitis patients as compared with the control group of healthy children. The mean hsCRP concentration was statistically significantly higher in children with allergic diseases (0.65 \pm 0.55 mg/L) than in control group children (0.28 \pm 0.16 mg/L). The patients with asthma showed hig-

Jedino je koncentracija CRP mjenenog uobičajenim postupkom bila statistički značajno manja u bolesnika s rinitisom nego u bolesnika s astmom, dok se vrijednosti ostalih pretraga nisu značajno razlikovale među tim dvjema podskupinama.

Iz percentilnih vrijednosti (Slika 1) može se vidjeti da su bolesnici s alergijskim rinitisom imali koncentraciju hsCRP $\leq 1,57$ mg/L, a da je 5% bolesnika s astmom imalo koncentraciju hsCRP veću od 1,57 mg/L. Koncentracija komponenta C3 i C4 bila je u oko 40% bolesnika s astmom veća nego u bolesnika s alergijskim rinitisom. Broj trombocita bio je u bolesnika s alergijskim rinitisom $\leq 363 \times 10^9/L$, a u 5% bolesnika s astmom broj trombocita bio je $>450 \times 10^9/L$. Percentilne vrijednosti AAT bile su prosječno 8% veće nego u djece s alergijskim rinitisom.

Rasprava

Ovo je istraživanje pokazalo da djeca s astmom i alergijskim rinitisom imaju veću koncentraciju hsCRP nego klinički zdrava djeca. U dostupnoj literaturi samo je jedna skupina izraelskih autora na kongresu prikazala rezultate određivanja hsCRP u 63 djece s astmom (18). Ti su autori uspoređivali koncentraciju hsCRP u akutnoj egzacerbaciji astme i nakon primijenjene terapije te utvrdili da je koncentracija hsCRP značajno veća u akutnoj bolesti ($14,28 \pm 8,45$ mg/L) nego nakon terapije ($1,92 \pm 3,16$ mg/L), a da koncentracija hsCRP korelira s FEV1 (engl. *Forced Expiratory Volume in 1 second*, forsirani ekspiracijski volumen u 1. sekundi). U našem istraživanju su i djeca s astmom ($0,71 \pm 0,58$ mg/L) i djeca s alergijskim rinitisom ($0,53 \pm 0,50$ mg/L) imala prosječnu koncentraciju hsCRP manju nego djeca u citiranom istraživanju. Takemura i suradnici (13) su određivali koncentraciju hsCRP u odraslih astmatičara i pokazali da bolesnici bez terapije inhalacijskim kortikosteroidima ($1,33 \pm 1,48$ mg/L) imaju veću koncentraciju hsCRP i od zdravih ispitanika ($0,21 \pm 0,30$ mg/L) i od ispitanika na terapiji ($0,9 \pm 1,0$ mg/L). Usporedimo li vrijednosti hsCRP zdrave djece u našem istraživanju ($0,28 \pm 0,16$ mg/L) s vrijednostima u odraslih zdravih ispitanika u istraživanju Takemure i suradnika (13), može se vidjeti sukladnost rezultata.

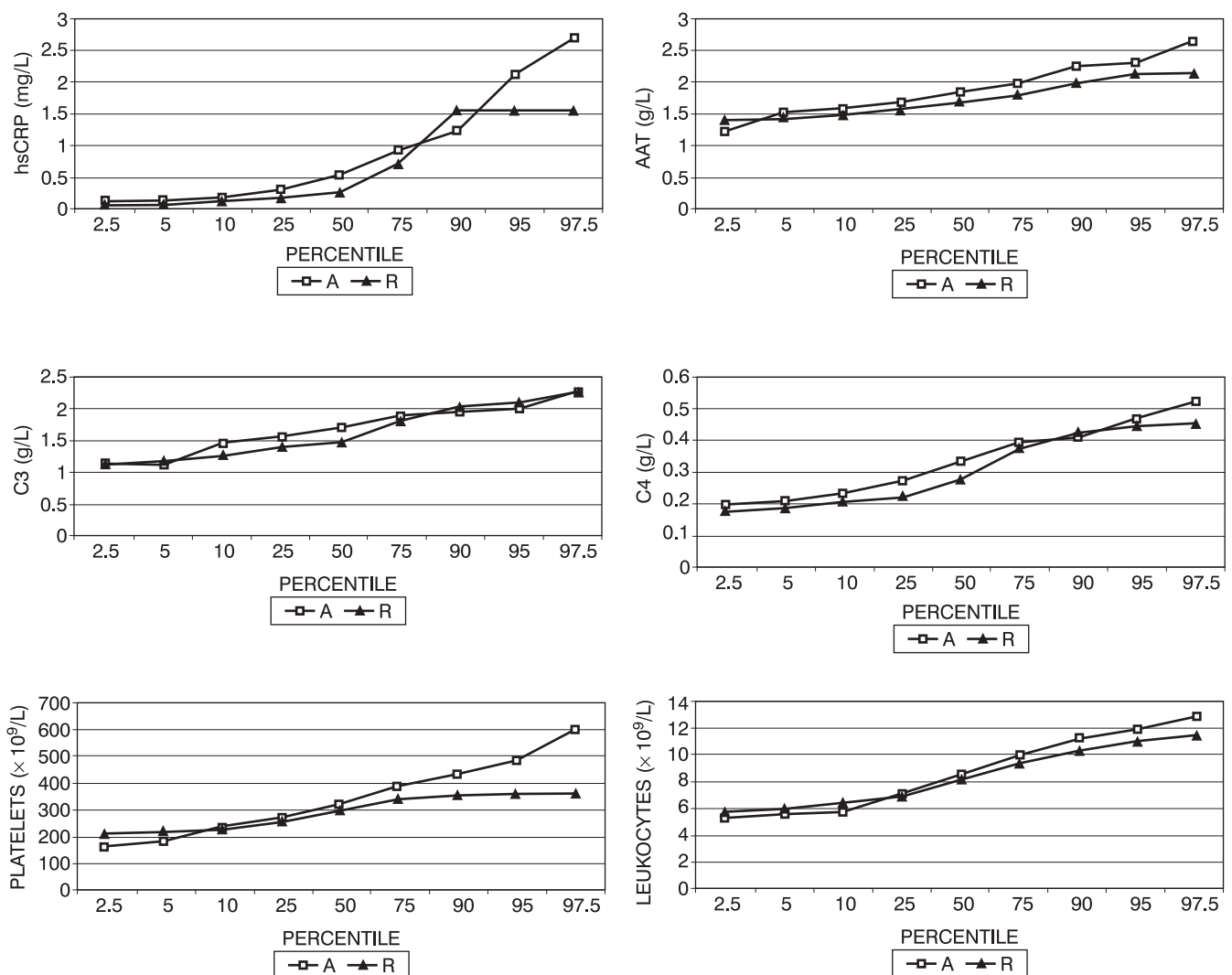
Prema nekim autorima (19) sistemska upala mogla se potvrditi i u bolesnika s astmom, budući da su ti bolesnici imali povećanu koncentraciju proteina akutne faze. I naše je istraživanje potvrdilo da djeca s astmom i alergijskim rinitisom imaju veći broj leukocita te veću koncentraciju $\alpha 1$ -antitripsina nego zdrava djeca, što ide u prilog postojanju blage sistemske upale u bolesnika s respiracijskim alergijskim bolestima. U odraslih ispitanika nije samo astma ključni činitelj povećanja koncentracije hsCRP. Na hsCRP mogu utjecati i drugi čimbenici, primjerice čimbenici rizika kardiovaskularnih bolesti (11), šećerna bolest (12), debljina (20), ateroskleroza i aterotromboza (21). Učestalost tih čimbenika rizika u dječjoj dobi je manja nego u odraslih, stoga pretpostavljamo da je vjerojatan uzrok

her values of the upper range limit for hsCRP (2.75 mg/L) than patients with allergic rhinitis (1.57 mg/L). Only the concentration of CRP measured by the conventional procedure was statistically significantly lower in rhinitis patients as compared with asthma patients, whereas the values of other tests did not differ significantly between these two subgroups.

Percentile values revealed the patients with allergic rhinitis to have an hsCRP concentration of ≤ 1.57 mg/L, whereas 5% of asthma patients had an hsCRP concentration greater than 1.57 mg/L (Fig. 1). In some 40% of asthma patients, the concentration of the complement components C3 and C4 exceeded the concentration recorded in patients with allergic rhinitis. Platelet count was found to be $\leq 363 \times 10^9/L$ in patients with allergic rhinitis and $>450 \times 10^9/L$ in 5% of asthma patients. Percentile values of AAT were by 8% on an average greater in asthma children than in those with allergic rhinitis.

Discussion

The present study indicated the children with asthma and allergic rhinitis to have a higher concentration of hsCRP than healthy children. The search of the available literature revealed only one group of Israeli authors to have presented results of hsCRP determination in 63 asthma children. These authors compared hsCRP concentration in acute exacerbation of asthma and upon therapy administration, and found it to be significantly higher in acute disease as compared with post-therapeutic state (14.28 ± 8.45 mg/L vs 1.92 ± 3.16 mg/L). They also report on the correlation between hsCRP concentration and forced expiratory volume in 1 second (FEV1) (18). In our study, both the children with asthma and those with allergic rhinitis had the mean hsCRP concentration lower than the concentration from the above mentioned report (0.71 ± 0.58 mg/L and 0.53 ± 0.50 mg/L, respectively). Takemura et al. (13) determined hsCRP concentration in adult asthmatic patients and showed it to be higher in patients without therapy with inhalation corticosteroids (1.33 ± 1.48 mg/L) than either in healthy subjects (0.21 ± 0.30 mg/L) or in patients receiving therapy (0.9 ± 1.0 mg/L). The hsCRP levels recorded in our control group of healthy children (0.28 ± 0.16 mg/L) were comparable to those reported by Takemura et al. (13) in healthy adults. According to some authors (19), systemic inflammation could also be verified in asthma patients, since these patients had an elevated concentration of acute phase proteins. Our study demonstrated the children with asthma and allergic rhinitis to have a higher leukocyte count and A1-AT concentration than healthy children, supporting the existence of mild systemic inflammation in patients with respiratory allergic diseases. In adult patients, it is not asthma alone that is the key factor to increase the concentration of hsCRP, as it can also be influenced by other factors such as the



SLIKA 1. Percentilne vrijednosti koncentracije hsCRP (a), AAT (b), C3 (c), C4 (d), broja trombocita (e) i leukocita (f) u bolesnika s astmom (A) i alergijskim rinitisom (R).

FIGURE 1. Percentile values of hsCRP (a), AAT (b), C3 (c), C4 (d) concentrations, platelet count (e) and leukocyte count (f) in patients with asthma (A) and allergic rhinitis (R).

povećanim vrijednostima CRP djece u ovom istraživanju upravo bila upala nastala zbog respiracijskih alergijskih bolesti. Pokazalo se, uz to, da u alergijskoj upali stanovitu ulogu ima i komplement, budući da su vrijednosti C3 i C4 u bolesnika bile veće nego u zdrave djece. Poznato je da CRP može aktivirati komponente komplementa (22). Broj trombocita također je bio povećan u bolesnika s astmom, ali ne i u onih s alergijskim rinitisom, pa bi u nekom budućem istraživanju trebalo ispitati uzroke toj razlici između astme i rinitisa, jer trombociti mogu imati različitu ulogu u alergijskim reakcijama (23).

risk of cardiovascular disease (11), diabetes mellitus (12), obesity (20), atherosclerosis and atherothrombosis (21). The prevalence of these risk factors is by far lower in children; therefore, the elevated concentration of CRP in our children could have been ascribed to inflammation due to respiratory allergic diseases. It was demonstrated that complement also plays a role in allergic inflammation, as the C3 and C4 levels were greater in children with respiratory allergic diseases than in healthy controls. CRP is known to be able to activate complement components (22). Platelet count was also increased in patients with as-

Svjesni smo ograničenja ovoga istraživanja zbog nedostatka podataka o lipidnom statusu ispitanika, koji bi mogao utjecati na koncentraciju hsCRP. Rezultati ovoga istraživanja (koje je jedno od prvih u tom području) pokazali su da djeca s alergijskim bolestima dišnih putova imaju veću koncentraciju hsCRP u serumu nego klinički zdrava djeca. Buduća istraživanja trebala bi pokazati može li se određivanjem koncentracije hsCRP pratiti uspješnost terapije respiracijskih alergijskih bolesti u djece.

thma but not in those with allergic rhinitis. Future studies should therefore investigate the causes of this difference between asthma and rhinitis because platelets may have a varying role in allergic reactions (23).

We are aware of the limitations of the present study due to the lack of information on the lipid status that may influence the hsCRP concentration. Study results (one of the first in this area) demonstrated that children with respiratory allergic diseases had greater concentrations of hsCRP in serum as compared with healthy children. Further studies are needed to demonstrate whether determination of hsCRP concentration could be useful in therapeutic monitoring of children with respiratory allergic diseases.

Adresa za dopisivanje:

Daniela Galez
Novaki 55
47000 Karlovac
e-pošta: danielagalez@net.hr
tel: 047/ 637-919

Corresponding author:

Daniela Galez
Novaki 55
47000 Karlovac, Croatia
e-mail: danielagalez@net.hr
Phone: +385 47 637-919

Literatura / References

- Kolbas V, Lokar R, Stanić M, Krznarić-Sučić Z. Prevalencija astme u djece školske dobi na području grada Zagreba. *Arhiv Zast Majke Djeteta* 1979;23:351-63.
- Aberle N, Reiner-Banovac Z. Epidemiološko ispitivanje astme u djece. *Pediatr Croat* 1998;42:9-14.
- Togias A. Rhinitis and asthma: evidence for respiratory system integration. *J Allergy Clin Immunol* 2003;111:1171-83.
- Casale TB, Dykewicz MS. Clinical implications of the allergic rhinitis-asthma link. *Am J Med Sci* 2004;327:127-38.
- Asthma management and prevention: a practical guide – 1996. (An information booklet for public health officials and health care professionals). NIH Publication No. 96-3659 B.
- Global strategy for asthma management and prevention, 2002. Scientific information and recommendations for asthma programs. NIH Publication No. 02-3659.
- Čepelak I, Dodig S, Štraus B, Labar B. Medicinsko-biokemijske smjernice. Zagreb: Medicinska naklada, 2004; str. 89.
- Pepys MB, Baltz MC. Acute phase proteins with special reference to C-reactive protein and related proteins (pentaxins) and serum amyloid A protein. *Adv Immunol* 1983;34:141-212.
- Silverman LM, Christenson RN. Amino acid and proteins. U: Burtis CA, Ashwood ER, ur. *Tietz Fundamentals of clinical chemistry*, 4. izdanje. Philadelphia: WB Saunders Company, 1996; str. 240-82.
- Whicher J. C-reactive protein (CRP). U: Thomas L, ur. *Clinical laboratory diagnostics*. Prvo izdanje. Frankfurt/Main: TH-books, 1998; str.700-6.
- Ridker PM. Clinical application of C-reactive protein for cardiovascular disease detection and prevention. *Circulation* 2003;107:363-9.
- Pradhan AD, Manson JE, Rifai N, Buring JE, Ridker PM. C-reactive protein, interleukin 6, and risk of developing type 2 diabetes mellitus. *JAMA* 2001;286:327-34.
- Takemura M, Matsumoto H, Niimi A, Ueda T, Matsuoka H, Yamaguchi M, Jinnai M, Mauro S, Hirai T, Ito Y, Nakamuro T, Mio T, Chin K, Mishima M. High sensitivity C-reactive protein in asthma. *Eur Respir J* 2006;27:908-12.
- World Medical Association Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects, August 2005. Available at <http://www.wma.net/e/policy/b3.htm>.
- Dupuy AM, Badiou S, Descomps B, Cristol JP. Immunoturbidimetric determination of C-reactive protein (CRP) and high sensitive CRP on heparin plasma. Comparison with serum determination. *Clin Chem Lab Med* 2003;41:948-9.
- Zar JH. *Biostatistical analysis*, 2. izd. Englewood Cliffs, NJ: Prentice-Hall, 1984.
- MedCalc Download, available June 15, 2006, www.medcalc.be/download.php.
- Soferman R, Gladshtein M, Weisman Y. C-reactive protein levels, a measurement of airway inflammation in asthmatic children. XXV Congress of the European Academy of Allergology and Clinical Immunology, Vienna, Austria, June 10-14, 2006. Abstract Book, str. 59.
- Jousilahti P, Salomaa V, Hakala K, Rasi V, Vahtera E, Palosuo T. The association of sensitive systemic inflammation markers with bronchial asthma. *Ann Allergy Asthma Immunol* 2002;89:381-5.
- Visser M, Bouter LM, McQuillen GM, Wener MH, Harris TB. Elevated C-reactive protein levels in overweight and obese adults. *JAMA* 1999;282:2131-5.
- Pepys MB. CRP or not CRP? That is the question. *Arterioscler Thromb Vasc Biol* 2005;25:1091-4.
- Wolbink GJ, Brouwer MC, Buysmann S, tenBerge IJ, Hack CE. CRP-mediated activation of complement in vivo: assessment by measuring circulating complement-C-reactive protein complexes. *J Immunol* 1996;157:473-9.
- Sullivan PJ, Jafar ZH, Harbinson PL, Restrck LJ, Costello JF, Page CP. Platelet dynamics following allergen challenge in allergic asthmatics. *Respiration* 2000;67:514-7.