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UČESTALOST POREMEĆAJA U REGULACIJI GLUKOZE KOD GOJAZNE DECE I ADOLESCENATA U SRBIJI

Sažetak: Prekomerna uhranjenost u populaciji dece i adolescenata predstavlja jedan od najznačajnijih javno zdravstvenih problema današnjice. Sa pandemijom gojaznosti kod mladih je uočeno povećanje prevalencije komplikacija gojaznosti koje su nekada primećivane samo kod odraslih, poput tipa 2 dijabetesa melitusa i drugih poremećaja u regulaciji glukoze. Učestalost ovih komorbiditeta gojaznosti u populaciji dece i adolescenata značajno se razlikuje u različitim delovima sveta, sa znatno većom prevalencijom u SAD u odnosu na Evropu. Ispitivanjem koje je obavljeno u Institutu za zdravstvenu zaštitu majke i deteta Srbije „Dr Vukan Čupić“, kod 301 deteta i adolescenata, utvrđena je prevalencija tipa 2 dijabetesa melitusa od 0,3%, a ukupna prevalencija drugih poremećaja u regulaciji glukoze, odnosno povećane glikemije naše i poremećaja tolerancije na glukozu iznosila je 16%. Iako ovi nalazi ne ukazuju na epidemiju tipa 2 dijabetesa melitusa kod dece u Srbiji, utvrđena je velika prevalencija drugih poremećaja u regulaciji glukoze, što ukazuje na potrebu za unapređenjem mera prevencije i ranog lečenja gojaznosti, kako bi se izbeglo smanjenje prosečne dužine i kvaliteta života u narednim generacijama odraslih u Srbiji.

Ključne reči: gojaznost, deca, poremećaji u regulaciji glukoze, tip 2 dijabetesa melitusa.

Uvod

Prekomerna uhranjenost, odnosno gojaznost, kako u populaciji odraslih, tako i u populaciji dece i adolescenata predstavljaju poremećaje zdravlja od izuzetnog

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epidemiološkog i kliničkog značaja i jedan od najvećih javno-zdravstvenih problema današnjice (1). Trend porasta prevalencije gojaznosti dovodi do povećanja rizika za nastanak udruženih endokrinoloških, kardiovaskularnih i drugih poremećaja zdravlja u populaciji dece i adolescenata. Tip 2 dijabetesa melitusa i drugi poremećaji u regulaciji glukoze jesu jedne od najznačajnijih komplikacija gojaznosti u populaciji dece i adolescenata, a sa pandemijom gojaznosti uočava se i nesporn porast ovih poremećaja zdravlja u populaciji najmlađih (2, 3).

Epidemija gojaznosti kod mladih širom sveta, sa posledičnim povećanjem prevalencije komorbiditeta gojaznosti poput tipa 2 dijabetesa melitusa, utiče na značajan porast morbiditeta od metaboličkih, kardiovaskularnih i drugih bolesti ne samo u pedijatrijskoj populaciji, već i u adultnom dobu. Naime, gojaznost u detinjstvu značajan je prognostički pokazatelj za gojaznost u starijim uzrastima. Prekomerna telesna masa u populaciji predškolske dece i osnovaca povezana je sa značajno većim rizikom za prekomernu uhranjenost u populaciji adolescenata, a žene i muškarci u trećoj deceniji života su u više nego desetostruko većem riziku da budu prekomerno uhranjeni ako su u uzrastu od 15 do 17 godina imali indeks telesne mase ≥ 85 . percentila za odgovarajući uzrast i pol (4, 5). Na osnovu ovih nalaza moglo bi se zaključiti da gojazna deca i adolescenti odrastaju u gojazne odrasle, a uzrast od 7 do 13 godina smatra se najznačajnijim za prevenciju i lečenje prekomerne uhranjenosti i gojaznosti (6). Pored toga, najnovija istraživanja ukazuju da proces ateroskleroze počinje već u adolescenciji, a da učestalost faktora rizika za kardiovaskularna oboljenja u detinjstvu, koja je u direktnoj proporciji sa stepenom prekomerne uhranjenosti, odnosno gojaznosti, utiče na povećanje učestalosti akutnih manifestacija kardiovaskularnih oboljenja u adultnom dobu (6–9).

Značaj porasta prevalencije predgojaznosti i gojaznosti u populaciji dece i adolescenata širom sveta možda se najbolje može sagledati kroz nalaz ispitivanja učinjenog u SAD koji ukazuje na to da se zbog sve veće prevalencije gojaznosti u populaciji dece i adolescenata može očekivati smanjenje očekivane prosečne dužine života u narednoj generaciji odraslih. Drugim rečima, očekuje se da će zbog pandemije gojaznosti u populaciji mladih, deca današnjice biti prva koja će živeti kraće od svojih roditelja (1, 10).

Učestalost gojaznosti kod dece i adolescenata u Evropi je nesporno velika sa uočenim trendom rasta, ali je prevalencija ovog poremećaja zdravlja u populaciji mladih i dalje značajno veća u SAD (11, 12). Prema nalazima istraživanja, ukupna prevalencija predgojaznosti i gojaznosti kod mladih u SAD iznosi i do 54,3% (12, 13). U severnoevropskim zemljama učestalost prekomerne uhranjenosti u populaciji dece i adolescenata je znatno manja, od 10 do 20%, dok je na jugu Evrope učestalost ovih poremećaja veća (20–35%), ali ipak skoro dvostruko manja od učestalosti u SAD (3). Pored socioekonomskih i kulturoloških razlika, značajan uzrok manje prevalencije gojaznosti u populaciji dece i adolescenata u Evropi u odnosu na SAD jeste činjenica da su deca određenih etničkih subpopulacija u većem riziku za razvijanje ovih

poremećaja zdravlja, sa najvećom prevalencijom gojaznosti u subpopulacijama dece i adolescenata afričkog i meksičkog porekla (3, 12). Istraživanje zdravlja stanovnika Srbije u 2006. godini pokazalo je da je skoro petina mladih (18%) u našoj zemlji prekomerno uhranjena (11,6%) ili gojazna (6,4%), što je u skladu sa prevalencijom prekomerne uhranjenosti i gojaznosti mladih u drugim zemljama regiona (14).

Učestalost poremećaja u regulaciji glukoze kod gojazne dece i adolescenata

Sa povećanjem prevalencije gojaznosti, u populaciji dece i adolescenata su sve učestalije komplikacije gojaznosti koje su nekada primećivane samo kod odraslih, kao što su tip 2 dijabetesa melitusa (T2DM) i drugi poremećaji u regulaciji glukoze (1, 3, 15). Iako su pozitivna porodična anamneza i etnička pripadnost nesporni faktori rizika, gojaznost se smatra najznačajnijim faktorom rizika za razvoj T2DM kod dece i adolescenata (3, 16, 17). Uočen porast prevalencije dijabetesa melitusa tipa 2 u populaciji dece i adolescenata u svetu još uvek ne dostiže epidemijske razmere, ali se odvija uporedo sa pandemijom gojaznosti u detinjstvu (15, 18). Rezultati pojedinih istraživanja iz SAD beleže izuzetno povećanje prevalencije tipa 2 dijabetesa i skoro izjednačenu incidenciju tipa 1 i tipa 2 dijabetesa melitusa u populaciji dece i adolescenata, dok su u drugim zemljama rezultati ispitivanja manje izraženi ali ukazuju na nesumnjiv porast učestalosti ovog oboljenja u populaciji najmlađih (19–22).

Učestalost tipa 2 dijabetesa melitusa u populaciji dece i adolescenata značajno se razlikuje u različitim delovima sveta, sa znatno većom prevalencijom u SAD i zemljama Azije u odnosu na Evropu (23). Prema nalazima više istraživanja u populaciji gojazne dece i adolescenata u SAD prevalencija dijabetesa melitusa tipa 2 iznosi od 1,3% do 6%, a učestalost poremećaja tolerancije na glukozu 17–25% (24–26). Rezultati studija učinjenih u Evropi ukazuju na značajno manju učestalost T2DM i drugih poremećaja u regulaciji glukoze u populaciji gojazne dece i adolescenata u Evropi u odnosu na SAD. Prema rezultatima ovih istraživanja, u Italiji učestalost tipa 2 dijabetesa melitusa u populaciji gojazne dece i adolescenata iznosi 0,1%, a poremećaja tolerancije na glukozu 4,5%, u Poljskoj 0,1%, odnosno 7,1%, u Francuskoj 0,2%, odnosno 5,0%, u Nemačkoj 1,5%, odnosno 5,3%, u Mađarskoj 1,9% odnosno 17,3%, a u Velikoj Britaniji je prevalencija ovih poremećaja u ispitivanoj grupi prekomerno uhranjene dece i adolescenata iznosila 0%, odnosno 11% (2, 3, 27–31).

Veća prevalencija tipa 2 dijabetesa u pedijatrijskoj populaciji SAD i Azije u odnosu na Evropu je velikim delom posledica činjenice da su određene etničke grupe, odnosno deca afričkog, meksičkog, azijskog i indijanskog (“Native-americans“) porekla u znatno većem riziku za obolevanje od ovog tipa dijabetesa u odnosu na ostatak populacije (3, 16, 21, 23).

Učestalost poremećaja u regulaciji glukoze kod gojazne dece i adolescenata u Srbiji

Ispitivanjem obavljenim u Institutu za zdravstvenu zaštitu majke i deteta Srbije „Dr Vukan Čupić“ u Beogradu obuhvaćeno je 301 dete i adolescent (176 devojčica i 125 dečaka) uzrasta od 5,2 do 18,9 godina, koji su imali indeks telesne mase veći od 90. percentila za odgovarajući uzrast i pol. Ispitivanjem nisu obuhvaćena deca sa genetskim sindromima i drugim uzrocima sekundarne gojaznosti, a cilj istraživanja je bila procena učestalosti tipa 2 dijabetesa melitusa i drugih poremećaja u regulaciji glukoze kod dece i adolescenata sa prekomernom telesnom masom u Srbiji. Prikupljeni podaci obuhvatali su demografske, antropometrijske i druge nalaze iz fizikalnog pregleda, a od laboratorijskih ispitivanja svima je obavljen test oralnog opterećenja glukozom i određeni nivoi glukoze, insulina, transaminaza, triglicerida, HDL, LDL i ukupnog holesterola. U cilju utvrđivanja faktora povezanih sa poremećajima u homeostazi glukoze, grupa gojazne dece sa poremećajima u regulaciji glukoze i grupa gojazne dece sa normalnom homeostazom glukoze poređene su parametarskim i neparametarskim testovima razlike.

Od ukupno 301 deteta i adolescenata kod 49 (16,3%) otkriven je neki od poremećaja u homeostazi glukoze. U grupi dece sa poremećajima u regulaciji glukoze T2DM je otkriven kod jedne adolescentkinje, 13 je imalo povećanu glikemiju našte, 25 poremećaj tolerancije na glukozu, a desetero je istovremeno imalo i povećanu glikemiju našte i poremećaj tolerancije na glukozu. U poređenju sa ispitanicima koji su imali normalnu homeostazu glukoze, deca sa poremećajima u regulaciji glukoze imala su statistički značajno više insulinemije u 120. minutu testa oralnog opterećenja glukozom, više nivoe triglicerida i HOMA indeksa rezistencije na insulin (tabela 1). Takođe, utvrđeno je da su devojčice bile u većem riziku za poremećaje u regulaciji glukoze, kao i da su ovi poremećaji bili učestaliji kod ispitanika u kasnijim stadijumima pubertetskog razvoja. Deca sa i bez poremećaja u regulaciji glukoze nisu se značajno razlikovala u pogledu uzrasta, stepena gojaznosti i drugih ispitivanih karakteristika.

Tabela 1: Razlike u fenotipu gojazne dece i adolescenata sa i bez poremećaja u regulaciji glukoze

	Normalna homeostaza glukoze	Poremećaj u regulaciji glukoze	p
Insulinemija u 120. minutu OGTT-a (mIJ/l) ¹	115,2 ± 100,6	181,9 ± 144,5	< 0,01
Trigliceridi (mmol/l)	1,3 ± 0,8	1,5 ± 0,7	< 0,05
HOMA indeks rezistencije na insulin	4,9 ± 4,3	6,7 ± 5,3	< 0,01

¹ OGTT – test oralnog opterećenja glukozom

Zaključak

Učestalost tipa 2 dijabetesa melitusa kod ispitivane prekomerno uhranjene dece i adolescenata može se porediti sa prevalencijom ovog poremećaja zdravlja u drugim zemljama Evrope. Sa druge strane, prevalencija tipa 2 dijabetesa melitusa u subpopulaciji gojazne dece i adolescenata u SAD je i do 20 puta veća u odnosu na utvrđenu učestalost ovog poremećaja zdravlja u Srbiji. Velika razlika u učestalosti T2DM u populaciji predgojazne i gojazne dece i adolescenata u Srbiji u odnosu na SAD je najverovatnije posledica različitog etničkog sastava i posledično većeg rizika za obolavanje od T2DM u populaciji dece i adolescenata u SAD. Rezultati našeg ispitivanja ukazuju na značajnu učestalost povećane glikemije naše i poremećaja tolerancije na glukozu kod ispitivane gojazne dece i adolescenata, što zajedno sa povećanjem učestalosti gojaznosti mladih u našoj zemlji ukazuje na potrebu za unapređenjem mera prevencije i ranog lečenja gojaznosti, kako bi se uz smanjenje učestalosti komplikacija gojaznosti kod dece izbeglo i smanjenje prosečne dužine i kvaliteta života u narednim generacijama odraslih u Srbiji.

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PREVALENCE OF DISTURBANCES IN GLUCOSE REGULATION IN OBESE CHILDREN AND ADOLESCENTS IN SERBIA

Summary: Childhood obesity is one of the most important present public health issues. Complications of obesity once observed only in the population of obese adults, like type 2 diabetes and other disturbances in glucose regulation, are emerging in the pediatric population along with the pandemic of obesity. Prevalence of these co-morbidities of obesity varies widely in the populations of children and adults in different regions, with significantly higher observed prevalence in USA compared with European countries. Results of the study performed in Institute for Mother and Child Health Care of Serbia “Dr Vukan Čupić” in a group of 301 obese children and adolescents, discovered prevalence of type 2 diabetes was 0,3%, and of other disturbances in glucose regulation, namely impaired glucose regulation and impaired glucose tolerance 16%. Although these results are not suggestive of pediatric type 2 diabetes epidemic in Serbia, high established prevalence of other disturbances in glucose homeostasis emphasizes the need for prevention and early treatment of obesity in order to avoid a decline in life expectancy in future generations of adults in Serbia.

Keywords: obesity, children, impaired glucose regulation, type 2 diabetes

Introduction

Overweight and obesity in population of adults as well as in children and adolescents, are health disorders of substantial epidemiological and clinical significance, thus

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representing one of the most important public health issues (1). Rise in the prevalence of obesity is followed by an increased risk of associated endocrine, cardiovascular and other diseases in the population of children and adolescents. Type 2 diabetes mellitus and other disturbances in glucose regulation are important complications of childhood obesity. Increase in the prevalence of these co-morbidities has been observed in the youth along with worldwide epidemic of obesity (2, 3).

Pandemic of childhood obesity and associated co-morbidities, including type 2 diabetes, is associated with a substantial increase in incidence of metabolic, cardiovascular and other diseases not only in pediatric population, but also in the adult life. Obesity in childhood is a significant prognostic factor for adult obesity. Overweight in the population of preschool and school-aged children is associated with substantially increased risk for overweight in adolescence. Also, women and men in their twenties are at more than ten times greater risk for overweight if their body mass index in the age of 15-17 years was ≥ 85 . percentile for the appropriate age and gender (4, 5). According to these findings, it could be concluded that obese children and adolescents become obese adults, and timing in the age of 7 to 13 years is considered to be of greatest importance for the prevention and treatment of overweight and obesity (6). It has also been established in recent studies that atherosclerosis starts in adolescence and that prevalence of cardiovascular risk factors in childhood, directly associated with the degree of obesity, results in increased number of cardiovascular events in the adulthood (6-9).

The best understanding of the consequences of worldwide childhood obesity epidemic may be acquired through the results of the research performed in USA. These results indicate that due to observed increase in the prevalence of obesity amongst children and adolescents, a potential decline in life expectancy in future generations of adults could be expected. In other words, as a result of obesity pandemic in youth, the children of today could be the first generation of children to live a shorter life than their parents (1, 10).

Prevalence of obesity in the population of children and adolescents in Europe is definitely high and rising, but this disorder is still most frequent in the youth living in USA (11, 12). Research results indicate that total prevalence of overweight and obesity in children and adolescents in USA is as high as 54.3% (12, 13). The prevalence of overweight in children and adolescents in countries of northern Europe is significantly lower, ranging between 10% and 20%, and although observed prevalence in countries of southern Europe is higher (20-35%), it is still two times lower compared to USA (3). Besides well established socioeconomic and cultural differences, the fact that children of certain ethnic origins, namely African-american and Hispano-american, are much more prone to obesity significantly influences the prevalence of obesity to be higher in American children and adolescents compared to their European peers (3, 12). According to the results of the "Study of population health in Serbia" performed in 2006. 18% of children and adolescents aged 7-19 years were overweight, with

one third of them being obese, which correlates with established prevalence of other countries in the region (14).

Prevalence of impaired glucose regulation in obese children and adolescents

Complications of obesity once observed only in the population of obese adults, like type 2 diabetes mellitus (T2DM) and other disturbances in glucose regulation, are emerging in the pediatric population along with the pandemic of obesity (1, 3, 15). Although positive family history and ethnic origin are certain risk factors, obesity is considered to be the most important risk factor for the development of T2DM in children and adolescents (3, 16, 17). Along with pandemic of obesity in youth, an increase in the prevalence of type 2 diabetes has been observed in the pediatric population, though still not regarded as epidemic (15, 18). Substantial rise in the prevalence of pediatric type 2 diabetes and nearly equal incidence of type 1 and type 2 diabetes in children and adolescents has been observed in several studies performed in USA, while available data regarding other regions are less pronounced, but still confirm the certain increase in the prevalence of this disease in youth (19-22).

The prevalence of type 2 diabetes mellitus widely varies in different regions, with significantly higher observed prevalence of this disease in USA and Asian countries compared to Europe (23). According to the results of several studies performed in USA, the prevalence of type 2 diabetes in obese children and adolescents ranges from 1.3% to 6%, and the prevalence of impaired glucose tolerance 17-25% (24-26). Results of the studies performed in Europe suggest that the prevalence of these disorders in obese children and adolescents is significantly lower compared to USA. According to the results of these studies, the prevalence of type 2 diabetes and impaired glucose tolerance in obese children and adolescents is 0.1% and 4-5% in Italy, 0.1% and 7.1% in Poland, 0.2% and 5.0% in France, 1.5% and 5.3% in Germany, 1.9% and 17.3% in Hungary and 0% and 11% in Great Britain (2, 3, 27-31).

Higher observed prevalence of pediatric type 2 diabetes in USA and Asia compared to Europe is largely due to the fact that certain ethnic groups, namely African-american, Mexican, Asian and Native-american children, are at significantly higher risk for type 2 diabetes compared to the rest of the population (3, 16, 21, 23).

Impaired glucose regulation in obese children and adolescents in Serbia

Research performed in the Mother and Child Health Care Institute of Serbia "Dr Vukan Čupić" in Belgrade investigated a group of 301 children and adolescents (176

girls and 125 boys) aged 5.2 – 18.9 years, with body mass index value greater than 90. percentile for the appropriate age and gender. Children with genetic syndromes and other causes of secondary obesity were excluded from the study, and the main goal of the research was to investigate the prevalence of type 2 diabetes and other disturbances in glucose homeostasis in overweight children and adolescents in Serbia. Acquired data included demographics, anthropometric and other clinical exam data, while laboratory analyses included the oral glucose tolerance test with glucose and insulin levels, serum transaminases, triglycerides, HDL, LDL and total cholesterol levels. In order to assess the factors associated with impaired glucose regulation, group of obese children with disturbances in glucose regulation and group of the obese children with normal glucose homeostasis were compared by means of parametric and non-parametric statistical tests.

In total of 301 investigated children and adolescents, 49 (16.3%) had impaired glucose regulation. Within the group of children with disturbances in glucose regulation, T2DM was discovered in one adolescent girl, 13 had impaired fasting glucose, 25 impaired glucose tolerance, while ten had both impaired fasting glucose and impaired glucose tolerance. It was observed with statistical significance that when compared to subjects with normal glucose homeostasis, children with impaired glucose regulation had higher levels of insulin at 120. minute during oral glucose tolerance test, higher levels of triglycerides and higher values of HOMA insulin resistance index (Table 1). It was also observed that girls were at higher risk for disturbances in glucose homeostasis and that impaired glucose regulation was more frequent in later stages of pubertal development. There were no statistically significant differences between children with and without disturbances in glucose regulation regarding the degree of obesity and other investigated characteristics.

Table 1: Phenotype differences in groups of obese children with and without disturbances in glucose regulation

	Normal glucose homeostasis	Impaired glucose regulation	p
Insulin at 120. minute during OGTT (mIJ/l) ¹	115.2 ± 100.6	181.9 ± 144.5	< 0.01
Triglycerides (mmol/l)	1.3 ± 0.8	1.5 ± 0.7	< 0.05
HOMA insulin resistance index	4.9 ± 4.3	6.7 ± 5.3	< 0.01

¹ OGTT – oral glucose tolerance test

Conclusion

Observed prevalence of type 2 diabetes in investigated group of overweight children and adolescents is in concordance with the established prevalence of this disease in other European countries. Known prevalence of type 2 diabetes in the subpopulation of obese children and adolescents in USA is up to 20 times higher compared to observed prevalence in Serbia. Such pronounced difference in the prevalence of T2DM in overweight and obese children and adolescents in Serbia compared to USA is most probably due to differences in ethnical composition and consequent higher risk for type 2 diabetes in the population of children and adolescents in USA. On the other hand, results of our study revealed a significant prevalence of impaired fasting glucose and impaired glucose tolerance in studied obese children, which together with the increasing prevalence of childhood obesity in our country, emphasizes the need for prevention and early treatment of obesity in order to avoid a decline in life expectancy in future generations of adults in Serbia

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