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Cardiac autonomic modulation in obese and eutrophic children: systematic review and meta-analysis

Modulação autonômica cardíaca em crianças obesas e eutróficas: revisão sistemática e metanálise

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Abstract – This study aimed to verify the influence of childhood obesity on the regulation of cardiac autonomic modulation through the heart rate variability of obese and eutrophic children. The study consisted of a systematic review and meta-analysis in five PubMed, Scielo, Cochrane Library, BVS/Lilacs and Medline databases. Of the 60 articles found, 15 met the pre-established criteria. These studies were submitted to evaluation of methodological quality and risk of bias, and the Joanna Briggs Institute Critical Appraisal Checklist for Prevalence Studies (JBI) was applied. Meta-analysis was performed with the Review Manager 5.3 software for variables related to the alteration of cardiac autonomic modulation. Fifteen studies were used for meta-analysis, all were classified with high methodological quality (7 to 9 points), 13 presented results showing alteration of autonomic cardiac modulation in obese children in comparison with eutrophic children, and only two presented indicatives that refute this hypothesis. The present study identified reduction in the parasympathetic activity of the obese group in relation to the eutrophic group through the variables studied. The use of RMSSD, pNN50 and SDNN variables is recommended in future studies, as their results were significant for this meta-analysis.

Key words: Autonomic nervous system; Heart rate; Pediatric obesity.

Resumo – *Este trabalho teve por objetivo verificar a influência da obesidade infantil na regulação da modulação autonômica cardíaca, por meio da variabilidade da frequência cardíaca de crianças obesas e eutróficas. O estudo consistiu em uma revisão sistemática e metanálise em cinco bases de dados PubMed, Scielo, Cochrane Library, BVS (Biblioteca Virtual em Saúde)/Lilacs e Medline. Dos 60 artigos encontrados, 15 atenderam aos critérios pré-estabelecidos. Esses estudos foram submetidos a avaliação da qualidade metodológica e risco de viés, sendo aplicado o Critical Appraisal Checklist for Prevalence Studies do Joanna Briggs Institute (JBI). Aplicou-se metanálise com o software Review Manager 5.3 para as variáveis que estão relacionadas à alteração da modulação autonômica cardíaca. Foram utilizados 15 estudos para a metanálise, todos foram classificados com alta qualidade metodológica (7 a 9 pontos), 13 apresentaram resultados mostrando alteração da modulação autonômica cardíaca em crianças obesas em comparação com crianças eutróficas e apenas dois apresentaram indicativos que refutam essa hipótese. O presente estudo identificou a redução da atividade parassimpática no grupo obeso em relação ao grupo eutrófico através das variáveis trabalhadas. Recomenda-se a utilização das variáveis RMSSD, pNN50 e SDNN em estudos futuros, pois seus resultados foram significativos para esta metanálise.*

Palavras-chave: *Frequência cardíaca; Obesidade pediátrica; Sistema nervoso autônomo.*

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INTRODUCTION

Obesity is a multifactorial disease characterized by excess body fat, generating metabolic, respiratory and locomotor disorders, as well as a risk factor for comorbidities, such as diabetes, cardiovascular diseases, dyslipidemias and some types of cancer[1,2].

Approximately 16% of the world's population of children and adolescents are considered obese[3]. In Brazil, this value reaches 14% for children and 5% for adolescents[4]. The increase in the obesity prevalence in childhood and adolescence is one of the factors responsible for the growing number of diseases of metabolic and cardiovascular causes that affect adults[3,5].

Based on this assumption, some studies have demonstrated the importance of identifying changes that may arise in cardiac autonomic modulation due to obesity early in childhood / adolescence in order to observe the impact of this comorbidity on individuals over time, which may affect the various systems of an organism[6].

Rodriguez-Colon et al.[7] and Tasçilar et al.[8] indicate that childhood obesity may cause greater sympathetic activity and lower parasympathetic activity. However, there are several studies that show results that corroborate this statement and results that refute this statement, such as the study by Ancona et al.[6].

Therefore, the present study sought to perform a systematic review with meta-analysis on cardiac autonomic modulation between obese and non-obese children in order to verify if the results found in studies confirm or contradict the hypothesis of the influence of childhood obesity on the regulation of autonomic modulation in children.

METHODOLOGICAL PROCEDURES

The study consisted of a systematic review with meta-analysis, whose search of articles occurred during the month of April of 2017, was carried out by two researchers in five databases: PubMed, Scielo, Cochrane Library, Virtual Health Library (BVS)/Lilacs and Medline. To find the articles with the characteristics desired for the study, the keywords used were "autonomic nervous system" AND "obese children". There was no determination of the publication period, and therefore, all studies from the beginning of the scientific platform until April 2017 were accepted. There was no determination of the language of studies; however, the terms used allowed the inclusion of articles written in English, Portuguese and Spanish.

All the works found from the above mentioned keywords were read in full, observing first the title, methodology, results and conclusion. For the selection of studies, some criteria were established: the study should present obese group and control group (eutrophic); the sample should be composed of children, but due to some specifications of some studies, adolescents were also included; and the study should contain at least 4 of the heart rate variability indexes.

To assess the methodological quality and risk of bias of studies, the Joanna Briggs Institute Critical Appraisal Checklist for Prevalence Studies (JBI)[9], of the University of Adelaide, Australia (JBI, 2016) was used. This evaluation consists of 9 questions that will compose the final methodological quality score, from 0 to 6 classified as moderate or low quality and from 7 to 9 classified as high quality. The classification indexes were based on the work of Kasten et al.[10].

The 14 indexes observed were: age (years), weight (kg), height (cm), BMI (kg/m^2), rest systolic blood pressure (SBP) and diastolic blood pressure (DBP) (mmHg), mean resting heart rate (HR) (bpm), mean RR interval (iRR) (ms), mean square root of the sum of differences between iRRs (RMSSD) (ms), percentage of adjacent iRRs greater than 50ms (pNN50), Low Frequency (BFu.n.) and High Frequency (AFu.n.) of normalized units, BFu.n./AFu.n. ratio and the standard deviations of iRRs in milliseconds (SDNN).

The low frequency oscillatory components (BFu.n.) reflect the sympathetic activity at the time of recording, and the high frequency components (AFu.n.) show the parasympathetic activity of the recorded period. High HR also demonstrates the sympathetic activity, which consequently rises in the bipedal position. However, high resting HR demonstrates stimulated sympathetic activity[11]. Ancona et al.[6] reported that RMSSD and pNN50 are variables corresponding to the parasympathetic response.

Analysis of R-R intervals (iRR) of successive heart beats recorded under controlled conditions may give us an interpretation of the cardiac vagus-sympathetic modulation and indicate whether or not there are changes in the cardiac autonomic function. The most used measures for heart rate variability are RMSSD and pNN50. They are short-term measures that estimate the variation of the high heart rate and are strongly correlated[12]. Ancona et al.[6] reported that the RMSSD and pNN50 are variables corresponding to the parasympathetic response. The SDNN variable corresponds to sympathetic activity and global variability[13].

The Review Manager 5.3 software (Copenhagen: The Nordic Cochrane Centre) was used, and a fixed-effect analysis was performed on data collected from the selected studies. Florest plots were generated. In order to measure effect size, the global Z effect size test was applied, where 95% confidence interval was used, the results inserted and presented in order to evaluate also heterogeneity, Chi^2 and p> 0.01 and the inconsistency I^2 for each set of data of the studied variables. For the meta-analysis, the following variables were used: RMSSD, iRR, pNN50, HR, BF u.n. and AF u.n., SBP, DBP and SDNN. The significance level stipulated for the meta-analysis was P> 0.01.

RESULTS

Initially, 60 articles were found, 12 were duplicates, 6 were not found with complete content for free and 26 did not meet the pre-established criteria

to compose the study, since they were literature reviews, were not adequate to the aims of the present study or did not have control group composed of eutrophic children. There were 15 articles remaining (Figure 1).

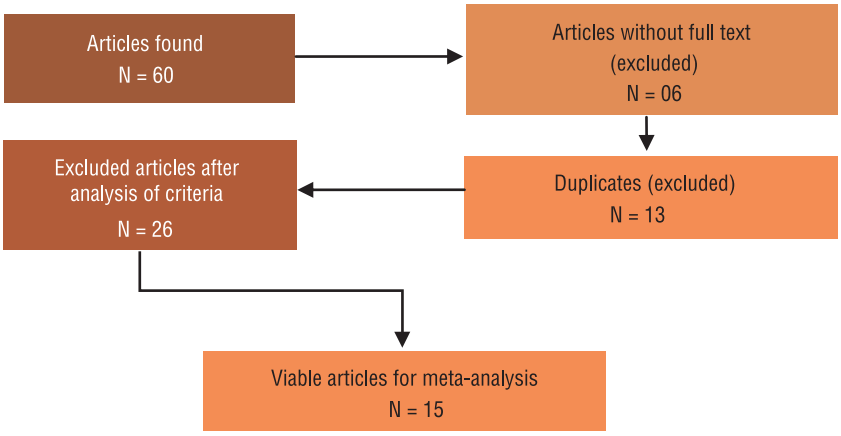

Figure 1. Flowchart of the selection of studies on autonomic modulation in obese and eutrophic children for the systematic review and meta-analysis

In the meta-analysis, the 15 selected articles included 14 indexes of HR variability, each selected article should contain at least four indexes to be introduced in the statistical analysis. Box 1 presents the characterization of these studies and the results found in each study.

Box 1. Description of selected studies for the systematic review of cardiac autonomic modulation in obese and eutrophic children

Author	Title	Sample	Assessed Indexes	Conclusion
Ancona et al.[6]	Heart rate variability in eutrophic and obese children in the supine and bipedal positions	15 obese 15 eutrophic	Anthropometric characteristics, mean iRR (ms), RMSSD (ms), pNN50, BF, AF, mean HR	The cardiac autonomic modulation in situations of controlled rest and in biped position is not influenced by this degree of childhood obesity.
Cozzolino et al. [22]	Cardiac Autonomic Regulation in Response to a Mixed Meal Is Impaired in Obese Children and Adolescents: The Role Played by Insulin Resistance.	33 obese 30 eutrophic (35 obese insulin-resistant patients excluded from the study)*	Anthropometric measurements, BF, AF, mean iRR (ms), RMSSD (ms), pNN50, BF, AF, mean HR	The findings of the present study demonstrate that cardiac autonomic regulation both at rest and in response to mixed meal intake is abnormal in obese children and adolescents, despite the normality of conventional cardiac reflex tests.
Freitas et al. [20]	Cardiac autonomic dysfunction in obese normotensive children and adolescents.	31 obese 35 eutrophic	Anthropometric measures, BF, AF, mean iRR (ms), RMSSD (ms), pNN50, mean HR, SDNN	Obese normotensive children and adolescents present compromised cardiac autonomic control
Kaufman et al. [21]	Relationships of Cardiac Autonomic Function With Metabolic Abnormalities in Childhood Obesity.	16 obese 10 eutrophic (10 overweight excluded from the study)*	Anthropometric measures, BF, AF, mean HR	The present study presents new data indicating that obese children, but not overweight children, are characterized by dysfunction of the cardiac autonomic system compared to normal weight children and that the relationship between the cardiac autonomic system function and leptin, insulin resistance, oxidative stress and inflammation, are mainly mediated by fat mass.
Lira et al. [17]	Influence of vitamin C on cardiac modulation autonomy at rest and during isometric exercise in obese children	21 obese 8 eutrophic	Anthropometric measures, BF, AF, mean HR	Obese children have greater sympathetic activity and lower vagal activity at rest and during isometric exercise when compared to eutrophic children.

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Author	Title	Sample	Assessed Indexes	Conclusion
Latchman et al. [19]	Impaired autonomic function in normotensive obese children.	18 obese 19 eutrophic	Anthropometric measures, BF, AF, mean HR	It presents direct clinical implications of the apparent baroreflex sensitivity regulated in obese children, independently of the fact that they are normotensive, in addition to an unfavorable change in the autonomic modulation.
Lazarova et al. [23]	Baroreflex sensitivity is reduced in obese normotensive children and adolescents.	20 obese 20 eutrophic	Anthropometric measurements, mean iRR (ms)	Baroreflex sensitivity is significantly reduced in obese children and adolescents compared to non-obese controls.
Martini et al. [16]	Heart rate variability in childhood obesity.	32 obese 13 eutrophic	Anthropometric measures, mean iRR (ms), RMSSD (ms), pNN50, mean HR	They suggest that a sympathetic-vagal imbalance, characterized by a primary decrease in parasympathetic activity with relative prevalence of sympathetic activity, is present in pediatric obesity.
Nagai et al. [15]	Autonomic Nervous System Activity and the State and Development of Obesity in Japanese School Children.	42 obese 42 eutrophic	Anthropometric measurements, mean HR	They indicate that childhood obesity is closely related to the reduction of activities of the Sympathetic Nervous System and Parasympathetic Nervous System.
Paschoal et al. [18]	Variability of Heart Rate, Lipids and Physical Ability of Obese and Non-Obese Children	15 obese 15 eutrophic	Anthropometric measures, mean iRR (ms), RMSSD (ms), pNN50, BF, AF, mean FC, SDNN.	Presence of greater cardiac sympathetic activity when in biped position and great reduction of physical capacity documented in incremental effort protocol.
Paschoal and Pereira [11]	Cardiac autonomic modulation in the supine and biped positions in non-obese, obese and morbidly obese children	10 obese 10 eutrophic (10 morbidly obese excluded from the study) *	Anthropometric measures, mean iRR (ms), RMSSD (ms), pNN50, BF, AF, mean HR	There was no significant result that could confirm the interference of childhood obesity on HRV during MPA or during the permanence in the bipedal position.
Rodriguez-Colon et al. [7]	Obesity is associated with impaired cardiac autonomic modulation in children.	91 obese 420 eutrophic	Anthropometric measures, mean HR, RMSSD, SDNN.	Childhood obesity is significantly associated with lower HRV, indicative of sympathetic overflow without opposition to parasympathetic modulation.
Tasçilar et al. [8]	Cardiac Autonomic Functions in Obese Children.	32 obese 30 eutrophic	RMSSD (ms), pNN50, BF, AF, SDNN.	Sympathetic dominance in obese children, which was more significant in the insulin resistant subgroup.
Vanderlei et al. [14]	Geometric Indexes of Heart Rate Variability in Obese and Eutrophic Children	61 obese 72 eutrophic	Anthropometric measurements	They suggest that obese children have autonomic nervous system modifications, characterized by reduction in parasympathetic activity and general variability.
Vanderlei et al.[13]	Analysis of cardiac autonomic modulation in obese and eutrophic children.	56 obese 65 eutrophic	Anthropometric measures, mean iRR (ms), RMSSD (ms), pNN50, BF, AF, SDNN	Obese children presented changes in heart rate variability, characterized by a reduction in sympathetic and parasympathetic activity.

* Studies that contained in addition to the obese and eutrophic groups, the sample relative to another previous group was discarded.

All articles selected presented obese group and control group (eutrophic). Studies included these two groups because they showed the criteria previously mentioned and had the necessary data to acquire information regarding the study objective. Some articles have analyzed cardiac modulation in both bipedal position and supine position. For the present study, only supine position data were included in the meta-analysis.

Studies were submitted to evaluation of methodological quality and risk

of bias, and the "Joanna Briggs" Institute (JBI) Critical Appraisal Checklist for Prevalence Studies was applied. All articles were within the stipulated range of high methodological quality and risk of bias (7 to 9 points) (Box 2). The results show the variables used in the meta-analysis regarding changes in cardiac autonomic modulation in obese and eutrophic children, indicated in the studies of this systematic review.

For the RMSSD variable, nine articles were used, with a total sample of 298 obese children and 613 eutrophic children. $Chi^2 = 6.50$, df = 8 (P = 0.59), $I^2 = 0\%$, Z = 6.00 (P <0.00001) and standardized mean difference -0.46 [-0, 61; -0.31ms] were observed. Low heterogeneity and significant overall effect

Box 2. Evaluation of methodological quality and risk of bias on cardiac autonomic modulation in obese and eutrophic children

(JBI Critical Appraisal Checklist for Prevalence Studies)										
Study	1	2	3	4	5	6	7	8	9	Total (No. S)
Ancona et al. [6]	Y	Y	Y	Y	Y	Y	Y	Y	Y	9
Cozzolino et al. [22]	Y	Y	Y	Y	Y	Y	Y	Y	Y	9
Freitas et al. [20]	Y	Y	Y	Y	Y	Y	Y	Y	Y	9
Kaufman et al. [21]	N	Y	Y	Y	Y	Y	Y	Y	Y	8
Latchman et al. [19]	Y	Y	Y	Y	Y	Y	Y	Y	Y	9
Lazarova et al. [23]	Y	Y	Y	Y	Y	Y	Y	Y	Y	9
Lira et al. [17]	N	Y	N	Y	Y	Y	Y	Y	Y	7
Martini et al. [16]	N	Y	Y	Y	Y	Y	Y	Y	Y	8
Nagai et al. [15]	Y	Y	Y	Y	Y	Y	Y	Y	Y	9
Paschoal et al. [18]	Y	Y	Y	Y	Y	Y	Y	Y	Y	9
Paschoal e Pereira [11]	N	Y	Y	Y	Y	Y	Y	Y	Y	8
Rodriguez-Colon et al. [7]	Y	Y	N	Y	Y	Y	Y	Y	Y	8
Tasçilar et al. [8]	Y	Y	Y	Y	Y	Y	Y	Y	Y	9
Vanderlei et al. [14]	Y	Y	Y	N	Y	Y	Y	Y	Y	8
Vanderlei et al. [13]	Y	Y	Y	Y	Y	Y	Y	Y	Y	9

Responses to criteria: Y = yes; N = No, O = Obscure, NO = Not Applicable. 1. Was the sample representative of the target population? 2. Were the study participants adequately recruited? 3. Was the sample size adequate? 4. Have the individuals studied and the recruitment environment been described in detail? 5. Was the data analysis done with sufficient coverage of the identified sample? 6. Were objective standard criteria used to measure the condition? 7. Was the condition reliably measured? 8. Was the statistical analysis appropriate? 9. Was the response rate adequate, and if not, was the low response rate adequately managed?

Table 1. Variables used in the meta-analysis regarding changes in cardiac autonomic modulation in obese and eutrophic children (RMSSD, rest HR, pNN50 and SDNN).

Root mean square of sum of the differences between the iRR (RMSSD) (ms)								
	Obese Children			Euthophic Children				
Study	Mean	SD	Total	Mean	SD	Total	Weight	Standardized mean difference Fixed, 95% CI
Ancona et al.[6]	50.5	40.1	15	62.08	23.6	15	4.4%	-0.34 [-1.06. 0.38]
Vanderlei et al. [13]	27.45	12.7	56	31.92	10.34	65	17.6%	-0.39 [-0.75. -0.03]
Freitas et al.[20]	56.0	28.0	31	69.0	32.0	35	9.6%	-0.43 [-0.91. 0.06]
Kaufman et al.[21]	63.7	21.5	16	85.8	18.1	10	3.2%	-1.05 [-1.90. -0.21]
Martini et al.[16]	45.8	13.6	32	56.5	15.8	13	5.2%	-0.74 [-1.40. -0.07]

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Paschoal e Pereira[11]	63.3	39.9	10	54.8	28.5	10	3.0%	0.23 [-0.65. 1.12]
Paschoal et al.[18]	64.9	36.9	15	69.9	29.8	15	4.5%	-0.15 [-0.86. 0.57]
Rodriguez-Colon et al.[7]	58.8	30.7	91	77.0	34.5	420	43.6%	-0.54 [-0.77. -0.31]
Tasçilar et al.[8]	73.2	37.4	32	89	45	30	9.1%	-0.38 [-0.88. 0.12]
Total (95% CI)			298			613	100%	-0.46 [-0.61. -0.31]
Heterogeneity: Chi² = 6.50, df = 8 (P = 0.59); I² = 0% Test for overall effect: Z= 6.00 (P < 0.00001)								
Rest Heart Rate (HR)								
	Obese Children			Euthophic Children				
Study	Mean	SD	Total	Mean	SD	Total	Weight	Standardized mean difference IV, Fixed, 95% CI
Ancona et al.[6]	92.8	14.1	15	80.8	8.9	15	4.4%	0.99 [0.23. 1.75]
Cozzolino et al.[22]	71.0	9.0	33	71.0	10.0	30	10.5%	0.00 [-0.49. 0.49]
Freitas et al.[20]	78.0	9.9	31	74.0	11.0	35	10.8%	0.39 [-0.10. 0.88]
Latchman et al.[21]	96.3	12.9	18	78.0	13.1	19	4.8%	1.42 [0.69. 2.15]
Lira et al.[17]	83.0	2.0	21	81.0	1.0	8	3.4%	1.08 [0.22. 1.95]
Martini et al.[16]	77.1	18.1	32	76.0	10.3	13	6.2%	0.07 [-0.58. 0.71]
Nagai et al.[15]	90.7	1.5	42	84.3	1.0	42	3.3%	4.97 [4.09. 5.86]
Paschoal e Pereira[11]	81.6	9.1	10	85.1	9.7	10	3.3%	-0.35 [-1.24. 0.53]
Paschoal et al.[18]	84.6	11.2	15	80.2	7.4	15	4.9%	0.47 [-0.26. 1.20]
Rodriguez-Colon et al.[7]	81.5	7.9	91	76.1	8.0	420	48.4%	0.68 [0.45. 0.91]
Total (95% CI)			308			607	100%	0.70 [0.54. 0.86]
Heterogeneity : Chi² = 114.28. df = 9 (P < 0.00001); I² = 92% Test for overall effect: Z = 8.54 (P < 0.00001)								
Percentage of adjacent iRRs greater than 50ms (pNN50)								
	Obese Children			Euthophic Children				
Study	Mean	SD	Total	Mean	SD	Total	Weight	Standardized mean difference IV, Fixed, 95% CI
Ancona et al.[6]	10.8	11.7	15	17.5	9.2	15	8.0%	-0.62 [-1.35. 0.12]
Vanderlei et al. [13]	9.65	10.14	56	12.08	8.91	65	33.7%	-0.25 [-0.61. 0.10]
Freitas et al.[20]	29.0	21.0	31	43.0	23.0	35	17.6%	-0.63 [-1.12. -0.13]
Martini et al.[16]	20.7	9.6	32	28.0	9.0	13	9.8%	-0.76 [-1.43. -0.09]
Paschoal e Pereira[11]	15.9	11.7	10	12.3	8.3	10	5.5%	0.34 [-0.54. 1.22]
Paschoal et al.[18]	15.7	10.3	15	19.1	8.9	15	8.3%	-0.34 [-1.07. 0.38]
Tasçilar et al. [8]	26.8	16.4	32	34.0	13	30	17.0%	-0.48 [-0.98. 0.03]
Total (95% CI)			191			183	100%	-0.41 [-0.62. -0.20]
Heterogeneity : Chi² = 5.70. df = 6 (P = 0.46); I² = 0% Test for overall effect: Z = 3.87 (P = 0.0001)								
Standard deviations of iRRs in milliseconds (SDNN)								
	Obese Children			Euthophic Children				
Study	Mean	SD	Total	Mean	SD	Total	Weight	Standardized mean difference IV, Fixed, 95% CI
Vanderlei et al. [13]	37.18	26,26	56	42.58	10.48	65	19.8%	-0.28 [-0.64. 0.08]
Freitas et al.[20]	49.0	21,0	31	55.0	21.0	35	10.8%	-0.28 [-0.77. 0.20]
Martini et al.[16]	129.4	27,6	32	149	51.0	13	6.0%	-0.54 [-1.19. 0.12]
Paschoal et al.[18]	64.9	28,7	15	68.6	23.7	15	5.0%	-0.14 [-0.85. 0.58]
Rodriguez-Colon et al. [7]	79.2	25,0	91	98.0	27.0	420	48.1%	-0.70 [-0.93. -0.47]
Tasçilar et al. [8]	137.8	35,1	32	142	29	30	10.3%	-0.13 [-0.63. 0.37]
Total (95% CI)			257			578	100%	-0.48 [-0.64. -0.32]
Heterogeneity: Chi² = 8.32. df = 5 (P = 0.14); I² = 40% Test for overall effect: Z = 5.83 (P < 0.00001)								

* SD: Standard Deviation; CI: Confidence Interval.

in this variable among the selected studies could be identified, showing the reliability of articles for this measurement tool.

The mean iRR variable included seven articles (179 obese children and 173 eutrophic children), and showed Chi^2 = 33.51, df = 6 (P <0.00001), I^2 = 82%, Z = 4.64 (P <0.00001), standardized mean difference -0.52 [-0.75; -0.30], which demonstrated heterogeneity in this variable. For the pNN50 variable, seven articles were analyzed (191 obese children and 183 eutrophic children), Chi^2 = 5.70, df = 6 (P = 0.46), I^2 = 0%, Z = 3.87 (P = 0.0001), standardized mean difference -0.41 [-0.62; -0.20] identifying low heterogeneity.

Resting HR was analyzed in 10 studies (308 obese and 607 eutrophic children), where Chi^2 = 114.28, df = 9 (P <0.00001), I^2 = 92%, Z = 8.54 (P <0.00001), standardized mean difference 0.70 [0.54; 0.86], showing high heterogeneity. The SDNN variable resulted in Chi^2 = 8.32, df = 5 (P = 0.14), I^2 = 40%, Z = 5.83 (P <0.00001), standardized mean difference -0.48 [-0.64; -0.32]. In addition to variables presented in table 1, other variables were submitted to meta-analysis.

The variable related to Low Frequency (BF) in normalized units presented Chi^2 = 53.68, df = 7 (P <0.00001), I^2 = 87%, Z = 3.53 (P = 0.0004), standardized mean difference 0.28 [0.13; 0.44]. The variable that characterizes High Frequency (AF) in normalized units, obtained Chi^2 = 53.83, df = 7 (P <0.00001), I^2 = 87%, Z = 2.60 (P = 0.009), standardized mean difference -0.21 [-0.37; -0.05]. SBP variable presented Chi^2 = 55.21, df = 6 (P <0.00001), I^2 = 89%, Z = 8.08 (P <0.00001), mean standardized difference 0.74 [0.56; 0.92]. The DBP obtained Chi^2 = 43.36, df = 6 (P <0.00001), I^2 = 86%, Z = 3.54 (P = 0.0004), mean standardized difference 0.31 [0.14; 0.49]. SDNN resulted in Chi^2 = 8.32, df = 5 (P = 0.14), I^2 = 40%, Z = 5.83 (P <0.00001), standardized mean difference -0.48 [-0.64; -0.32].

DISCUSSION

The systematic review and meta-analysis aimed to analyze the cardiac autonomic variables of the selected studies, verifying the presence of increased or decreased sympathetic and parasympathetic activity in obese and eutrophic children. Of the 15 selected studies, 13 presented corroborative indications of altered cardiac autonomic modulation in obese children compared to eutrophic children, and only 2 presented results that refute the indication of this hypothesis.

We can observe that two variables, RMSSD and pNN50, the second indicates vagal modulation, may present lower values in obese individuals[6,8,13,16,18,20], both presented heterogeneity indexes of 0% and test for overall (Z) significant effect. The alteration of these two highly correlated variables[12] suggest changes in parasympathetic activity[6,7]. In obese children, RMSSD can undergo a significant progressive reduction[7]. Vanderlei et al.[13] and other authors corroborate this assertion, indicating reduction of parasympathetic activity in the obese group[14-18].

The reduction of parasympathetic and sympathetic activity in children can negatively impact the health of individuals later in adulthood[19]. Nagai et al.[15] indicates that the degree of these autonomic reductions depends on the duration of obesity, regardless of age. Cardiovascular complications and reduction of life expectancy are serious consequences of childhood obesity in the long term[20-23].

Autonomic changes occur both in the time domain and in the frequency domain; the frequency domain parameters may be decreased in early childhood in obese children, specifically when an elevation of the sympathetic nervous system occurs, this could be associated with factors related to insulin resistance in childhood[8].

The SDNN variable presented low heterogeneity (40%), with reduction in the obese group when compared to the eutrophic group[13]. This result shows a decrease in sympathetic activity in the obese group[7]. The mean iRR variable of the obese group was reduced when compared to the eutrophic group[23].

Resting HR had a slight increase, as well as BFu.n. and AFu.n. variables. However, as in the present analysis, only the supine position was verified and the heterogeneity of studies was considered high, which makes it impossible to suggest the interference of childhood obesity in these results. Paschoal et al.[18] and Paschoal and Pereira[11] did not find changes in resting HR in their studies and indicated that the number of samples could have altered the result, since other authors suggest an increase in this variable in the obese group[19]. SBP increased in obese children and DBP did not present significant alterations between groups[18].

Some limitations of the present meta-analysis can be pointed out: aspects such as gender, age, family history, other medical complications, life habits, level of physical activity or stress were not controlled for the analysis of variables. Studies with a discrepant number of samples between groups of interest (obese and eutrophic group) contributed to increase the heterogeneity of six of the nine variables presented (mean iRR, resting HR, BFu.n., AFu.n., SBP and DBP). We also recognize that the indexes evaluated, as well as other indexes, had limitations on their precise measurement. However, there is evidence in studies that suggest that these indexes are adequate to analyze what was proposed in the present work.

The autonomic nervous system actively participates in the homeostatic processes of the human body, being the autonomic suppression a serious problem in adulthood. Although there is no consensus about the relationship between autonomic nervous system and childhood obesity, it could be identified that it can pose serious risks to autonomic functioning, including important metabolic alterations for body homeostasis[15]. Therefore, greater investments in health education are recommended, especially in early childhood, where life habits are beginning to be formed in order to prevent future risks.

CONCLUSION

Reduction in the parasympathetic activity of the obese group in relation

to the eutrophic group could be verified in variables included in this meta-analysis, mainly for values obtained in RMSSD, pNN50, SDNN and resting HR. The use of these four variables in further studies related to this subject is recommended. However, due to the heterogeneity of some variables, more research is needed to address childhood obesity and its interconnection with cardiac autonomic modulation, in the search for a better understanding of the long-term health risks for these individuals.

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