

The impact of infancy antibiotic intake on childhood obesity; review of studies

Abstract

The prevalence of childhood obesity has been grown up since 1990s for about 3% in 2010 both in developed and developing countries. There are several factors impacting childhood weight one of which is antibiotic exposure during infancy. In the current review we aimed to assess the conducted studies regarding this topic. We searched databases such as Medline, EBSCO, Cochrane Library, Scopus with the key words of “infancy antibiotic exposure” and “Childhood obesity” and “antibiotic” and “childhood obesity”. There have been 5 studies conducted on humans, investigating the effect of antibiotic intake before childhood. The studies represented the association between wide spectrum antibiotic and early overweight was significant even after adjustment, however, these results were stronger among boys. The type of the effective antibiotics was wide spectrum in all 5 studies which strengthens the recommendation of narrow spectrum antibiotics for the first line treatment. More studies must be conducted to attain more consistent results.

Keywords: infancy, antibiotic exposure, childhood obesity

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Abbreviations: BMI, body mass index; SAGE, study of asthma genes and the environment; ALSPAC, avon longitudinal study of parents and children; DNBC, danish national birth cohort

Introduction

The prevalence of childhood obesity has been grown up since 1990s for about 3% in 2010 and it is predicted that the same trend will lead to a 9% prevalence which equals 60 million preschool obese children.¹ For all higher concern of childhood obesity and overweight is pointing the developed societies, recent review studies on the epidemiology of early obesity in low income countries such as Sub Saharan Africa, represented that in rural areas with higher socioeconomic status the proportion of obesity and overweight has increased along with the consistent challenge of underweight in this area.²

Several underlying factors have been hypothesized to be effective on obesity in children representing the prominent significance of maternal and infantile health, such as the effect of antibiotic exposure during infancy on childhood obesity and the current study aims to summarize the recent research projects carried out in this area. In spite of the vital therapeutic effect of antibiotics since the 1940s,³ imbalanced prescription in either childhood or adolescence leads to resistance to antibiotics and perturbing the balance between the natural microbiota which improves immune system and have positive effects on metabolism and cell differentiation.⁴ The over-prescription of antibiotics is not equal among countries and in Europe the percentage of prescription modifies from 18% to 55% in 2000 based on the country⁵ and the worldwide antibiotic use has been elevated in the last decades.⁶ Back in 1940s the farmers in USA were adding antibiotics to their animal's food to fatten them for the market not conscientious about the underlying mechanism.⁷

Methods

Our surfing through the medical databases including Medline, EBSCO, Scopus and Cochrane yielded five studies aiming to investigate the effect of antibiotic exposure on childhood obesity.

There is no review study in this area. The total number of studies found with the key words “Infancy antibiotic exposure” and “childhood obesity”, “antibiotic” and “childhood obesity” was 5 studies in PubMed without any particular search limitations for time or article category. As mentioned Cochrane library did not find any review study in this regard. 17 studies of EBSCO were consisting of some unrelated studies, animal studies and the same studies as the mentioned five eligible studies. Two studies of Scopus were repeatedly found in PubMed. Our inclusion criteria for election of the studies were human studies, studies on children intake or prescription of antibiotics and human studies.

Statistics

The general results of the five studies are illustrated in the table. Among the studies five articles were included to be reviewed. All of them studied the topic with a big sample size and the independent variable was intake of wide spectrum antibiotics. Only one study (Bailey) considered the frequency of antibiotic exposure. The obesity determinant was BMI and in SAGE study central obesity was evaluated as well. Two studies adjusted the analysis for gender and represented the significant effect in boys in comparison with girls.

Results

The probable effect of antibiotic exposure on early preadolescence obesity has been investigated in human studies applying various methods and criteria such as the particular time of antibiotic utilizing, the variety of antibiotics, the gender of the studied subjects, etc.

The Canadian study on 616 children participated SAGE survey (Study of Asthma, Genes and the Environment) classified the consumption of wide spectrum antibiotic in the first year of life in 4 sub-groups of zero, one to two, three to four and five or more courses of prescription and the time of first exposure in 3 groups of after the first year, 3-6 or 6-12month and before 3month. According to this study antibiotic exposure was significantly associated with childhood overweight at the age of 9 and 12year old even after adjustment for

confounding variables and it is noteworthy that the association was stronger among boys and the relationship was more significant in the subjects with first exposure in 6-12months or 3-6months.⁸ In other words, the mentioned study found the earlier antibiotic exposure more significant in obesity.

Avon Longitudinal Study of Parents and Children (ALSPAC) cohort study in UK including 11532 infants represented that before 6months prescription of antibiotic leads to higher BMI during 10 to 38months and not in 7year old age, whereas later intake of antibiotic (6-14 and 15-23months) did not demonstrate any significant association with BMI during childhood periods.⁹

Studying a greater sample size, Bailey and coworkers found the significant association of antibiotic utilization in infancy and

preadolescence obesity with 69% of 65480 children who had taken antibiotic during first 23months of their life and the association was more considerable in the case of 4times or more exposures besides earlier exposures. Considerably, the aforementioned study found the antibiotic consumption effective on other obesity risk factors such as male sex, living in better socioeconomic circumstances.¹⁰ A large cross sectional study (ISSAC) on 74946 children between 5-8year old residing in New Zealand, demonstrated that the boys who had taken antibiotics in primary year of their life had higher BMI.¹¹

The Danish study by Ajslev and colleagues (DNBC), included antibiotic administration before 6months of age among the post and pre-natal factors affecting childhood obesity. The follow up of 28364 subjects until 7years yielded the significant association only for boys and not girls after adjustment for other maternal covariates¹² (Table 1).

Table 1 The summary of studies and the differences among the measurement of outcome and exposure Y, year, BMI, body mass index

Study	Sample Size	Exposure time significant	Age of significant outcome	Obesity determinant	Frequency of exposure studied	Gender specific	Significant association
SAGE	616	6-12 or 3-6month	9 and 12y	BMI, Central Obesity	No	No	yes
ALSPAC	11532	Before 6months	10-38months	BMI	No	No	No
Bailey	65480	23month	24-59months	BMI	yes	No	Yes
ISAAC	74946	12months	5-8y	BMI	No	Yes	For boys
DNBC	28364	Before 6months	7y	BMI	No	Yes	For boys

Discussion

Surfing through several databases we found the 5 mentioned studies around the effect of antibiotic exposure on obesity. All of the studies found the association of wide spectrum antibiotics in obese children. None of the assessments reported non-significant association of antibiotic with obesity. However differences related to the gender, time of the stronger relationship and the frequency of prescriptions was visible in outcomes. Generally, the results were consistent with their former ones.

Regarding the gender dependency of the effect of antibiotic use, the majority of the studies found non-significant relationship between antibiotic exposure and obesity in girls, whereas some others (ISAAC & DNBC) only found the relationship stronger in boys and still significant in girls. The mechanism of gender specific effect of antibiotic on obesity is hidden, however, it is probable that the metabolism of antibiotics and the microbiota varieties are not similar in both genders;¹³ on the other hand, the gut microbiota plays role in metabolism of sex steroid hormones resulting in the adjustment of adipose tissue.^{14,15} The male gender is one of the risk factors for obesity¹⁰ and other words some studies investigated the effect of antibiotic on obesity in females and males separately;^{11,12} however the comparison of boys exposed to antibiotic versus non-exposed, represented that the prevalence of obesity in exposed boys was significantly 5times higher.⁸

The effect of antibiotic on obesity was significant not only in BMI but in central obesity which is a better determinant of obesity.⁸ The frequency of antibiotic exposure during infancy is the matter of importance about which, Bailey and coworkers found significant effect in more than 4times of exposure. The mechanism behind the mentioned exposure and outcome is not diagnosed yet. However there are some probable hypotheses that can explain the reason by which

the gut microbial modification of antibiotherapy results in obesity and overweight. The reason to support the hypothesis is that the growth boosting effect of antibiotics has not been observed in microbiota-free animals.^{16,17} Ascribing the aforementioned mechanism to modification of gut microbiota, using remained polysaccharides in colon, fat digestion (production of bile salt hydrolase by Commensal bacteria)^{18,19} and absorption of nutrients conducted by mucosa bacteria,^{20,21} affecting gut hormones and appetite balanced insulin activity.²²

Conclusion

The review of several studies on antibiotic utilization in the primary year of life in relation with childhood obesity have represented consistent results yielded with few differences; such as stronger effect of antibiotic in the first half-year of life⁹ which the authors ascribe to the probable differences in antibiotic variety and method of prescription whether intravenous or oral. In all of the mentioned studies, early exposure to antibiotics was significantly effective on higher prevalence of obesity. Obese girls demonstrated weaker association with antibiotic intake during their infancy, which lost their significance after adjustment for confounding factors effective on childhood obesity versus obese boys. All of the studies investigated the obesity developing effect in wide spectrum antibiotics and recommended the prescription of narrow spectrum antibiotics for the first line treatment.

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Conflict of interest

The author declares no conflict of interest.

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