Vitamin A: the functionality of supplementation for children of all ages

Vitamina A: a funcionalidade da suplementação para crianças de todas as idades

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ABSTRACT
Objective:to analyze scientific production in the search for the best scientific evidence for vitamin A supplementation in children at different growth and development stages. Methodology: This is a systematic literature review that followed the protocol proposed by the Cochrane Center of Brazil. Data collection was performed in Pubmed, Scopus, Cinahl, Web of Science, and Cochrane databases, using the English descriptors, selected Medical Subject Headings (MeSH). Thus, from the 10 selected studies, according to the criteria, their methodological characteristics were analyzed through globally validated instruments and the degree of scientific evidence was identified. Results: As regards the analysis of the results it was evidenced that vitamin A supplementation should be as follows: first analyze the social characteristics of the population, thus defining the nutritional profile; and supplementation should be above the stimulated age, recommending the dosage of vitamin A in growth and development appointments. Conclusion: Studies show the benefit of using vitamin A in populations said to be vulnerable. However, studies show that this practice must be analyzed according to the social vulnerability of each country and region.

Keywords: vitamin A, food supplementation, children.

RESUMO
Objetivo: analisar a produção científica na busca da melhor evidência científica para a suplementação de vitamina A em crianças em diferentes estágios de crescimento e desenvolvimento. Metodologia: Trata-se de uma revisão sistemática da literatura que seguiu o protocolo proposto pelo Centro Cochrane do Brasil. A coleta de dados foi realizada nas bases de dados Pubmed, Scopus, Cinahl, Web of Science e Cochrane, utilizando os descritores em inglês, Medical Subject Headings (MeSH) selecionados. Assim, dos 10 estudos selecionados, de acordo com os critérios, foram analisadas suas características metodológicas por meio de instrumentos validados mundialmente e identificado o grau de evidência científica. Resultados: Com relação à análise dos resultados, evidenciou-se que a suplementação de vitamina A deve ser da seguinte forma: primeiro analisar as características sociais da população, definindo assim o perfil nutricional; e a suplementação deve ser acima da idade estimulada, recomendando a dosagem de vitamina A nas consultas de crescimento e desenvolvimento. Conclusão: Estudos mostram o benefício do uso da vitamina A em populações consideradas vulneráveis. Entretanto,

os estudos mostram que essa prática deve ser analisada de acordo com a vulnerabilidade social de cada país e região.

Palavras-chave: vitamina A, suplementação alimentar, crianças.

1 INTRODUCTION

Vitamin A is characterized by being a fat soluble macromolecule, composed of 20 carbons, which is called retinol. It is an essential nutrient for the proper functioning of metabolic functions, such as vision, growth and development, gene expression, maintenance of cellular epithelial integrity, antioxidant defense, improves immunity and reproduction[1]. In addition to participating as an activation co-enzyme for the absorption of other substances, it participates in the metabolic balance process[2].

The supply of Vitamin A must be through a diversified diet, whether from foods of animal origin, such as liver, egg, milk, tuna and cheese, and in dark green leafy vegetables, yellow-orange and red fruits. Thus, about 90% of this substance is stored in the liver, as well as in other places, between these eyes and lungs[3-4].

Vitamin A deficiency leads to changes in the absorption of some substances, such as iron, reducing its incorporation in red blood cells, which leads to the development of anemia, such as iron deprivation[5]. Another relevant factor is that for a good metabolic activity, this substance must be ingested with Zinc, as deficiency leads to reduced availability of vitamin A, thus requiring a diversified diet, different in some social niches[6].

It is estimated that 250 million children worldwide have some vitamin A deficit, and that 250,000 children are blinded due to deficiency[7]. Supplementation is ableto reduce the risk of death for children aged 6 to 59 months. However, a study developed by the University of the United Kingdom showed that, in addition to blindness, the lack can lead to morbidity and mortality, due to half weight-height growth deficiency, worsening of the immune response and failed antioxidant defense. Inaddition, the study points out that supplementation can exceed the established age, and that health policies must analyze the socioeconomic situation of the geographical area, so that it can thus institute measures[8].

In Brazil, which is one of the most affected countries among the regions of the Americas[9-10], in which the disability mainly affects children of the pre-school age group, between 2 and 6 years old, and thus a global agreement was signed to eradicate the problem. And in 1994, the Ministry of Health of Brazil, through Ordinance No. 2,160, instituted the

program to combat Vitamin A deficiency, intensifying promotion, prevention and protection actions in areas at risk[11].

For example, supplementation should be as follows: From 6 to 11 months 100,000 IU single dose, and from 12 to 59 months, a dose of 200.00 every 6 months[12]. In a study carried out by the University of Mexico, researchers realized that vitamin supplementation should be up to 6 years of age and with serial monitoring of vitamin A up to 8 years, as the justification in which the study population presented a deficit in the retinol, due to several factors, including accessibility to a diversified diet[13].

Another study, it was shown that in addition to supplementation in Brazil being up to 59 months, it is necessary to carry out nutritional monitoring until the end of the school phase, and the beginning of puberty, as in this period of growth and development it is essential to complement food, to meet nutritional needs[14].

Thus, the objective of the study is to analyze scientific productions in the search for the best scientific evidence for vitamin A supplementation in children in different growth and development ranges.

2 METHOD

This is a study of systematic literature review that followed the protocol proposed by the Cochrane Center of Brazil, composed of the following steps: Formulation of the research question, which used the PICO strategy; location and selection of studies; critical evaluation of studies; data collect; analysis and presentation of data; and interpretation of results[15].

In formulating the research question, the PICO strategy was adopted, which is characterized by four important components for the formulation of the research question, being P: participant (patient); I: intervention; C: comparison and O: outcome.However, it is necessary to have the participant item (P) and the intervention (I)[16]. So the question that guided the systematic review study was: what is the time limit for vitamin A supplementation in children?

Data collection took place in the second half of 2019, by two researchers in a paired manner. For Pubmed, Scopus, Cinahl, Web of Science, and Cochrane databases, the following descriptors were used in English, selected Medical Subject Headings (MeSH), which are: Food Supplementation, Vitamin A, Children. In the searches for the Latin American and Caribbean Literature in Health Sciences database (LILACS), the Health Sciences Descriptors (DeCS), Vitamin A, Food supplementation were used. In addition, Boolean operators AND were used in the search strategy in each database

For the selection and inclusion of articles in the systematic review, the following eligibility criteria were adopted, such as: original articles from research published in full, with no language limit published in national and international databases. The exclusion criteria were: articles focused on another population, other than children; not from research.

Thus, through the search strategy, 13 articles were identified in the international and national databases, 25 articles. Soon after, after the selection by the aforementioned criteria, two researchers analyzed the titles and summary, with the intention of filtering the studies that did not collaborate with the objective of this research, only 10 articles made up the final sample. In possession of the pre-selected article bank, an instrument was used to collect data with the respective information, author / year, type of method applied, level of evidence and result.

Soon after cataloging, studies were carried out to analyze, evaluate and study quality through Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) for observational research and the Consolidated Standards of Reporting Trials (CONSORT,) to clinical trial studies; And analysis of the level of evidence through the Grading of Recommendations Assessment, Developing and Evaluation (GRADE), which ranks the quality of evidence in the study as high, moderate, low or very low.

Regarding the analysis by STROBE, it was adopted that each of the 22 criteria obtained a score of 0 - described and 1 - not described. For CONSORT, which consists of 22 items, the score was 0 - not described, 1 - partially described and adequate and 2 - adequate[17-18]. Thus, the score generated per article was transformed into a percentage, and those with a percentage greater than 60%, or considered relevant characteristics in this evaluation process, were considered quality.

3 RESULTS

From the analysis of the sample of selected articles, it is noted that the year of publication was between 2012 and 2017, being distributed as follows: one in the year 2012 and 2013, four in the year 2015, two in 2016 and 2017.In relation to the journals that showed greater prominence in the research, it was the Lancet Magazine with (05).

Table 1 summarizes the information provided by the articles that were included in the systematic review.

Source	Method	Result	Conclusion
01-Katz J, West KP Jr, Khatry SK, Thapa MD, LeClerq SC, Pradhan EK. et al.	A stratified, random sample of 40 wards with 4766 children in Sarlahi district of Nepal was	There were 1871 (84%) surviving children in the vitamin A group and 1711 (85%) in the placebo group examined at follow-up.	Supplementation was effective at reducing the prevalence and incidence of xerophthalmia

	selected to participate in a randomized, controlled, community trial	After adjustment for the baseline prevalence of xerophthalmia, vitamin A reduced the prevalence at follow-up by 63% (95% confidence interval, 21% to 83%).	
02 - Schmitz J, West KP Jr, Khatry SK, Wu L, Leclerq SC, Karna SL, et al.	Follow-up study of adolescents and young adults who, as preschool aged children in 1989, were enrolled into a cluster randomised, double blinded, placebo controlled trial of vitamin A supplementation	Among participants with any ear discharge in early childhood, vitamin A supplementation was associated with a reduced risk of hearing loss, by 42% (0.58, 0.37 to 0.92) compared with controls, after adjusting the confidence interval for the design effect of the original trial.	In undernourished settings, periodic, high dose vitamin A supplementation may reduce the risk of hearing loss associated with purulent ear infections in early childhood
03 - Awasthi S, Peto R, Read S, Clark S, Pande V, Bundy D.	Participants in this cluster-randomised trial were pre-school children in the defined catchment areas of 8338 state-staffed village child-care centres (under-5 population 1 million) in 72 administrative blocks	Estimated compliance with 6-monthly retinol supplements was 86%.	DEVTA contradicts the expectation from other trials that vitamin A supplementation would reduce child mortality by 20-30%, but cannot rule out some more modest effect.
04-Imdad A, Mayo-Wilson E[2], Herzer K[3], Bhutta ZA[4].	In March 2016 we searched CENTRAL, Ovid MEDLINE, Embase, six other databases, and two trials registers. We also checked reference lists and contacted relevant organisations and researchers to identify additional studies.	We identified 47 studies (4 of which are new to this review), involving approximately 1,223,856 children. Studies took place in 19 countries: 30 (63%) in Asia, 16 of these in India; 8 (17%) in Africa; 7 (15%) in Latin America, and 2 (4%) in Australia.	Vitamin A supplementation is associated with a clinically meaningful reduction in morbidity and mortality in children. Therefore, we suggest maintaining the policy of universal supplementation for children under five years of age in populations at risk of VAD.
05-Edmond KM, Newton S, Shannon C, O'Leary M, Hurt L, Thomas G.	This study was a population-based, individually randomised, double-blind, placebo-controlled trial in the BrongAhafo region of Ghana.	We assessed 26,414 livebirths for eligibility between Aug 16, 2010, and Nov 7, 2011. We recruited 22,955 newborn infants, with 11,474 randomly assigned to receive	The results of this trial do not support inclusion of newborn vitamin A supplementation as a child survival strategy in Ghana.

		vitamin A and 11,481 to receive placebo	
06-.Masanja H, Smith ER, Muhihi A, Briegleb C, Mshamu S, Ruben J, et al.	We did an individually randomised, double-blind, placebo-controlled trial of infants born in the Morogoro and Dar es Salaam regions of Tanzania.	We did not find any evidence for a beneficial effect of vitamin A supplementation on mortality in infants at 6 months	Neonatal vitamin A supplementation did not result in any immediate adverse events, but had no beneficial effect on survival in infants in Tanzania
07-Mazumder S, Taneja S, Bhatia K, Yoshida S, Kaur J, Dube B. et al.	We undertook an individually randomised, double-blind, placebo-controlled trial in Haryana, India.	We noted no significant interactions between the intervention effect and sex on mortality at 6 months (p=0·409).	The findings of this study, done in a population in which vitamin A deficiency is a moderate public health problem, are consistent with a modest reduction in mortality between supplementation and 6 months of age
08-Gogia S, Sachdev HS.	Randomised or quasi-randomised or cluster randomised, placebo controlled trials evaluating the effect of prophylactic	The six included trials were from developing countries. There was no convincing evidence of a reduced risk of mortality during infancy	here is no convincing evidence of a reduced risk of mortality and possibly morbidity or of increased early adverse effects after neonatal supplementation with vitamin A
09-Elemraid MA, Mackenzie IJ, Fraser WD, Harper G, Faragher B, Atef Z	A case-control study of 75 children with CSOM and 74 healthy controls.	Cases had lower mean Z-scores for weight-for-age, weight-for-height, body mass index and mid-upper arm circumference (MUAC) (all P<0.05), and lower mean concentrations of serum Zn.	Children with CSOM were more undernourished than controls with lower mean serum Zn, Se and calcium concentrations. Vitamin D-deficient and iron-replete children had longer duration of infection, although this association was lost with age adjustment.
10- Unal M, Oztürk C, Aslan G, Aydin O, Görür K.	Experimental maxillary sinusitis in rabbits was induced by blocking the left noses and direct inoculation of Staphylococcus aureus into the left maxillary sinuse cavities	All of the infected sinuses displayed various degrees of inflammation but there was no statistically significant difference between the study and control groups	The adjuctive therapeutic role of vitamin A in acute sinusitis was found doubtful but this topic is worth to investigate more comprehensively.

Source: Pubmed, Scopus, Cinahl, Web of Science, e Cochrane

Regarding the analysis of the results, it was shown that the supplementation of Vitamin A must be as follows: first analyze the social characteristics of the population, thus defining the nutritional profile; and supplementation should be over the stimulated age, recommending the dosage of vitamin A in growth and development consultations

4 DISCUSSION

The present investigation provides a dimension on the relevance of Vitamin A supplementation in children's survival and in reducing the rate of morbidity and mortality. For the World Health Organization (WHO) the recommendation is that the practice of supplementation should be between 6 to 59 months, but a multicenter study developed in some cities like Nepal, states that the practice must be based on the identification of social variables , that is, the condition of food assistance, income, accessibility to health services. And so he recommends that the dose of Vitamin A should exceed 59 months and reach the school stage[19].

In another study, which has high scientific evidence, instituting a randomized, double-blind, controlled clinical trial, developed in the city of Neovita, India, performed early supplementation in neonates, in which supplementation with 50,000 IU of vitamin A in the first few 72 hours of life was generally safe and well tolerated, with the exception of a small excess risk of protruding fontanelle[20].

In addition, the findings of this study, carried out in a population in which vitamin A deficiency is a moderate public health problem, are consistent with a modest reduction in mortality between supplementation and 6 months of age. These findings should be seen in conjunction with similar trials in other populations, to allow the determination of appropriate public health policies[20].

Already under study, with a moderate level of evidence, developed in North India, in which vitamin A deficiency is common in preschool children, the objective was to assess whether periodic vitamin A supplementation based on plasma retinol dosage, in which the dose was calculated from this indicator, the research proposal was that the vitamin A correction should be based on the dosage found. And, it was observed that such practice leads to a reduction in mortality indirectly[21].

In summary, it is clear from the results of the studies that vitamin supplementation should be put into practice early and that it is regularly monitored by health professionals, and that vitamin deficiency in the country may be related to the processes structural aspects of society and the immediate environment of the child, not the individual. Thus, the control of this nutritional deficiency, which still persists as a moderate public health problem, requires investments not only in the health area, but also in other segments[22].

5 CONCLUSION

Studies show the benefit of using vitamin A in populations said to be vulnerable. However, studies show that this practice must be analyzed according to the social vulnerability

of each country and region. In addition, the study was intended to contribute to national and international literature on the practice of vitamin A supplementation and that these results may serve as a basis for further studies. As well, it can directly contribute to the decision making, of health professionals, and generating the best evidence.

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