Plasma retinol-binding protein predicts plasma retinol concentration in both infected and uninfected Cameroonian women and children.

Engle-Stone R, Haskell MJ, Ndjebayi AO, Nankap M, Peerson JM, Erhardt JG, Gimou M-M, Brown KH. J Nutr 141: 2233-41, 2011.

Introduction

Accurate and robust indicators of vitamin A (VA) status are needed to assess the risk of vitamin A deficiency in populations, and to evaluate the impact of VA interventions. Serum or plasma retinol concentration is recommended by the World Health Organization for population-level assessment of VA status [WHO, 1996], but measurement of retinol can be costly and samples must be collected and processed carefully to avoid degradation of retinol. Retinol-binding protein (RBP), which is the primary carrier of retinol in blood, can be used as an alternative indicator of VA status [Erhardt, 2004], and RBP is less costly to measure and less sensitive to specimen handling conditions. However, consensus is lacking on the RBP cutoffs that are indicative of VA deficiency, which complicates the interpretation of RBP concentrations. Additionally, the relationship between plasma retinol and RBP concentrations may vary by factors, such as VA status, presence of infection, obesity, and others, which could affect the comparability of retinol and RBP cutoffs used to define VA deficiency.

The authors of the study reviewed in this month's edition of Nutrition News for Africa compared plasma retinol and RBP concentrations in a sub-sample of women and children who were included in a nationally representative sample survey in Cameroon. Specifically, the authors assessed whether selected factors affected the relationship between plasma retinol and RBP concentrations, and they derived new deficiency cutoffs for plasma RBP concentration that are equivalent to the commonly used plasma retinol cutoffs of 0.70 and 1.05 µmol/L for VA deficiency and VA depletion, respectively.

Methods

RBP was measured by ELISA in plasma samples from women 15-49 years of age (n=872) and children 12-59 months of age (n=838), who were included in a nationally-representative, cross-sectional, cluster survey of in the Republic of Cameroon [HKI, 2011]. C-reactive protein (CRP) and alpha-1-acid-glycoprotein (AGP) were also measured as indicators of infection, which can temporarily lower both plasma retinol and RBP concentrations. In a randomly selected subset of women (n=80) and children (n=83), plasma retinol was measured by HPLC. The investigators also selected additional samples from specific population sub-groups of interest (obese women, women with elevated acute phase proteins, and older children aged 3-4 y (n=41 women; n=40 children) to assess whether these factors affected the relationship between retinol and RBP.

Results and conclusions

Plasma retinol and RBP concentrations were highly correlated with each other, both among women ($r=0.94$; $p<0.001$) and children ($r=0.96$; $p<0.001$); and RBP showed excellent ability to predict low plasma retinol concentrations. However, plasma RBP concentrations were consistently higher than plasma retinol concentrations; therefore, new cutoffs for RBP were derived using regression analysis. The

derived cutoffs were 1.17 µmol/L for women (equivalent to plasma retinol <1.05 µmol/L) and 0.83 µmol/L for children (equivalent to plasma retinol <0.70 µmol/L). The sensitivity and specificity of these cutoffs for predicting low plasma retinol concentrations were high: 82% and 93% for women and 95% and 89% for children, respectively.

Among women, physiological status (i.e., whether the woman was pregnant, lactating, or non-pregnant, non-lactating) altered the relationship between plasma RBP and retinol. However, using specific cutoffs for each category of women did not improve sensitivity or specificity, as compared to using a single RBP cutoff for all women. Elevated CRP and AGP, VA status, obesity and age did not affect the relationship between RBP and retinol in women.

Among children, child age altered the relationship between plasma RBP and retinol, but using age-specific cutoffs for children did not improve the sensitivity or specificity for predicting low plasma retinol concentrations. Elevated CRP and AGP, VA status, and stunting did not affect the relationship between RBP and retinol in children.

Adjusting retinol and RBP concentrations for elevated acute phase proteins (or excluding individuals with elevated acute phase proteins) did not affect sensitivity and specificity. Using the derived RBP cutoffs, the infection-adjusted national prevalence of VAD in Cameroon was 21.9% among women (plasma RBP <1.17 µmol/L) and 35.0% among children (plasma RBP <0.83 µmol/L).

Program and Policy Implications

The results of this study show that plasma RBP can be used in place of plasma retinol to assess population VA status in large surveys. Moreover, the relationship between plasma RBP and retinol concentrations was not affected by VA status, or the presence of infection, obesity (in women), or stunting (in children). More research is needed in different settings to determine whether these results are population-specific, especially with regard to pregnant and lactating women, obese women, and children of different age groups. In any case, the use of specific cutoffs for these population sub-groups did not improve the predictive capacity of RBP in the Cameroonian population.

RBP has a number of potential advantages over plasma retinol for large surveys, including lower susceptibility to degradation under field conditions, such as light and heat, smaller required sample volume, and generally lower cost of analysis. However, in the absence of recommended RBP cutoffs to indicate VA deficiency, it may be advisable to measure retinol in a subset of the study sample to derive population-specific RBP cutoffs. Also, although CRP and AGP did not affect the relationship between RBP and retinol, both RBP and retinol decrease transiently in the presence of infection. Thus, indicators of infection (such as CRP and AGP) should be measured concurrently to permit correct interpretation of both RBP and retinol concentrations in populations with a high prevalence of infection.

NNA Editors' comments*

Studies such as this are important to facilitate comparison of results across studies that use different indicators of nutritional status, and to harmonize global data on the prevalence of micronutrient deficiency. RBP is a useful indicator of population VA status, and RBP has several advantages over plasma retinol for large surveys. However, consensus is still needed on the appropriate RBP cutoffs to use for determining the presence of VA deficiency and comparing the results of VA status assessment surveys in different countries and over time.

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* These comments have been added by the editorial team and are not part of the cited publication.

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