Austin Journal of Nutrition and Food Sciences

Open Access

Austin Publishing Group

Perspective

Recommended use of Cut-off Folate Concentrations in Serum and Erythrocyte (Red Blood Cell) as Expressed by Folic Acid Equivalent for the Diagnosis of Deficiency in Deliberating the Creation of Dietary Reference Intakes

Ihara H[1]*, Hirota K[2], Watanabe T[3], Totani M[4], Hashizume N[5], Aoki Y[6], Nagamura Y[7], Kamioka K[8], Onda K[8], Sunahara S[8], Suzuki T[9], Itabashi M[9], Ishibashi M[10], Ito S[11], Ohashi K[12], Ohta Y[13], Nobori T[14], Fujishiro K[15], Maekawa M[16], Miura M[17], Miyano H[18], Ando T[18] and Nishimura K[19]

[1]Faculty of Science, Toho University/Faculty of Risk and Crisis Management, Chiba Institute of Science, Japan
[2]Information Center, National Institute of Health and Nutrition, Japan
[3]Department of Dietary Environment Analysis, University of Hyogo, Japan
[4]Graduate School of Human Life Science, Showa Women's University, Japan
[5]Department of Health and Nutrition, University of Human Arts and Sciences, Japan
[6]Kanagawa Health Service Association, Japan
[7]Department of Clinical Nutrition, Suzuka University of Medical Science, Japan
[8]LSI Medience Corporation, Japan
[9]SRL, Inc., Japan
[10]Department of Laboratory Medicine, New Tokyo Hospital, Japan
[11]Department of Clinical Laboratory Sciences, Nitobe Bunka College, Japan
[12]Department of Clinical Chemistry, Fujita Health University, Japan
[13]Department of Chemistry, Fujita Health University, Japan
[14]Department of Molecular and Laboratory Medicine, Mie University Graduate School of Medicine, Japan
[15]Kyowa Medex Co., Ltd., Japan
[16]Department of Laboratory Medicine, Hamamatsu University School of Medicine, Japan
[17]Faculty of Pharmaceutical Sciences, Hokuriku University, Japan
[18]Ajinomoto Co., Inc., Japan
[19]Beckman Coulter Japan Co., Japan

***Corresponding author:** Hiroshi Ihara, Faculty of Science, Toho University, 2-2-1 Miyama, Funabashi, Chiba 274-8510, Japan/Faculty of Risk and Crisis Management, Chiba Institute of Science, 15-8 Shiomi, Choshi, Chiba 288-0025, Japan, Email: ihara@med.toho-u.ac.jp/cyber_ihara@yahoo.co.jp

Received: January 07, 2015; **Accepted:** January 19, 2015; **Published:** January 19, 2015

Dietary Reference Intakes (DRIs) for folate in the US, Canada and Japan have been decided based on the dietary amounts of folate in populations in whom erythrocyte (Red Blood Cell: RBC) folate concentrations were higher than the cutoff value of 300 nmol/L (mass concentration of 140 ng/mL). This mass concentration was expressed as equivalent to 5-methyltetrahydrofolate.

We read an interesting new WHO technical consultation on folate and vitamin B_{12} deficiencies [1] describing cutoff values that indicated deficiency. The cutoff values were < 10 nmol/L (4 ng/mL) for serum folate, < 340 nmol/L (151 ng/mL) for RBC folate, and < 150 pmol/L (203 pg/mL) for plasma vitamin B_{12}. These values were the lowest concentrations of serum and RBC folate capable of repressing an exponential increase in plasma homocysteine, and of serum vitamin B_{12} capable of repressing an exponential increase in serum methylmalonic acid [2]. We created Dietary Reference Intakes (DRIs) for folate in Japan in 2000 [3] with the use of a previous cutoff value from WHO that indicated 7 nmol/L (3 ng/mL) of serum folate for deficiency [4]. The DRIs created were revised in 2010 with the use of RBC folate (300 nmol/L; 138 ng/mL rounded to 140 ng/mL) obtained from US and Canadian DRIs [5].

Upon closer reading of WHO technical consultation, we realized that both the cutoff mass concentrations for serum and RBC folate were expressed as equivalent to folic acid (FA: molecular mass of 441.40 Da). In the US and Canadian DRIs, however, the mass concentration of RBC folate was expressed as equivalent to 5-methyltetrahydrofolate (5-MTHF: molecular mass of 459.46 Da). In our previous study [6] as well as other studies [7-9], the mass concentrations of serum folate were permitted to be expressed as equivalent to FA for the international standardization of serum folate measurement.

For the standardization of RBC folate measurement, WHO developed a new standard (IS 03/178) in 2006 [7,8], and its assigned values were determined by the Reference Measurement Procedure (RMP) using a Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS). Since IS 03/178 could be used as a calibration material for both measurements of serum and RBC folate, WHO proposed a way to use IS 03/170 independently from their previous international standard for RBC folate (IS 95/528) [10]. The IS 95/528 had an assigned value of the mass concentration for RBC folate, but the molar concentration related to FA or 5-MTHF was not defined. Furthermore, its mass concentration was a mean value (e.g., consensus value) calculated from data collected from 13 laboratories employing different methods and different standards comprised of 5-MTHF and/or FA.

Nowadays, both serum and RBC folate are determined by automated methods; however, the assay values of serum total folate (the sum of all folate vitamers including 5-MTHF and FA) in not all

Citation: Ihara H, Hirota K, Watanabe T, Totani M, Hashizume N, Aoki Y, et al. Recommended use of Cut-off Folate Concentrations in Serum and Erythrocyte (Red Blood Cell) as Expressed by Folic Acid Equivalent for the Diagnosis of Deficiency in Deliberating the Creation of Dietary Reference Intakes. Austin J Nutri Food Sci. 2015;3(1): 1055.

of the automated methods, are expressed as equivalent to FA as we previously reported [6]. While, the assay values of RBC folate in the automated methods (some of which used IS 95/528 as a calibrator) were not clearly disclosed by the manufacturers, whether they are expressed as equivalent to FA or 5-MTHF. When 340 nmol/L of RBC folate is expressed as equivalent to FA and 5-MTHF, its mass concentrations related to FA and 5-MTHF are calculated to be 150 and 156 ng/mL, respectively. Even using mass concentration of either FA or 5-MTHF bias was negligibly small in the nutritional assessment, but was considerably different in deliberating the creation of DRIs. Therefore, in the US and Canadian DRIs, as well as in the Japanese DRIs, we recommend that the FA equivalent mass concentrations for serum and RBC folate be used as measured by the automated methods related to IS 03/178 (not IS 95/528).

References

1. Conclusion of a WHO technical consultation on folate and vitamin B_{12} deficiencies. Food Nutr Bull 2008; 29: 238–244.
2. Selhub J, Jacques PF, Dallal G, Choumenkovitch S, Rogers G. The use of blood concentrations of vitamins and their respective functional indicators to define folate and vitamin B_{12} status. Food Nutr Bull. 2008; 29: 67-73.
3. Shibata K, Fukuwatari T, Imai E, Takashi Hayakawa, Fumio Watanabe, Hidemi Takimoto, et al. Dietary Reference Intakes for Japanese 2010: Water-soluble vitamins. J Nutr Sci Vitaminol. 2013; 59: 67-82.
4. Nutritional anaemias. Report of a WHO scientific group. World Health Organ Tech Rep Ser. 1968; 405: 5-37.
5. Institute of Medicine of the National Academies of Science. Dietary reference intakes for thiamine, riboflavin, niacin, vitamin B_6, folate, vitamin B_{12}, panthotenic acid, biotine and choline. Washington, DC: National Academies Press. 1998.
6. Ihara H, Watanabe T, Hashizume N, Totani M, Kamioka K, Onda K, et al. Commutability of National Institute of Standards and Technology standard reference material 1955 homocysteine and folate in frozen human serum for total folate with automated assays. Ann Clin Biochem. 2010; 47: 541-548.
7. Thorpe SJ, Heath A, Blackmore S, Lee A, Hamilton M, O'broin S, et al. Second international standard for vitamin B_{12} and first international standard serum folate. Corrected and Updated Report of the International Collaborative Study to Evaluate a Batch of Lyophilised Serum for B_{12} and Folate Content. WHO/BS/06, 2052. 2006.
8. Thorpe SJ, Heath A, Blackmore S, Lee A, Hamilton M, O'broin S, et al. International standard for serum vitamin B_{12} and serum folate: international collaborative study to evaluate a batch of lyophilised serum for B_{12} and folate content. Clin Chem Lab Med. 2007; 45: 380–386.
9. Satterfield MB, Sniegoski LT, Sharpless KE, Welch MJ, Hornikova A, Zhang NF, et al. Development of a new standard reference material: SRM 1955 (homocysteine and folate in human serum). Anal Bioanal Chem. 2006; 385: 612-622.
10. Thorpe SJ, Sands D, Heath AB, Hamilton MS, Blackmore S, Barrowcliffe T. An International Standard for whole blood folate: evaluation of a lyophilised haemolysate in an international collaborative study. Clin Chem Lab Med. 2004; 42: 533-539.

Austin J Nutri Food Sci - Volume 3 Issue 1- 2015
ISSN : 2381-8980 | www.austinpublishinggroup.com

Citation: Ihara H, Hirota K, Watanabe T, Totani M, Hashizume N, Aoki Y, et al. Recommended use of Cut-off Folate Concentrations in Serum and Erythrocyte (Red Blood Cell) as Expressed by Folic Acid Equivalent for the Diagnosis of Deficiency in Deliberating the Creation of Dietary Reference Intakes. Austin J Nutri Food Sci. 2015;3(1): 1055.