Plasma and erythrocyte Magnesium Levels in a French Population

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Zusammenfassung

Plasma- und Erythrozyten-Mg wurden bei 971 Blutspendern im Alter von 18 bis 60 Jahren mittels AAS bestimmt. Beide Parameter wiesen eine *Gauß*sehe Verteilung auf. Die arithmetischen Mittelwerte (±Standardabweichung) betrugen 0.80±0.06 mmol (Plasma) und 2.11± 0.24 mmol (Erythrozyten). Die mittleren Konzentrationen lagen bei Männern jeweils über denen der Frauen. Die Ergebnisse zeigen bei beiden Geschlechtern eine signifikante Korrelation zwischen Plasma- und Erythrozyten-Mg sowie jeweils altersbezogene Unterschiede. Die Meßergebnisse liegen in derselben Größenordnung, die von anderen Autoren gefunden wurde; dennoch wurden kürzlich höhere Werte bei gesunden Kontrollen in Frankreich gemessen. In zukünftigen Studien sollten exakt die Kriterien definiert werden, die der Auswahl normaler Kontrollpersonen zugrundegelegt wurden.

Summary

Plasma and RBC Mg levels were determined by AAS in 971 blood donors aged 18 to 60 years. The distribution of values for the Mg concentration in the plasma and RBC is gaussian. The means (±SD) of plasma and RBC Mg of the total population are 0.80±0.06 and 2.11±0.24 mM respectively. The mean levels of plasma and RBC Mg for men were significantly greater than the mean levels for women. The results indicate a significant correlation between plasma and RBC Mg in both sexes and age related differences in plasma and RBC Mg. Our results concerning plasma and RBC Mg correspond to the range given by previous authors; however higher values have been previously reported in healthy controls in France. Future studies concerning reference intervals for Mg have to define preeisely the criteria for selecting normal suhjects.

Résumé

Les valeurs du Mg plasmatique et érythrocytaire ont été déterminées par spectrophotometric d'absorption atomique chez 971 donneurs de sang âgés de 18 à 60 ans. Les distributions des valeurs du Mg plasmatique et erythrocytaire sont gaussiennes. Les valeurs moyennes (±SD) du Mg plasmatique et erythrocytaire sont respectivement de 0,80±0.06 et 2.11±0.24 mM. Les valeurs moyennes du Mg plasmatique et erythrocytaire chez l'homme sont significativement plus élevées que chez les femmes. Les résultats indiquent une corrélation significative entre les valeurs du Mg plasmatique et erythrocytaire et des différences en fonction de l'âge. Ces résultats sont en accord avec des études précédentes, cependant des sujets français en bonne santé présentaient des valeurs nettement plus élevées. Il serait nécessaire de définir de façon précise les critères permettant de sélectionner des sujets normaux si l'on veut établir les intervalles de référence pour les valeurs du Mg plasmatique et erythrocytaire.

Introduction

A considerable amount of data has been reported on the roles of magnesium on cellular processes and magnesium deficiency has been implicated as a factor in a number of diseases [3, 13, 14], in neuromuscular and psychological disorders, cardiovascular diseases and diabetes mellitus. The magnesium concentration in plasma and red blood cell (RBC) has been used clinically to assess the magnesium status of patients [3]. However interpretation of clinical chemical results depends in large part on the use of reference intervals in a population. Various blood Mg levels have been reported in population from different countries [3, 10, 11, 12, 18] reflecting genetic differences and mesologic factors. However, few studies are currently available concerning reference values for plasma and RBC Mg in french population [3, 11]. In addition age and sex are important variable to take into account in interpreting biological [11, 12] data and only few studies have a large enough sample size to compare trends in different age groups in both sexes.

Material and Methods

Plasma and RBC Mg were determined on 971 blood donors [Fig. 1] aged 18–60 years, all residents of the Clermont-Ferrand area in France. They included

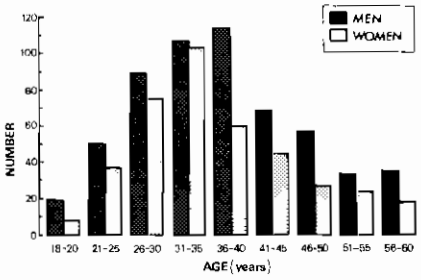

Fig. 1: Number of subjects in each age group.

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587 men (37.6 ± 9.7 years) and 384 women (36.0 ± 7.8 years). The criteria for selecting blood donors were as following, no past diseases characterized by lasting sequels, no concomitant diseases, no alcohol or drug abuse.
Blood sampling was done at the beginning of summer during a period of 15 days. Samples were collected from donors after breakfast, at their place of work between 10 and 12 a.m. Blood samples were collected into tubes containing heparin and centrifuged (2000 × g, 15 min) at 4° C. Plasma was diluted 50 fold with a 1.17 g/l solution of lanthanum chloride. After separating the plasma, we carefully removed the buffy coat then washed the erythrocytes twice in saline solution (0.9 % NaCl). Erythrocytes were lysed 10 fold with de-ionized water and diluted 20 fold with lanthanum chloride solution.
Plasma and RBC Mg were measured by atomic absorption spectrometry (Perkin Elmer 420) in duplicate. All samples were measured in a one large serie at the end of the protocol.
Statistics: Asymetry and linearity test were applied to determine the normality of the population. The male and female population were compared by analysis of variance and the "F-test". Correlations between plasma Mg and RBC Mg and influence of age and sex were studied by regression analysis. Student's t-test was used for comparing the means [15].

Results

Fig. 2 and 3 indicate the frequencies of distribution of plasma and RBC Mg in each group (total population, men and women). The coefficients of skewness and kurtosis listed in the figure indicate the gaussian distribution of plasma and RBC Mg. The arith-

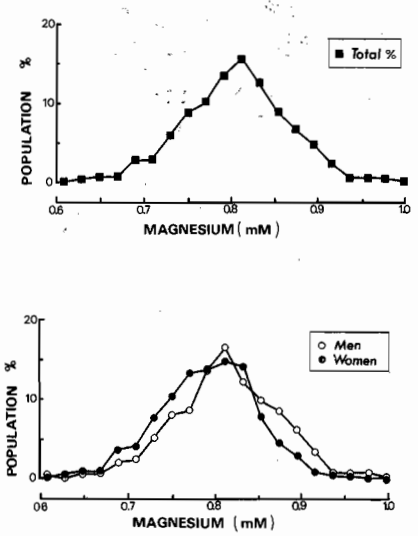

Fig. 2: Distributions of concentrations of magnesium in plasma of total, men and women populations.

	Coefficient of skewness	Coefficient of kurtosis
Total	−0.149	0.267
Men	−0.171	0.362
Women	−0.229	0.090

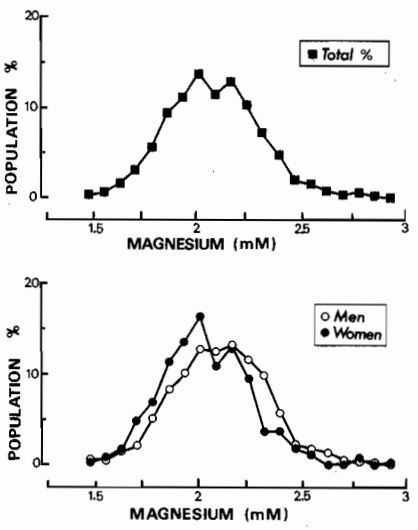

Fig. 3: Distributions of concentrations of magnesium in RBC of total, men and women populations.

	Coefficient of skewness	Coefficient of kurtosis
Total	0.232	0.150
Men	0.166	0.122
Women	0.315	0.343

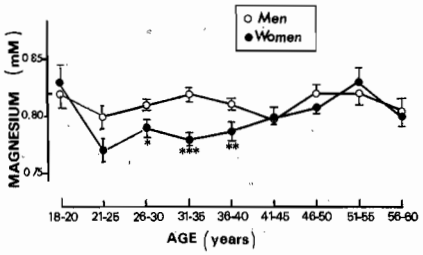

Fig. 4: Distribution of means (±SEM) for plasma concentration of magnesium with age.
*P<0.05; **P<0.01; ***P<0.001

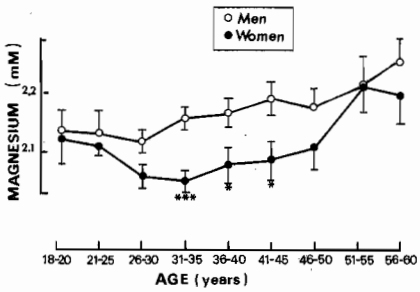

Fig. 5: Distribution of means (±SEM) for RBC concentration of magnesium with age.
*P<0.05; ***P<0.001

Tab. 1: Reference intervals for plasma and RBC magnesium

	Total population	Men	Women
Number	971	587	384
Plasma Mg *(mM)*	0.69 − 0.92 (0.80 ± 0.06) [a]	0.69 − 0.93 (0.81 ± 0.06)	0.68 − 0.90 (0.79 ± 0.06)**
RBC Mg *(mM)*	1.64 − 2.58 (2.11 ± 0.24)	1.67 − 2.62 (2.14 ± 0.24)	1.62 − 2.52 (2.07 ± 0.23)**

[a] (means ± SD). Significant difference between men and women.
** p < 0.01

Tab. 2: Regression equations for plasma and RBC Mg

Men	RBC Mg (y) = 0.003 x + 2.034 [a]	(r = 0.14; P < 0.01)
Women	Plasma Mg (y) = 0.001 x + 0.757 [a]	(r = 0.16; P < 0.01)
	RBC Mg (y) = 0.003 x + 1.953	(r = 0.14; P < 0.01)
Total	y = 0.023 x + 0.686 [b]	(r = 0.22; P < 0.01)
Men	y = 0.024 x + 0.684 [b]	(r = 0.23; P < 0.01)
Women	y = 0.014 x + 0.718 [b]	(r = 0.14; P < 0.01)

[a] Regression equations for plasma or RBC Mg (y) and age (x)
[b] Regression equations for plasma Mg (y) and RBC Mg (x)

metic means ± SD of plasma and RBC Mg of the total population are 0.80 ± 0.06 and 2.11 ± 0.24 mM respectively. The distribution of plasma and RBC Mg for men and women were found to differ statistically. The mean levels of plasma Mg and RBC Mg for men were significantly greater than the mean levels for women ($P < 0.01$) (Tab. 1).

Our results also indicate a significant correlation between plasma and RBC Mg in both sexes and age related differences in plasma and RBC Mg (Tab. 2). Fig. 4 and Fig. 5 indicate the distribution of means for plasma and RBC magnesium with age. The mean plasma Mg remains stable in men from 18 to 60 years whereas in women, plasma Mg shows a slight decrease from 18 to 21 – 25 years ($p < 0.05$); then plasma Mg levels increase slightly with age. From 21 to 40 years, women show plasma values which are lower than in men (Fig. 4). The mean RBC Mg in men increases slightly with age. In women, the RBC Mg shows a decrease from 18 to 26 – 30 years whereas an increase in RBC Mg was found after 40 – 50 years. Women show RBC values which are lower than in men from 26 to 50 years (Fig. 5).

Discussion

The majority of the data for Mg status is based upon serum or plasma and RBC concentration. These parameters probably have clinical utility even if plasma and RBC Mg concentrations have been shown to be poor indicators of intracellular Mg concentration (4 – 5). Our results confirm that the distribution of values for the Mg concentration in the plasma and RBC of normal people is gaussian. In hospitalized patients however, it is non gaussian and shows a broader ranges of values than in healthy people [19]. Our values satisfy the criteria required for comparison of male and female distribution of plasma and RBC Mg. It has been previously documented that the Mg concentration in plasma [7, 10, 11, 12] and RBC [10, 11] is less in women than in men. The differences in mean values for men or women when expressed as a percentage of our reference interval are 8.9 % for plasma Mg and 7.9 % for RBC Mg. The use of a separate reference interval for men and women should therefore be considered.

Our results also indicate age related differences in plasma and RBC Mg. In men, *Henrotte* et al. [11] show a decline of plasma Mg with age form 25 to 58 years while our results show little variations in agreement with previous studies in American men [12]. The present study indicates a slight decline of plasma Mg in women before 25 years. Then, plasma Mg levels increase slightly with age. These modifications correspond to results obtained in American women [12]. However differences between mean plasma Mg values with age are small. The maximum change in the mean plasma Mg value with age represent 2 % of the difference between the upper and lower limits of the reference range in men and 6 % in women. The mean concentrations of RBC Mg increase slightly with increasing age in men. This effect has not been previously reported [11]. The existence of two variable factors of RBC Mg in women, one being linked with age and the other with menopause have been previously demonstrated [11]. *Henrotte* et al. [11] indicate a decline from 18 to 25 years, and an increase after 25 years. A further increase in RBC Mg was found in women after menopause. However in our study, the maximum changes in the mean RBC Mg value with age are small and represent 3 % of the difference between upper and lower limits of the reference range in men and 4 % in women.

Significant correlations between plasma Mg and RBC Mg were found in both sexes. It has been previously recognized that correlation between plasma Mg and RBC Mg is small or inexistant [1]. It is well known that plasma Mg and RBC Mg depend as much on mesologic factors as on genetic factors [8]. These genetic factors account for a major part of the variability of both RBC Mg and plasma Mg.

Our results concerning plasma and RBC Mg correspond to the range given by previous authors in France [1, 10, 11, 16, 17], Israel [18] or USA [12]. However, *Durlach* [3], in France, found highest values. In this study [3], the normal levels of plasma and erythrocyte Mg are very close to 0.9 and 2.3 mmol/L and hypomagnesemia begins at 0.8 and 1.8 mmol/L respectively. In trying to explain these differences, consistent higher mean Mg values may be due to criteria for selecting normal subjects. The individual showing latent tetany or any pathology, any history of morbidity and any treatment capable of disturbing Mg metabolism have been exclued in the control group of *Durlach* [3]. In the present experiment and in other studies, blood donors and apparently healthy people may include among them a large proportion of individual with latent tetany which may reduce somewhat the average value of the reference group [3].

Dietary Mg in many regions and particularly in France appears to be insufficient to satisfy daily requirements [2]. Mg deficiency at least at a marginal level is probably quite common in our society. The present results show a substancial difference between healthy subjects (reference group

of 3) and blood donors in their Mg distribution. This supports arguments against the practice of using data from blood donors or apparently healthy subjects to determine reference ranges for mg. Future studies concerning reference intervals of Mg have to define precisely the criteria for selecting normal subjects.

Acknowledgements

We are indebted to Mrs *Annie Bellanger* (Laboratoire des Maladies Métaboliques, INRA) for assistance with this work.

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