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CIRCADIAN RHYTHMICITY OF CIRCULATING VITAMIN CONCENTRATIONS

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A b s t r a c t

The aim of the study was to assess whether circulating vitamin concentrations are circadian periodic, and if so, to estimate the phase relations among vitamins A, E, C, and beta-carotene. Plasma concentrations of vitamins A, E and C, and of beta-carotene are circadian periodic, with peak values found in the early morning hours.

K e y   w o r d s

Circadian rhythmicity, Circulating vitamin concentrations, Vitamins A, E, C

INTRODUCTION

Fructose represents a stronger reducing capacity than glucose and mightly induced the glycation reaction. The aldehyde groups of unbound sugars react with free amino groups of proteins, forming Schiff bases which further undergo various rearrangements to generate advanced glycosylation end-products *(1). Wolff et al. (2)* suggested that transition metals catalysed auto-oxidation of free sugars in glycosylation. This process, called auto-oxidative glycosylation, seems to be accelerated by transition metals and contributes to the structural damages in diabetes *(3).* Glucose auto-oxidation and protein oxidation have a major role of auto-oxidative glycosylation in diabetes mellitus and are also involved in the process of ageing *(2).* There is also other evidence that free oxygen radicals are present in diabetic patients *(4,5)* and advanced glycosylation endproducts play a role in diabetic and non-diabetic vascular disease *(1).* An anti-oxidant activity of vitamins E and C was described. We assess whether circulating vitamin concentrations are circadian periodic, and if so, we estimate the phase relations among vitamins A, E, C, and beta-carotene.

MATERIALS AND METHODS

In Moradabad, India, 28 clinically healthy men, 30 to 61 years of age (mean ± SD: 44.8 ± 8.2 years; average weight = 64.0 ± 3.8 kg and height = 164.0 ± 4.7 cm) provided 4 blood samples at about 6-hourly intervals during 24 hours for the determination of plasma concentrations of vitamins A, E, C, and beta-carotene. Samples were collected around 06:30, 12:00, 19:00 and 00:00. Magnesium was determined at the latter 3 timepoints, whereas lipid peroxides were assessed in the morning sample. The daily dietary intake of vitamins A, E and C and of beta-carotene was also recorded along with blood pressure. Each data series was analyzed by single cosinor *(6).* Results were summarized by population-mean cosinor.

RESULTS

With the sparse sampling available, a circadian rhythm could be demonstrated with statistical significance ($P<0.05$) on an individualized basis in only 2 cases for vitamin A, and in only 4 cases for vitamin C and for beta-carotene. For vitamin E, a circadian rhythm was statistically significant for 9 of the 28 subjects. The individual acrophases clustered relatively tightly among all subjects for all variables examined. A summary of individual results by population-mean cosinor finds the circadian rhythm to be statistically significant for all 4 variables ($P<0.001$) (*Table 1*). The circadian variation for circulating Mg, assessed by single cosinor across all subjects, is of borderline statistical significance ($P=0.067$), with a similar acrophase (ϕ = -21 dg ± 40 dg), peaking around 01:24.

Table 1

Circadian rhythmicity of circulating vitamin concentrations

Vitamin	PR	MESOR ± SE	Amplitude (95% CI)	Φ (95% CI, in dg)
A	76	2.20 ± 0.02	0.07 (0.05; 0.09)	-42 (-29; -56)
E	85	20.93 ± 0.37	1.38 (1.04; 1.73)	-18 (-7; -28)
C	83	34.90 ± 0.70	2.26 (1.78; 2.73)	-31 (-19; -44)
b-carotene	85	0.45 ± 0.01	0.019 (0.015;0.023)	-20 (-8; -31)

PR: percent rhythm (proportion of variability accounted for fitted curve)
MESOR:midline-estimating statistic of rhythm
Amplitude.: double amplitude is a measure of extent of predictable change within a day
Acrophase: measure of timing of overall high values recurring each day, expressed in negative degree, with 360 degree equated to 24 hours and 0 degree set to local midnight

The well-known increase in blood pressure with body weight was mostly replicated (SBP: r=0.363; P=0.057; DBP: r=0.428; P=0.023). The MESOR of circulating vitamins E and C was negatively correlated with weight (E: r=-0.419; P=0.026; C: r=-0.375; P=0.050). The MESOR of circulating vitamin C correlated positively with the daily intake of this vitamin (r=0.381; P=0.045). The MESORs of circulating vitamins A, E and C and of beta-carotene were further correlated among each other (P<0.05 invariably), the strongest associations being between vitamin A on the one hand and beta-carotene (P<0.001) and vitamin E (P=0.002) on the other hand.

DISCUSSION

Plasma concentrations of vitamins A, E and C, and of beta-carotene are circadian periodic, with peak values found in the early morning hours (around 02:00). These inter-related variables depend on the amount and timing of daily dietary supplementation.

An earlier study on patients with suspected acute myocardial infarction (the Indian Experiment of Infarction Survival-3) showed that combined treatment with the antioxidant vitamins A, E, C, and beta-carotene may be protective against cardiac necrosis and oxidative load and could be beneficial in preventing complications in such patients. The therapy can be useful also in patients with type 2 diabetes mellitus *(2,4)*. Whether such treatment can be optimized by timing the administration of vitamins according to their circadian (and other) rhythms remains a task for future investigations.

A c k n o w l e d g e m e n t

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CIRKADIÁNNÍ RYTMICITA KONCENTRACÍ CIRKULUJÍCÍCH VITAMINŮ

S o u h r n

Cílem studie bylo posoudit, zda koncentrace cirkulujících vitaminů A, E, C, a beta-karotenu jsou cirkadiánně periodické, a pokud ano, stanovit jejich fázové vztahy. Zjistili jsme, že plasmatické koncentrace vitaminů A, E, C, a beta-karotenu jsou cirkadiánně periodické a jejich vrcholy byly nalezeny v časných ranních hodinách.

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