Influence of the state of ozonosphere on the risk of acute myocardial infarction

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Received March 19, 2007

The results of the studies of the influence of the ozonosphere state, controlling the level of near-ground shortwave UV–*B* radiation in temperate belt of the Northern Hemisphere, on the risk of acute myocardial infarction (AMI). The mechanism of influence of UV–*B* radiation on the risk of AMI development is suggested, based on its exceptional role in creation of active form of vitamin D_3, which regulates the homeostasis of calcium in the human organism. Statistically significant interrelation between the state of ozonosphere in period of maximum insolation and the number of AMI accidents, recorded during subsequent period of light starvation, is shown.

Introduction

Studies of the problem of how the variations of the level of total ozone influence the frequency of accidents of the acute myocardial infarction (AMI) in Tomsk, where the epidemiology of the disease is studied among the city dwellers older 20 years, have been initiated by us in 2003.[1,2] It is clear that the immediate influence on the frequency of AMI accidents is exerted not by ozone itself, 85% of which resides in ozone layer located at altitudes about 10–50 km above sea level, but rather by the dose of near-ground solar UV–*B* (280–315 nm) radiation. It was shown in Ref. 3 that at temperate latitudes of the northern hemisphere, the near-ground level of shortwave ($\lambda < 310$ nm) UV–*B* radiation is practically totally controlled by the total ozone (TO) content. Thus, by studying the influence of the ozonosphere state variations on the frequency of AMI accidents we can see the indirect interrelation of these processes, caused by the statistically high (for confidence probability 0.99) negative correlation between the near-ground UV–*B* radiation ($\lambda < 310$ nm) and TO variations.

The myocardial infarction is an acute form of ischemic cardiac disease which, in its turn, is a consequence of atherosclerosis of coronary arteries of heart.[12]

The existing data suggest that the effect of UV–*B* radiation may favor the improvement of the health state at the atherosclerotic cardiosclerosis,[4] the decrease of the level of cholesterol, intensification of the tissue breath, and improvement of metabolic processes (http://www.ill.ru/cgi-bin/form.news.). At the first stage of the studies[1,2] we revealed the presence of interrelation between the number of recorded AMI and TO level, which modulates the fluxes of shortwave near-ground UV–*B* radiation in the summer period, characterized by increased insolation. The obtained results well agree with data of international cooperative study of epidemiology of acute myocardial infarction as a part of the World Health Organization (WHO) program "World Health Organization Myocardial Community Registers," demonstrating obvious latitudinal dependence of this disease in European countries.[5–7] It was found that the countries of northern hemisphere with a high TO level and low insolation, such as Finland and Sweden, despite quite high living standard and medicine development level, suffer the largest number of myocardial infarction accidents yearly. However, considering solar UV–*B* radiation as a factor favoring reduction of the AMI risk, the authors did not analyze the mechanism of this phenomenon.

Analysis of results of the performed studies and data of scientific literature allowed us to suggest a mechanism explaining the influence of TO variations, controlling the level of shortwave near-surface UV–*B* radiation, on the risk of AMI development.

Mechanism of influence of near-ground UV–*B* radiation on the homeostasis of calcium in human organism and acute myocardial infarction risk

Under influence of solar UV–*B* radiation ($\lambda = 280$–313 nm) in human skin the cholecalciferol (the vitamin D_3) is synthesized from inactive provitamin D_3 (7-dehydrocholesterol), contained in secretions of skin sebaceous glands. In this case, the spectrum of biologic action has a maximum in the wavelength range 295–300 nm.[8,9] It is well known that the D-avitaminosis leads to child rickets, adult osteoporosis because of removal of calcium from bone tissue.[10] However, in recent years researchers have found that the functions of the vitamin D_3 are much more multiform.[10–12] In particular, deficit of D_3 in human organism may be one of the factors increasing the risk of cardiovascular diseases including AMI.

0235-6880/07/10 862-05 $02.00

In essence, the hydroxylated forms of vitamin D_3 (1,25-$(OH)_2D_3$ or calcitriol and 24,25-$(OH)_2D_3$), forming in kidneys as a result of complex reactions, represent hormones, playing a key role in regulation of metabolism and maintenance of homeostasis of calcium in human organism. The calcium concentration in blood plasma is one of the constants of human organism rigidly maintained. Calcium participates in coagulation of blood, clonus, and excitation of nerve. Changes of the intracellular calcium metabolism cause disturbance of the rhythm of the heart. It is found that the calcium deficit in the organism increases the risk of cardiovascular diseases. Organs that immediately control the calcium concentration in blood plasma are parathyroid gland, which synthesize two polypeptide hormones, namely parathyreoid hormone (parat) and calcitonin.[10,11]

The block-diagram in Fig. 1 shows the mechanism of action of active metabolites of vitamin D_3 in regulation of calcium homeostasis in human organism and explains the role of shortwave UV–*B* radiation in this process.

Under influence of biologically active UV–*B* radiation ($\lambda < 310$ nm), whose level in the temperate belt of the northern hemisphere is controlled predominately by the variability of ozonosphere (TO) state, in epidermis, the vitamin D_3 is synthesized from inactive provitamin 7-dehydrocholesterol. Subsequent scheme follows the principle of feedback. It is clear that moderate doses of solar UV–*B* radiation constitute the factor favoring reduction of AMI risk. The dose of ultraviolet radiation, required for compensation of vitamin D_3, for aged human, as data of the site http//rc.nsu.ru/distance /Biology/Archives/0.34html.url suggest, is about 60 minimum erythemal doses (MED) per year upon exposed sections of the body (1 MED is on average about 200 J/m^{-2}). Therefore, relatively regular 20–30-min stay with exposed extremities and back under scattered sun beams is enough. However, excessive sunburn prevents penetration of UV–*B* radiation to the internal skin layers and, therefore, disturbs the synthesis of vitamin D_3.[11] At the same time, the increased calcium level in blood plasma has considerable negative consequences, causing calcification of vitally important organs and tissues, kidneys, blood vessels, and heart, with irreversible dysfunctions.[10–12]

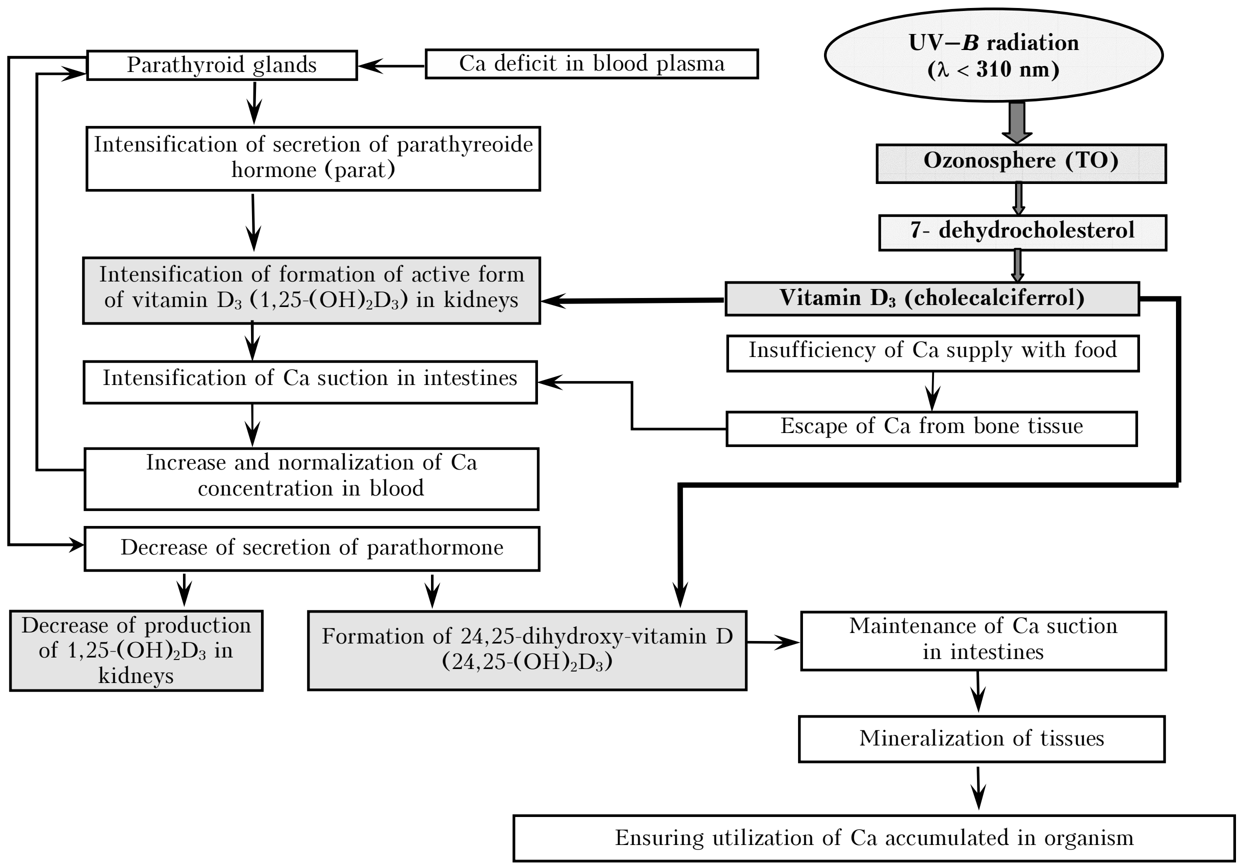

Fig. 1. Block-diagram of the mechanism of action of UV–*B* radiation and active metabolites of vitamin D_3 in regulation and maintenance of Ca homeostasis in human organism.

Results of correlation analysis of TO time series and acute myocardial infarction accidents in Tomsk for period 1986–2004

The climatic conditions of Tomsk correspond to the regions with quite limited insolation. In fall–winter period, the light starvation, especially in the UV range, is particularly noticeable. The calculations based on data of the site http://www.woudc.org. for Edmonton, Canada, the region quite close to Tomsk in latitude location and climatic conditions, have shown that in the winter period the daily mean total dose of UV–B radiation (295–315 nm) is only 0.56 kJ · m^{-2} · nm^{-1}. At the same time, the spectral interval 295–310 nm accounts only for 16.4%. From the middle of October to the end of February, the radiation at a wavelength of 295 nm is so small that it cannot be determined instrumentally, while at 300 nm it contributes only 0.03%. In the summer period, the daily mean total dose of UV–B radiation increases to 7.06 kJ · m^{-2} · nm^{-1}. In the range 295–310 nm, the total percentage of radiation is 33.10%, while at 295 and 300 nm it already reaches 0.67% of the daily mean total dose for the summer period.

Figure 2 presents the climatic norms of the radiation dose at 295, 300, 305, and 310 nm, as well as 295 and 300 nm for Edmonton.

Evidently, the total dose of radiation at 295 and 300 nm for period January–March and October–December, i.e., on the whole for period October–March, is negligibly small. The total dose of radiation at 295–310 nm is quite low in these periods as well. The total doses of UV–B radiation reach their maximum in period of maximum of summer solstice. At the same time, the lower levels in June are associated with still quite high (in comparison with July) TO level, which is, naturally, more clearly manifested itself for shortwave radiation.

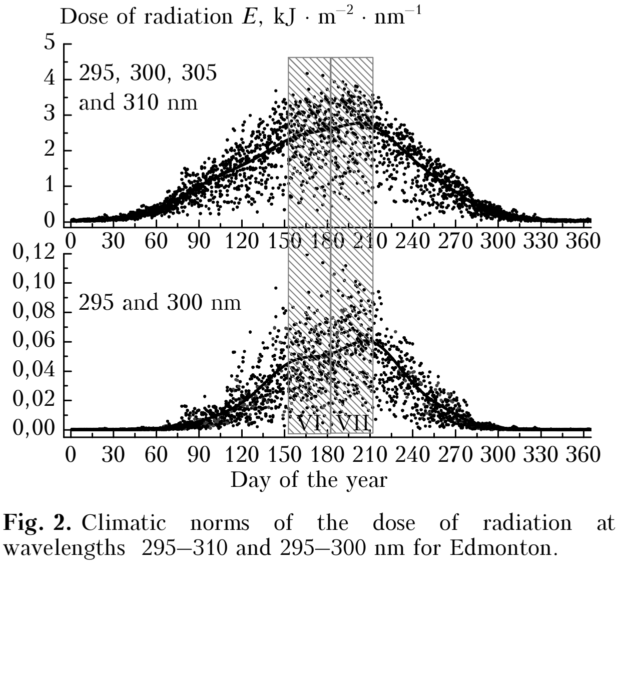

Fig. 2. Climatic norms of the dose of radiation at wavelengths 295–310 and 295–300 nm for Edmonton.

Thus, we can conclude that under conditions of Tomsk, the synthesis of vitamin D_3 in human skin and its accumulation in the organism are possible mostly in the period of insolation maximum, and in this case the problem of UV–B effect prolongation to the period associated with light starvation becomes urgent.

The monthly mean TO time series for Tomsk were obtained from data of TOMS satellite instrument (http://toms.gsfc.nasa.gou/ozone/ozone_v8.html) and complimented with data of ground-based observations.[13] Clinical and epidemiological fragment for the study was taken from the database of epidemiological WHO program "World Health Organization Myocardial Community Registers" (Fig. 3*a*).

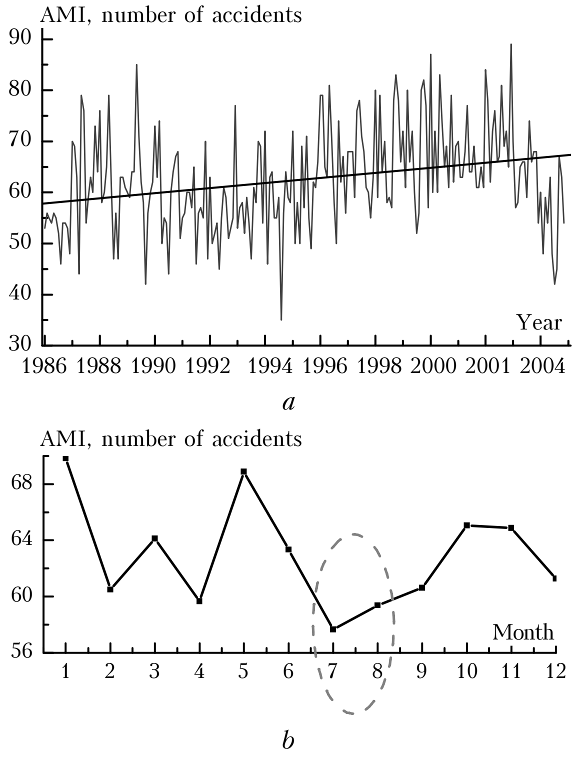

Fig. 3. Month-by-month distribution of acute myocardial infarction accidents (shown as a linear trend) (*a*) and monthly mean distribution of AMI accidents (*b*) for observation period January 1986–November 2004 in Tomsk.

The data series cover the time period from 1986 to 2004. The growth of the number of AMI cases in this period most probably reflect the influence of socioeconomic factor because the age composition of the population and ecological background in the region did not change.

Figure 3*b* shows the annual behavior of many-year means (over the analyzed period) of monthly AMI cases. Despite the absence of pronounced seasonality for AMI, it is clear that the annually least number of myocardial infarctions is recorded in period near maximum of summer solstice, in July–August (see Fig. 2). At the same time, we clearly see a larger (than in the summer months) number of recorded AMI cases for period fall–spring, indirectly confirming the role of UV–*B* radiation in reduction of the risk of the disease.

The correlation analysis of time series of relative deviations of diurnal TO values and dose of UV-*B* radiation in period of annual maximum, performed for Edmonton, demonstrated statistically quite high correlation coefficients in July, at least for the range of maximum of the spectrum of biological action for synthesis of vitamin D_3, and in July (Table 1). The obtained results allow us to use TO time series as an adequate substitution in the study of influence of UV–*B* radiation on reduction of the AMI risk in Tomsk. Moreover, the performed substitution is profitable because the accuracy of TO measurements in practice is more than an order of magnitude higher than the accuracy of direct measurements of UV–*B* radiation at wavelengths shorter than 305 nm.

In the course of the study, we performed the correlation analysis of normalized time series of monthly (June and July) mean TO values and the number of AMI cases, recorded monthly during year. In addition, we analyzed interannual variations of TO level at the maximum of summer solstice (June and July) and the number of AMIs, recorded in period of minimal doses of shortwave UV–*B* radiation (October–March). For convenience of correlation analysis, the compiled time series were standardized via detrending and conversion to dimensionless indices. In addition, removal of the linear trend made it possible to mitigate the social factor of risk of acute myocardial infarction. The statistical significance of the obtained results was estimated using Student's *t*-test.[14]

The results of the correlation analysis of the normalized time series of June-mean TO values and the number of monthly recorded AMI accidents recorded during year are presented in Table 2.

Obviously, the positive correlation is observed for January and May, i.e., months when the largest AMI number over year (see Fig. 3*b*) is observed. At the same time, for March the correlation coefficient also is close to (R_{min}) with confidence probability 0.95.

Estimates of prolongation of the effect of UV–*B* radiation in June on the number of AMI accidents, recorded in period of light starvation, have demonstrated statistically high coefficient of positive correlation of TO indices in June and AMI for period from October to March (Fig. 4) even for the confidence probability 0.99. It reaches $R = 0.739 \pm 0.216$ for the required minimum value $(R_{min})_{0.99} = 0.583$.

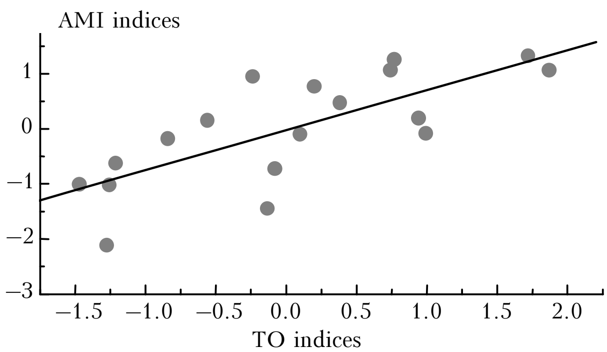

Fig. 4. Direct regression and scatter diagram of indices of TO level for June versus number of AMI accidents, recorded for period October–March.

Table 1. Correlation coefficients between time series of relative deviations of monthly mean dose of UV–*B* radiation at wavelengths 295–310 nm and TO time series for period of maximum of summer solstice

Year	June				July			
	295 nm	300 nm	305 nm	310 nm	295 nm	300 nm	305 nm	310 nm
1997	**−0.618**	**−0.552**	**−0.447**	**−0.366***	**−0.826**	**−0.767**	**−0.666**	**−0.566**
1998	**−0.718**	**−0.577**	**−0.390***	−0.301	–	–	–	–
1999	**−0.822**	**−0.748**	**−0.568**	**−0.389***	**−0.812**	**−0.759**	**−0.658**	**−0.566**
2000	**−0.784**	**−0.580**	−0.353	−0.200	**−0.832**	**−0.761**	**−0.648**	**−0.560**
2001	**−0.655**	**−0.515**	**−0.365***	−0.276	–	–	–	–
2002	**−0.747**	**−0.711**	**−0.574**	**−0.423***	**−0.789**	**−0.735**	**−0.581**	**−0.422***
2003	**−0.752**	**−0.661**	**−0.555**	**−0.476**	**−0.771**	**−0.693**	**−0.558**	**−0.441***
2004	**−0.588**	**−0.433***	−0.228	−0.127	**−0.784**	**−0.760**	**−0.698**	**−0.649**
N	**30**				**31**			
$(R_{min})_{0.95}$	**0.360**				**0.356**			
$(R_{min})_{0.99}$	**0.462**				**0.450**			

N o t e s: 1. We give in bold the statistically significant correlation coefficients for confidence probability 0.95 (denoted by asterisk) and 0.99. 2. *N* is the sample size, and $(R_{min})_{0.95}$ and $(R_{min})_{0.99}$ are correlation coefficients for this sample, required to reach the statistical significance at the level of confidence probability 0.95 and 0.99 respectively.

Table 2. Results of correlation analysis of normalized time series of June-mean TO values and monthly recorded AMI accidents from June of the current year to July of the next year

Month	VI	VII	VIII	IX	X	XI	XII	**I**	II	**III**	IV	**V**	VI	VII
Correlation coefficient	0.139	0.239	0130	0.293	0.304	0.337	0.370	**0.469**	0.373	**0.445**	0.321	**0.515**	0.404	0.070
N	19													
$(R_{min})_{0.95}$	0.466													

The analogous analysis of interrelation between interannual variations of TO level in July and the number of AMI cases recorded both in individual months and during entire period of light starvation from October to March has demonstrated an absence of correlation. We can speculate that the sunburn, i.e., increase of the number of melanoses and synthesis of melanin in July, prevents the penetration of UV–B radiation to the internal layers of skin and, hence, disturbs further synthesis of vitamin D_3.

Conclusions

Based on the results of the performed studies we can conclude the following:

1. Owing to the exceptional role of near-ground UV–B radiation in the synthesis of active forms of vitamin D_3 in human organism, especially in the interval 295–300 nm, a significant interrelation is created between the state of ozonosphere in the summer period and risk of acute myocardial infarction, because the D-avitaminosis is a significant factor increasing this risk.

2. For confidence probability 0.95, we found a statistically significant positive correlation between TO level in June and the number of acute myocardial infarction accidents for months when in Tomsk the annually maximal number of diseases is recorded (January and May).

3. We revealed the statistically high positive correlation at the 0.99 confidence level between TO in June and the number of acute myocardial infarction accidents, recorded in period of light starvation, which in the regions located in North Hemisphere at latitude of Tomsk lasts from October to March.

Acknowledgments

Authors express sincere thanks to Professor R.S. Karpov, Academician of Russian Academy of Medical Science, director of Scientific Research Institute of Cardiology of Tomsk Scientific Center of Siberian Branch of Russian Academy of Medical Science, for assistance and help in obtaining of confident data for research, and extra thanks to candidate of medical sciences Ya.I. Zyablov and candidate of medical sciences S.A. Okrugin for providing data on the number of acute myocardial infarction cases, recorded in Tomsk, and for useful suggestions at the initial stages of the studies.

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