Pathogenetic Mechanism of Alcohol's Effect on Academic Performance

M. O. Welcome, E. V. Pereverzeva, V. A. Pereverzev

Abstract**—**The regulatory competence of blood glucose homeostasis might determine the degree of academic performance. The aim of this study was to produce a model of students' alcohol use based on glucose homeostasis control and cognitive functions that might define the pathogenetic mechanism of alcohol's effect on academic performance. The study took six hours and thirty minutes on fasting, involving thirteen male students. Disturbances in cognitive functions, precisely a decrease in the effectiveness of active attention and a faster development of fatigue after four to six hours of mental work in alcohol users, compared to abstainers was statistically proven. These disturbances in alcohol users were retained even after seven to ten days of moderate alcohol use and might be the reason for the low academic performances among students who use alcoholic beverages.

Keywords**—**Alcohol, Academic performance, Pathogenetic mechanism.

I. INTRODUCTION

SEVERAL studies have noted the negative effect of alcohol use on academic performance [1]. In spite of the enormous epidemiological data on students' drinking behaviors, the fact that alcohol use reduces academic performance remains disputable [2].

Factors like cognitive abilities, competency in blood glucose maintenance, and stress might determine the level of academic performance [1], [3]. Decrease in the concentration of glucose leads to a lowering of cognitive functions [4]. Glucose is the main energy substrate for brain functions [4] – [6]. The intensiveness of brain glucose metabolism correlates with functional activity of the central nervous system [6] – [9].

Apart from the nervous system, the liver is the main target organ of the toxic effects of ethanol. The liver plays a central role in blood glucose homeostasis control [6], [10]. In this study we hypothesized that intensive mental activities under maximum stressed condition [4], [10], [11], even in a period of fasting, can lead to hypoglycemia or even hyperglycemia as a result of the increase in the energy support for brain functions [4] – [6], and this might allow to finding some peculiarities in blood glucose homeostasis control among alcohol users [7] – [11]. We therefore test a model of students' alcohol use based on blood glucose homeostasis control under long-term continuously stressed mental activities of alcohol users and non-alcohol users that might define the pathogenetic mechanisms of alcohol use on academic performance of students.

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II. MATERIALS AND METHODS

A. Participants

Twenty (ten non-alcohol users and ten alcohol users) seniors (fourth year male medical students) of the Belarusian State Medical University, Minsk, Belarus were at random explained the study aims and objectives one month before the experiment. All students were told not to use alcoholic beverages of any composition at least one week before the study. Two weeks before the study, consent forms were given to each of the twenty (20) medical students to approve their participation, seven (7) of them refused to participate for unknown reasons. The following criteria were used in the selection of the students:

1) Participants were randomly selected based on a screening survey conducted in the Belarusian State Medical University. Out of 1499 respondents, 87.7% (1314) students were alcohol users and 12.3% (185) were non-alcohol users. The criteria used in the screening were based on the following AUDIT scores: 1 through 40 – alcohol users; 0 (zero) – non-alcohol users [1].
2) Only male medical students were considered.
3) Abstinence for at least a week before the experiment day. This was based on the fact that acute effects of alcohol have been greatly studied, however, its aftereffects (even after a week's interval of alcohol use is unknown).
4) No cases of chronic alcohol intoxication, antisocial behavior, and psychiatric anamnesis or multidrug use (two or more, except alcohol) during the period of study in the university. Good daily regime – at least 6-7 hrs of rest per day, 3-4 times daily food intake (daily calorie intake of 2200-2600kcal for one person per day) and good physical activeness.
5) Absence of hearing and visual impairments.

B. Procedures

The Ethics and Research Committee of the Belarusian State Medical University approved the study protocol. All medical students confirmed their consent form on participation on the day of the experiment.

C. General Outline of the Experiment

The experiment was divided in three phases (phase I – from $0^{00} – 2^{30}$ hrs; phase II - from $2^{30} – 4^{30}$ hrs; phase III - from 4^{30}– 6^{30} hrs) and took 6.5 hrs of intensive mental work of increasing difficulty in a condition of fasting. Mental work of increasing difficulty involved two types of works – performing standard memory and attention tasks by determining the Success Index (SI), as well as mental work of increasing difficulty (filling of various questionnaires to reading of texts and providing answers to the questions on the read texts). Two texts were considered for use in the study. The first text "Physiology of Bone Tissue" [12] was administered in the second phase, while the second text "Physiology of Autonomic Nervous System" [12] was used in the third phase. These two texts were selected for this study since they were of significantly huge information and included items that had been taught students in their first to third school year syllabus.

The tests on SI, results of blood glucose determination, including all questionnaires filled by the participants were marked and numbered by ordinal numbers as the study was anonymous.

The rationale for using multiple memory tests and many questionnaires in this study was to produce a maximum stressed condition for the subjects. This was based on the assumption that 2-4 hrs unstressed mental activities might not show any significant differences in both the blood glucose level and the mental activities between alcohol users and non-alcohol users [6], [13]. All participants were confined during the study duration so as to ensure no contamination in the experiment. They were all subjected to standard mental activities of the same kind.

D. Order of the Experiment

The phases and order in which the experiment was conducted are described as follows:

1) Phase I (from $0^{00} – 2^{30}$ hrs of the experiment): The first phase of the experiment was conducted according to the following layout: The first 30 minutes involved the 1st blood sampling, followed by initial tests of Success Index, SI on various memory and attention tasks, as well as answering of the Big Five Trait questionnaire and State Trait Anxiety Inventory, STAI. For the next 1 hour 30 minutes the participants answered on the following questionnaires – AUDIT (Alcohol Use Disorders Identification Test), MAST (Michigan Alcohol Screening Test), CAGE (the Cut, Annoyed, Guilty and Eye questionnaire), "General", and Academic Performance (results were filled from result cards). The last 30 minutes of the first phase involved the 2nd blood sampling followed by the 2nd test of SI on various memory and attention tasks, answering of the Big Five Trait questionnaire, and STAI.

2) Phase II (from $2^{30} – 4^{30}$ hrs of the experiment): As soon as the participants had finished answering on the last questionnaires in the 1st phase, for the next 1 hour 30 minutes, they worked with the first text (a 20 page text on Physiology of Bone Tissue) with subsequent performance of a control test exercise containing 43 questions. The last 30 minutes of the 2nd phase was meant for the 3rd blood sampling, 3rd test of SI on various memory and attention tasks, and answering of the Big Five Trait questionnaire, and STAI.

3) Phase III (from 4^{30}– 6^{30} hrs of the experiment): Immediately after filling the questionnaires on the 2nd phase, participants started reading the second text and subsequently performed a control test exercise that followed it. This took 1 hour 30 minutes. The last 30 minutes of the experiment was meant for the 4th blood sampling, 4th test of SI on various memory and attention tasks, answering of the Big Five Trait questionnaire, and STAI.

E. Data Collection

1) Scoring Pattern of the Questionnaires

i. MAST: A total score of 3 or more was considered problematic alcohol use [1].
ii. CAGE: Any positive score of 2 through 4 was considered problematic alcohol use [1].
iii. STAI: Is a highly reliable instrument for evaluation of the state of anxiety. The result of the STAI was conducted according [14], [15]. The test contains two subscales which clearly differentiate between the temporary condition of "state anxiety" (STAIS-Anxiety scale) and the more general and long-standing quality of "trait anxiety" – STAIT-Anxiety scale. The range of scores is 20-80. The higher the score the greater the anxiety level.
iv. The Big Five Trait questionnaire was modified according to [16] and was meant for the determination of the degree of intensity of neuropsychic stress, in the subjects. Normal scores range from 30 to 40%.

v. The questionnaire on *"General"* contained 53 questions for determination of general information (except name and surname) about the subjects, sex, age, physical activeness, daily routine, food regimen, religion.

vi. Academic performance questionnaire: All subjects entered their examination scores (including resit examination scores) from examination cards for all periods of study in the Belarusian State Medical University into the questionnaire on "academic performance". The name of examinations were not stated, but were coded by ordinal numbers in relation to the semesters. The filling of examination scores was controlled by Author M. O. W. The collected data were used as objective criteria for academic activities of the subjects. Two major criteria were calculated: Grade Point Average (GPA) of examination results for the 1st, 2nd, 3rd, 4th, 5th and 6th semesters; success or effectiveness to sit for examinations for the 1st time – 100%, 2nd time – 50% and 3rd time – 25%. Analysis of academic performances of students in Belarusian institutions is determined on the 10-point scale. An equivalent of this scale is the 100% scale. On the 10-point scale, a score of 1 = 10%; 2 = 20%; 3 = 30%; 4 = 40%; 5 = 50%; 6 = 60%; 7 = 70%; 8 = 80%; 9 = 90% and 10 = 100%. A minimum score in examination caries a total of 1 point on the 10-point scale. A maximum score is set at 10. A score of 1, 2, and 3 is considered unsatisfactory with a necessity of resit examination for that given subject or course [1].

2) Scoring Pattern of the Texts

i. The control test exercise on the first text "Physiology of Bone Tissue" contained 43 questions, so results were calculated as SI (Success Index), ability to master the read text with the formula: SI = 100 (43–M) / 43, where M – sum of two numbers (number of incorrect answers + number of questions without answers).

ii. The control test exercise on the second text "Physiology of Autonomic Nervous System" contained 46 questions. No student was able to finish the second text and the questions that followed it. As a result IC was calculated thus: SI = 100 (Q–M) / Q, where Q – number of questions with answers; M – number of incorrect answers.

3) Determination of Blood Glucose Level

Glucose concentration in the plasma of capillary blood was measured as initial and in course of the experiment (after 2, 4, and 6 hours of mental activities) in all students using the glucometer – Bionime (*Rightest*TM GM100) [17], with an accuracy up to 0.11mmole/L. Blood sampling was done in volumes of 20 microliter from the ring finger of the left hand by skin puncture with disposable lancets under sterile conditions. The blood test was performed by Author M. O. W.

4) Determination of Mental Activity (Success Index, SI on Various Tasks)

Standard tests for determining SI involved the following: estimation of visual short-term memory, auditory short-term memory and operative short-term memory and processes of thinking, as well as conduction of proof-correction tests on attention [18] – [26].

i. *Determination of Auditory Short-Term Memory (ASTM)*
ASTM was determined using single-digit numeral and two-digit vowel letters on increasing row from 3 to 10 numerals or letters, according to the following sequence [21] – [25]. The subjects were instructed to write down single-digit numeral into the blank spaces of increasing row (from 3 to 10) provided, immediately after they were voiced by Author M. O. W. Subsequently, after the numbers were voiced, the subjects were required to write down the remembered ones in the sequence in which they have heard it. The determination of ASTM for two-digit vowel letters was conducted the same way. The time interval to completing the task for each row on the average took 30-60 seconds. The first row, where any incorrectly or not sequentially written numbers or letters occur was considered a mistake with no possibility of calculating the results of other rows below. The number of correct answers was calculated according to the formula: SI = 100 (A-M) / 10, where A – number of answers to be written; M – number of mistakes (incorrectly written numbers or letters).

ii. *Determination of Visual Short-Term Memory (VSTM)*
Determination of VSTM was done according to the following layout [18], [19], [22] – [24] with modifications. The subjects within 40 seconds were introduced 10 two-digit numbers (any from 10th to 99th) in different sequences. Subsequently within 150 seconds after introduction of the numbers, the subjects were supposed to have reproduced all remembered numbers in unconditioned sequence. The number of correct answers was calculated according to the formula: SI = 100 (A-M) / 10, where A – number of answers to be reproduced; M – number of mistakes (incorrectly reproduced numbers).

iii. *Determination of Thinking Capacity/Operative Memory*
Determination of thinking capacity was carried out using simple arithmetic (on the level of simple logical deduction with a single correct answer: addition and subtraction). Operative memory calculation was carried out according to the results of solved arithmetical problems with a single-digit answer in the test "arithmetical calculation" [27], [28] which was carried out by the subjects within 20 seconds. The SI and the speed of calculation according to the average duration in accomplishing one problem (task) were analyzed. SI = 100 (S–M) / P, where S – total number of solved problems; M – number of mistakes (incorrectly solved problems).

iv. *Determination of Attention*
Attention was determined on the proof-correction test using Anfimov geometric tables [20], [25], [26] (the table contained 1600 symbols, where 200 symbols were needed to be marked or configured correctly, and time of completion of the test - not more than 5 minutes). The Success Index was calculated using the formula: SI = 100 (200–M) / 200, where 200 – number of symbols of required

configuration in the table; M – number of mistakes (un-configured symbols or incorrectly marked symbols). Visual Productivity Coefficient, VPC was calculated thus: VPC = (0.5436*N–2.807*M) / T, where N – number of viewed symbols (maximum number = 1600); 0.5436 (bytes/symbol) – average volume of information that equals one symbol; 2.807 (bytes/symbol) – loss of information that equals one un-configured symbol or incorrectly marked symbols; M – number of mistakes (un-configured or incorrectly marked symbols); T – time spent on the performance of the test in seconds (maximum of 300 seconds).

5) *Statistical Analysis*

Data were analyzed using the SPSS (The Statistical Package for the Social Sciences) 16.0 version for Windows and the Spearman rho, ρ for correlation analysis. The probability value for significance was set at $p<0.05$. All volumes of alcohol used are given in values of pure ethanol. A standard drink was set at 10 ml of absolute ethanol. Results are reported as means and standard error of means, M±m, as well as in percentages, %.

III. Results and Discussion

All participants in this study were Christians. The body weight for both groups showed no differences (average weight of alcohol users – 73.2kg; non-alcohol users – 72.5kg). Their age range was 21-23yrs. The overall response rate for the study was 65% (i.e. 13 of 20 students), which is more than the average number. According to the screening results 5 students were non-alcohol users (group № 1 – control group), while 8 were alcohol users (group № 2 – test group). The average statistical results of the participants in the control and test groups according to the AUDIT, CAGE and MAST, including volume of alcohol used are shown in table 1.

TABLE I
AVERAGE STATISTICAL RESULTS OF NON-ALCOHOL USERS (GROUP № 1) AND ALCOHOL USERS (GROUP № 2) ON THE AUDIT, CAGE AND MAST

Groups	AUDIT	CAGE	MAST	Alcohol use per month		
	Scores	Scores	Scores	Fre-quency	Quantity per session	Quantity per month
№ 1	0	0	0	0	0	0
№ 2	4.5	0.8	1.6	1.3	23.0ml	38.0ml

Among alcohol users, 37.5% cases of alcohol related injuries were reported. The average volume of alcohol use was reported as 23 ml per session with approximately 1.3 frequency of use per month.

According to the results of the Big Five Trait Questionnaire, there was increase in neuropsychological stress in course of the experiment, especially after the fourth hour among the alcohol users. Also, significant decrease in mood, activeness in the second and third phases of the experiment among the alcohol users was recorded.

The state anxiety (according to the STAIS-Anxiety scale – STAI first subscale) among the alcohol users increased by about 10% immediately after 2hrs of intensive mental activities ($p<0.05$). Increase in the trait anxiety (according to the STAIT-Anxiety scale – STAI second subscale) was noted only after the 4th hr of the experiment ($p<0.05$). Anxiety level among the non-alcohol users in both subscales remained generally low in all phases of the experiment ($p<0.05$).

The academic performance of the non-alcohol users was significantly higher than that of the alcohol users. The GPA and effectiveness to sit for examinations was significantly reduced among the alcohol users. Reduction in the GPA of group № 2 students (alcohol users) in relation to the results of the first semester was 1.3 points ($p<0.05$) on the second course and 1.4 points for third year of study. The effectiveness to sit for exams by non-alcohol users on the second and third courses was by 10.9 % and 11.4 % ($p<0.05$) respectively higher, compared to that of the alcohol users.

The results of the tests on short term visual and short term auditory memory in course of the experiment showed no significant change in the Success Index (SI) in both groups. There was no significant difference in the speed of calculation and the Visual Productivity Coefficient (VPC) between non-alcohol users and alcohol users in course of the experiment (Table 2).

TABLE II
VALUES OF MENTAL WORK CAPACITY ACCORDING TO THE RESULTS OF THE "PROOF-CORRECTION TEST" OF NON-ALCOHOL USERS (GROUP № 1) AND ALCOHOL USERS (GROUP № 2)

Parameters	Groups	Values in course of mental activities			
		Initial	After 2hrs	After 4hrs	After 6hrs
Speed of viewing symbols/s	№ 1	4.8	5.8	5.9	6.6^{O}
	№ 2	6.4*	6.8*	7.2*^{O}	6.9
Total number of errors	№ 1	2.2 ± 1.3	2.0 ± 0.9	2.6 ± 0.9	2.4 ± 1.2
	№ 2	25.0 ± 6.6**	28.1 ± 8.4**	33.0 ± 8.4**^{O}	43.0 ± 10.0**^{O}
Success Index, %	№ 1	98.9 ± 0.6	99.0 ± 0.5	98.7 ± 0.4	98.8 ± 0.6
	№ 2	87.5± 3.3*	86.2 ± 4.2 *	83.4 ± 4.3*	78.4 ± 4.9*
VPC, bytes/s	№ 1	2.5 ± 0.2	2.9 ± 0.07	3.0 ± 0.1	3.3 ± 0.3^{O}
	№ 2	2.8 ± 0.1	3.1 ± 0.1	3.2 ± 0.1	3.1 ± 0.2

*$p<0.05$; **$p<0.01$ in relation to the corresponding values in group № 1; $^{O}p<0.05$ in relation to the initial values of its own group;

Among alcohol users and non-alcohol users, there was significant increase in the quantity of solved task on the test "arithmetical calculation", as well as number of configured symbols and speed of viewing each symbol in the test "geometric tables" (Table 2). However, increase in VPC by

+0.9±0.3 bytes/s ($p<0.05$) was noted only among the non-alcohol users after the 6th hr of the experiment (Table 2).

The errors made on the test “geometric tables” among the students of the alcohol users (group № 2) was 12.5 – 40.0 times ($p<0.001$) higher in relation to the non-alcohol users during the experiment (Table 2). The result of success index (i.e. effectiveness of active attention) among non-alcohol users was significantly higher, compared to the alcohol users (Table 2). Some similarities were also recorded. In group № 1 the success index in the tests on attention and operative memory under repeated condition remained stable and high. The number of errors made on the “proof-correction test among students of the group № 2 after six hours of mental activities increased by 72% (i.e. from 25 to 43 errors) in relation to their initial value (Table 2).

Evaluation of the ability of learning new materials by the students, as well as reproduction of already learnt materials in 1 – 3 courses of school years showed high effectiveness among the non alcohol users (success index approximately 75 – 96 %) and lower than average among the alcohol users (success index 15 – 37 %). Reduction in the number of answers was noted among group № 2 students, regarding the questions on “physiology of autonomic nervous system”. The correctness of answers (i.e. success index) among them was not more than 25%.

The results of the blood glucose sampling showed increasing glucose level (in relation to their initial value: 4.02±0.22 mmole/l) among non-alcohol users (group № 1) according to the measure of increase in mental activities: +0.70 mmole/l increase ($p<0.001$) in blood glucose concentration after 2 hrs, +1.40 mmole/l ($p<0.001$) after 4 hrs, +1.74 mmole/l ($p<0.001$) after 6 hrs in relation to the initial level among these students. The increase in the blood glucose level of alcohol users was observed only within the first 2 hours of mental activities (+0.45 mmole/l, $p<0.05$). (The initial blood glucose level of alcohol users was 4.24±0.21 mmole/l.) Thereafter, a fall in blood glucose level after 4 hrs of work was observed. After 6 hours of mental work blood glucose level among students of the group № 2 dropped by –0.89 mmole/l ($p<0.05$) in relation to its level after 2 hrs of mental activities, and by –0.80 mmole/l ($p<0.05$) in relation to its level after 4hrs and had a tendency to fall even in relation to its initial level. The decrease in the blood glucose concentration after the first two hours of mental activities had negative effects on alcohol users. Therefore long-term intensive mental activities of students who use alcohol (even in episodic small doses) are not accompanied by increase in the blood glucose level and subsequently leading to inadequate energy supply for brain functions. The result of this was the increase in the total number of mistakes, decrease in effectiveness of mental activities (Table 2), and even rejection of performance of difficult tasks (after 4hrs of the experiment 3 students declined from answering on the texts as result of the severity of fatigue as their blood glucose level was less than 3.0 mmole/l). As noted by [6] blood glucose level less than 3.5mmole/l leads to symptomatic hypoglycemia. A steady increase in the blood glucose level is a necessary physiological mechanism for adequate supply of energy for brain functions under metal activities of increasing difficulties: from questionnaires to reading of texts and providing answers to the questions on the read texts. The blood glucose concentration is a direct predictor of the brain glucose level, which in turn determines brain functions. On the average the brain glucose concentration is about 30-50% of the blood glucose concentration.

Scientists have constantly reported that alcohol in large doses inhibits gluconeogenesis leading to hypoglycemia [5]. Up to date, little is still known about the aftereffects of alcohol even after a week’s interval of moderate alcohol use. This is the first study to show that alcohol (even in small doses), especially under intensive mental activities leads to decrease in blood glucose level. The resultant effect might be marked by decrease in the capacity of mental activities (significant increase in error commission). Table 3 shows negative correlation between blood glucose level and total number of errors during the 4th hour of mental activities ($\rho = -0.8$, $p<0.001$). This correlation increased slightly after 6th hr of the experiment ($\rho = -0.9$, $p<0.0001$).

TABLE III
CORRELATION ANALYSIS BETWEEN THE GLYCEMIC LEVELS AND THE TOTAL NUMBER OF ERRORS COMMITTED IN COURSE OF THE EXPERIMENT

Correlation (rho, ρ) values of blood glucose level versus total number of errors in course of the experiment			
Initial	After 2hrs	After 4hrs	After 6hrs
– 0.1	– 0.4	– 0.8*	– 0.9**

*p<0.001, **p<0.0001

TABLE IV
CORRELATION ANALYSIS BETWEEN THE BLOOD GLUCOSE LEVEL AMONG THE PARTICIPANTS AND THEIR ACADEMIC PERFORMANCE FOR THREE YEARS OF STUDY IN THE UNIVERSITY

Time of Blood Glucose Sampling	Correlation (rho, ρ) values of the participants (n=13)					
	Grade Point Average, GPA			Effectiveness to sit for examinations		
	1st course	2nd course	3rd course	1st course	2nd course	3rd course
Initial	–0.1	–0.6	–0.4	–0.1	–0.1	–0.1
After 2hrs	–0.1	–0.4	–0.1	–0.3	+0.1	+0.3
After 4hrs	+0.1	+0.4	+0.7 **	+0.3	+0.6*	+0.8$^{\Delta}$
After 6hrs	–0.1	+0.4	+0.8 **	+0.4	+0.7 ***	+0.8 #

*p< 0.05, **p<0.02, ***p< 0.01, $^{\Delta}$p< 0.005, #p<0.001

Table 4 shows the correlation analysis between glucose level on fasting under intensive mental activities and the academic performance of students in different courses of study. Statistically significant correlation between the glucose level and the academic performance (GPA and the effectiveness to sit for examinations) was noted after the 4th and especially the 6th hours of intensive mental activities, starting from the examination results of the 2nd and 3rd courses of study in the university.

The positive correlation noted (only on the 2nd and 3rd courses, but not on the 1st course) between the academic performance and blood glucose level in course of the experiment indicates on the dose-time response effect of alcohol use (6 of the 8 alcohol users started using alcohol only in the university) (Table 4).

The results of this study suggest that the reduced academic performance of students who use alcohol might be related to the incompetency in blood glucose regulation, which is accompanied by low cognitive functions. This is the basis of the pathogenetic mechanism of alcohol use on academic performance of students.

IV. CONCLUSION

1) The model presented in this study defines the pathogenetic mechanisms of alcohol use on academic performance of students.

2) Alcohol use, even in small doses by students leads to a decrease in the capacity of mental work, and subsequently a reduction in academic performance.

3) Disorders in cognitive functions, precisely a decrease in the effectiveness of thinking capacity and active attention and development of fatigue (after four to six hours of mental activities) are detected in students who use alcoholic beverages, even after seven to ten days of alcohol use in small doses.

4) The detection of glucose homeostasis disorders in episodic moderate alcohol users was possible in a condition of 6.5 hrs intensive mental activities.

5) The procedures used in this study could serve as a model and a new method for early detection of alcohol related problems.

Study limitation

The small sample size is a major limitation of this study.

Future Research

There is need for a more comprehensive research on the dose-time response of alcohol consumption on glucose homeostasis control under varying mental activities and state, putting into consideration the academic performance of students in various levels of study, as well as other factors that might necessarily affect their academic success. Future study will also consider likely gender differences that might exist when this model is applied.

Recommendation

The results of this study suggest the necessity of limiting time (by two or a maximum of four hours) on continuous stressed mental activities of people (students, lecturers and teachers, drivers etc) who use alcoholic beverages and the development of complex measures, aimed at preventing menace of the rise of symptomatic hypoglycemia.

PROJECT REGISTRATION NUMBER

This study is part of a large project, officially registered in the Ministry of Health of the Republic of Belarus. Registration Number: 20093122. Registration Date: 17th November, 2009.

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