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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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INVESTIGATION OF ALCOHOL DEHYDROGENASE (ADH3) GENE POLYMOPHISM IN PATIENTS WITH CHRONIC ALCOHOLIC PANCREATITIS IN AZERBAIJANI POPULATION

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Abstract.

Aim: The aim of the study is to determine the single nucleotide polymorphism of the ADH3 gene, which is involved in the development of chronic alcoholic pancreatitis in the Azerbaijani population.

Material and Methods: Seventy patients (51 with chronic alcoholic pancreatitis, 19 with chronic non-alcoholic pancreatitis) and 90 healthy individuals (55 smokers and 35 non- drinkers) were included in the study. Genomic DNA was isolated from venous blood based on the kit protocol. Genotypes were determined on agarose gel using PCR-RFLP (polymerase chain reaction-restriction fragment length polymorphism) methods.

Results: To study the specificity of the ADH3 gene polymorphism in alcohol-dependent people, genotypes and alleles were compared in patients with chronic alcoholic pancreatitis (CAP) and "practically healthy " alcohol abusers. It was found that in both groups, the ADH3*1/ADH3*2 genotype predominates. It was also found that in the Azerbaijani population the frequency of ADH3*1 and ADH3*2 alleles is equally divided. From the data obtained, it can be clearly stated that the correlation of the ADH3*1 allele of the ADH3 gene polymorphism with an increased risk of the disease is not detected (p=0.876). When comparing genotypes and alleles in patients with chronic pancreatitis of non-alcoholic origin and non-drinkers, the predominance of the heterozygous ADH3*1 gene in both groups was also revealed without statistical significance (p = 0.777).

Conclusion: In the Azerbaijani population, the association between the polymorphism of the ADH3 gene genotypes and the development of CAP was not revealed. The predominance of the ADH3*1/ADH3*2 genotype explains the low incidence of both CAP and alcohol-dependent people in the Azerbaijani population.

Key words. Chronic pancreatitis, genetic polymorphism, alcohol dehydrogenase.

Introduction.

Chronic pancreatitis (CP) is an inflammatory process that leads to progressive and irreversible destruction of the exocrine and endocrine glandular parenchyma of the pancreas, which is subsequently replaced by fibrous tissue [1,2]. It is well known that alcohol consumption is a risk factor for both acute and chronic pancreatitis [1]. CP develops in 5-10% of those who abuse alcohol [2], and in developed countries, alcohol is the cause of CP in at least 70-80% of cases [3,4]. Genetic factors play an important role in the predisposition to damage to the pancreas, the severity and evolution of inflammatory processes leading to chronic inflammation or fibrosis.

It is believed that individual differences in susceptibility to CAP are probably genetically determined differences in alcohol-metabolizing enzymes with different metabolic rates. There have been many studies of possible associations between polymorphisms of alcohol-metabolizing enzymes and the risk of CAP, the results were controversial [5-7]. It remains unclear whether genetic variations in these enzymes may increase the risk of CAP.

The metabolism of alcohol is mainly carried out by the oxidative pathway. The main enzyme of the oxidative pathway of alcohol metabolism is alcohol dehydrogenase (ADH), an adimeric zinc-containing protein with a subunit molecular weight of 40 kDa, and aldehyde dehydrogenase (ALDH) [8,9]. ADH is encoded by at least 7 genes located on the long arm of chromosome 4 (chromosome 4q22), in which ADH2 (ADH1B) and ADH3 (ADH1C) are highly polymorphic [9]. The polymorphic genes ADH1B and ADH1C encode different forms of b and g subunits with different functions each. The ADH1B gene occurs as three alleles, ADH2* 1, ADH2* 2, and ADH2* 3, responsible for encoding b1, b2, and b3 subunits [10,11]. ADH2* 1 and ADH2* 2 alleles are found in Caucasians and Asians, ADH2 * 3 in 25% of the African American population [12], i.e., relatively more often than among white Americans, Europeans and Chinese populations [13]. The b1 subunit is practically inactive in alcohol metabolism, while the b2 subunit is very active in this regard. The ADH3 gene has two alleles: ADH3 * 1 and ADH3 * 2, encoding the corresponding subunits g 1 (arginine at position 272 and isoleucine at position 350) - with a high level of activity and g 2 (glutamine at position 272 and valine at position 350) - with lower activity in relation to ethanol [9]. However, it is important that the presence of polymorphic ADH3 isoenzymes varies in different ethnic groups. ADH3*1 occurs in 50–60% of Caucasians and >90% of Asian populations [14]. To date, several studies have been published evaluating ADH polymorphism in European populations. These articles concern mainly the eastern race [14,15].

The aim of this study was to determine the frequency of ADH3 alleles and genotypes in the Azerbaijani population, as well as to identify their responsibility for susceptibility to CP, in particular to CAP. We studied the allele frequency and genotypes for ADH3 in the Azerbaijani population by comparing patients with CAP and non-alcoholic chronic pancreatitis (NCP), with “practically healthy” alcohol abusers and non-drinkers.

Material and methods.

The study involved 160 people of the Azerbaijani population (31 women and 129 men). The main group consisted of 51 patients with CAP and 19 patients with NCP who received therapeutic and surgical treatment at the Scientific Center of

Surgery named after M.A.Topchibashov from 2014 to 2019. The control group included 90 "practically healthy" individuals, 55 of them with chronic alcohol abuse (CA) and 35 healthy non-drinkers volunteers (HN). The subgroup of heavy drinkers included those who consumed on average more than 80 g of pure ethanol per day for at least 2 years.

Blood DNA was analyzed from 70 patients (including 54 men and 16 women) aged 23 to 80 years with CP, as well as 90 "practically healthy" individuals (of which 75 men and 15 women) aged 30 to 84 years. CP was classified according to the TIGAR-O etiological classification [16]. The diagnosis of chronic pancreatitis was made on the basis of generally accepted criteria: clinical signs, physical examination, abdominal ultrasonography, CT or MRI, and exocrine pancreatic function tests [17]. Basically, ultrasound and CT were enough to confirm the diagnosis. These studies demonstrated atrophy or diffuse calcification of the pancreas, irregularity, and dilated length of the main pancreatic duct. Alcoholic etiology of CP was identified from the anamnesis. All subjects were informed and gave consent for the study (Table 1).

Table 1. *Criteria for inclusion and exclusion of subjects.*

Subgroups	Inclusion Criteria	Exclusion Criteria
CAP	1. Alcohol anamnesis > 80 g for at least 2 years 2. Radiological evidence of CP 3. Elevated serum amylase 4. Absence of any other cause of pain	1. Pancreatic cancer 2. Rare drinking
NCP	1. Radiological evidence of CP 2. The presence of any etiological factors according to the classification TIGAR-O	1. Pancreatic cancer 2. Alcohol anamnesis
CA	1. "Practically healthy" 2. Alcohol anamnesis > 80 g for at least 2 years	1.Pathology of the abdominal organs 2. Rare drinking
HN	1. "Practically healthy"	1. Pathology of the abdominal organs 2. Alcohol anamnesis

DNA extraction and genotyping.

Extraction of DNA from blood samples was performed according to the protocol of the Italian kit Sacace DNA sorb B. DNA samples were amplified using polymerase chain reaction (PCR). The nucleotide sequences of the specific primers used in the amplification were in the form F: GCTTTAAGAGTAAATATTCTGTCCCC and R: AATTCTACCTCTTTCCAGAGC. PCR reaction with a total volume of 25 µl included the following: 2 µl DNA, 2.5 µl 10X buffer [10 mM Tris-HCl pH 8.0, 50 mM KCl], 2.5 µl MgCl2, 0.5 µl 10 mM dNTP mixture , 0.5 µl of 100 µM primer. and 0.3 µl of 5 U/µl Taq polymerase enzyme. The PCR reaction steps included 5 minutes at 95°C, 30 seconds at 95°C, 1 minute at 51°C, 2 minutes at 72°C and 5 minutes at 72°C, respectively. The amplified product was digested with the restriction enzyme SspI (37°C incubation), and the results were analyzed by electrophoresis on a 3% agarose gel stained with ethidium bromide [18]. As a result of cutting DNA fragments with a restriction enzyme; ADH3*1/ADH3*1 was 146 bp, ADH3*1/ADH3*2-146, 67 and 63 bp, and ADH3*2/ADH3*2 - 67 and 63 bp ADH3*1 ADH3*1 (Figure 1).

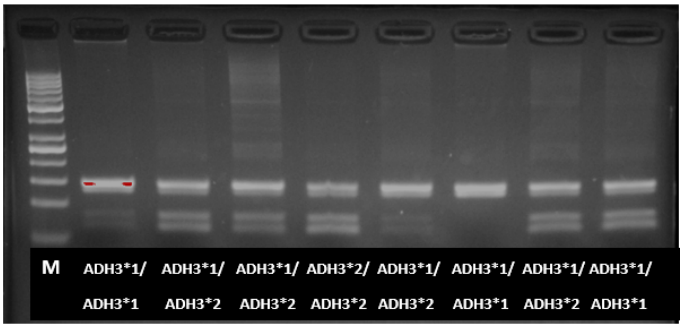

Figure 1. *Genotypes of ADH3 polymorphism determined from PCR-RFLP and analyzed by electrophoresis in 3% agarose gel stained with ethidium bromide and viewed under UV gel documentations. Lane M displays the 100 bp GeneRuler™ molecular weight marker; lanes designated ADH3*1/ADH3*1-homozygous, ADH3*1/ADH3*2-heterozygous, ADH3*2/ADH3*2 - mutant genotypes.*

Statistical analysis.

The results were studied statistically and tested against the hypotheses. All statistical analyzes were tested using IBM SPSS version 22.0. To test the significance of differences between the distributions of genotypes and alleles in the subjects, Fisher's exact test and Pearson's $\chi 2$ test were used. The association between case-control status and each polymorphism, measured by odds ratio (OR) and 95% confidence interval (CI), was assessed using an unconditional multiple logistic regression model. $p<0.05$ was considered statistically significant.

Results.

The desired study was aimed at determining the frequency of ADH3 alleles and genotypes in the Azerbaijani population, and identifying a possible association of ADH3 gene polymorphism with CP.

The distribution of genotype and allele frequencies of the ADH3 gene in patients and controls are shown in Table 2.

Table 2. *Distribution of genotypes, frequency of alleles of polymorphism ADH3 in patients with CP and controls.*

ADH3 gene	Patients N=70, (%)	Controls N=90, (%)	OR (95%CI)	*p*
Genotype ADH3*1/ADH3*1 ADH3*1/ADH3*2 ADH3*2/ADH3*2	6 (8.6) 63 (90) 1 (1.4)	10 (11.1) 78 (86.7) 2 (2.2)	Reference 1.35 (0.464-3.906) 0.83 (0.062-11.278)	 0.584 0.891
Allele ADH3*1 ADH3*2	 75 (53.6) 65 (46.4)	 98 (54.4) 82 (45.6)	Reference 1.04 (0.665-1.613)	 0.876

Heterozygous ADH3*1/ADH3*2 genotype was more common in both patients and controls (90% and 86.7%, respectively), but no significant difference was detected when comparing

study groups (OR = 1.385; 95% CI 0.464-3.906; p=0.584). In addition, there was no statistically significant difference between homozygous ADH3*1/ADH3*1 genotype and disease risk (OR = 0.83; 95% CI 0.062-11.278; p=0.891). In addition, no statistical correlation was found between the mutant ADH3*2 allele of the ADH3 gene and the risk of disease (p=0.876).

In order to study the specificity of the ADH3 gene polymorphism in alcohol-dependent people, genotypes and alleles were compared in patients with CAP and "practically healthy" alcohol abusers. This comparison shows that in both groups, the majority (96 and 92.8%, respectively) are dominated by the ADH3*1/ADH3*2 genotype. And the allele frequency of ADH3*1 and ADH3*2 is divided equally (Table 3).

Table 3. *Distribution of genotypes, frequency of alleles of polymorphism ADH3 in patients with CAP and controls.*

	CAP N=51, (%)	**CA N=55, (%)**	**OR (95%CI)**	***p***
Genotypes				
ADH3*1/ ADH3*1	1 (2)	2 (3,6)	Reference	
ADH3*1/ ADH3*2	49 (96)	51 (92,8)	1.92 (0.169-21.877)	0.599
ADH3*2/ ADH3*2	1 (2)	2 (3,6)	1.0 (0.034-29.809)	1.0
Allele				
ADH3*1	51 (50)	55 (50)	Reference	
ADH3*2	51 (50)	55 (50)	1.0 (0.583-1.714)	1.0

When comparing genotypes and alleles in patients with CP of non-alcoholic origin and in non-drinkers, the predominance of the heterozygous ADH3*1 gene in both groups was also revealed without statistical significance (p = 0.777) (Table 4).

Table 4. *Distribution of genotypes, frequency of alleles of polymorphism (rs698) ADH3 in patients with non-alcoholic CP and "practically healthy" non-drinkers (control).*

	NCP N=19, (%)	**HN N=35, (%)**	**OR (95%CI)**	***p***
Genotypes				
ADH3*1/ ADH3*1	5 (26,3)	8 (22,9)	Reference	
ADH3*1/ ADH3*2	14 (73,7)	27 (77,1)	0.83 (0.228-3.015)	0.777
ADH3*2/ ADH3*2	0	0	1.55(0.026-89.964)	0.834
Allele				
ADH3*1	24 (63,2)	43 (61,4)	Reference	
ADH3*2	14 (36,8)	27 (38,6)	0.93 (0.411-2.101)	0.860

The distribution of alleles showed the predominance of the ADH3*1 allele in both compared groups. However, the frequency of occurrence of this allele in both groups was not statistically significant (Table 4). Based on the obtained data showing the predominance of the ADH3*1 allele both in the group with ACP, also with CP of non-alcoholic genesis, as well as among “practically healthy” people who drink and non-drinkers, gives grounds for excluding the association between the polymorphism of the ADH3 gene genotypes and the development of ACP in the Azerbaijani population.

Discussion.

Genetic factors are involved in the development of alcohol dependence. These factors determine individual susceptibility to alcoholism and alcoholic lesions of the digestive tract. It is possible that those who are genetically predisposed become alcohol dependent, but the interaction between genetic factors and protection from environmental influences has not been identified [19]. It would be important to find the genes responsible for susceptibility to alcohol addiction and conduct screening tests to determine whether a particular individual has a genetic predisposition. And then people with a genetic predisposition will be able to consciously make a choice between an increased risk of drinking alcohol and abstaining from it. In Caucasians, ADH3*1 alleles occur in 50–60% of the population and their impact on the development of alcoholic liver disease varies. According to Kwast [20], in the Polish population, the frequency of ADH3*1 was 60.1%, while that of ADH3*2 was 39.9%. This frequency was calculated from phenotypic studies. And epidemiological data on the causes of death and the frequency of alcohol consumption in the study groups have not been described.

Borras et al. [21] evaluated ADH2 and ADH3 polymorphism in a European population of 876 individuals from 5 countries: Spain, France, Germany, Sweden, and Poland (193 individuals). On average, ADH3* 1 alleles were observed in 55.6% of healthy non-drinking volunteers and ADH3 * 2 in 44.4%. In alcohol-dependent people with cirrhosis of the liver and people without, damage to the liver parenchyma was 57.7 and 42.3%, respectively. Similar results were obtained by French scientists studying ADH3 in 46 alcohol-dependent patients with cirrhosis of the liver and 39 persons in the control group [22].

Our results show that the ADH3* 1 allele in patients with chronic alcoholic pancreatitis and in alcohol dependent patients without pancreatitis is equally distributed, which is closer to the results of the study by Borras et al. [21]. It should be noted that in non-drinkers, the presence of this allele is statistically slightly higher (61.4% in the CI group), while the ADH3* 2 allele is lower. Therefore, for the Azerbaijani population, the ADH3* 1 allele is not predisposing to the development of CAP. Similarly, the ADH3* 1/ADH3* 1 genotype cannot be associated with heavy alcohol users and the development of CAP.

The results for the Asian population showed that the ADH3 * 1 allele is more common in this population, its frequency is estimated at 90%. Coding for the extremely active g1 subunit is rare among Asian alcohol abusers, but there are studies demonstrating no difference in ADH3 polymorphism between heavy and non-abusive Asians [23]. These results are consistent with the results of our study since no association between the development of CAP and the ADH3 * 1 allele was found in the Azerbaijani population.

A similar study was conducted in the Chinese population, individuals who abused alcohol without liver damage had a lower frequency of the ADH3 * 1 allele compared to those who did not drink alcohol [24].

Orir et al [25], in their study, examined ADH3 polymorphism in a population of 371 Kenyans and found no statistically significant differences in alleles and genotypes between drinkers and non-drinkers. From the above, it can be concluded that the role of ADH3 polymorphism is ambiguous in different races and differs markedly in different populations. This probably involves the influence of coexisting environmental factors. There are many studies evaluating the association between alcohol-induced injury to other digestive organs and ADH3 polymorphisms.

Drenth et al. [26] demonstrated that ADH3 polymorphism may be a risk factor for chronic pancreatitis. Chronic pancreatitis was more common in homozygous ADH3*1 and ADH3*2 than in heterozygotes. The authors concluded that in the studied groups, the presence of heterozygous alleles has a protective role in the etiology of chronic pancreatitis [26]. In the Azerbaijani population, on the contrary, the heterozygous gene predominated both in the CAP group and in the CA.

The results of our research are different. In the group of patients with CAP, a higher frequency of the heterogeneous ADH3* 1 / ADH3 * 2 genotype was observed, while the presence of homozygous ADH3* 2 / ADH3* 2 was estimated at 2%. One might think that in the Azerbaijani population, the possession of this genotype usually does not contribute to alcoholism and protects against chronic pancreatitis.

The impact of ADH3 genetic polymorphism on the development of alcoholic pancreatic disease should be considered on an individual basis in terms of race. The presence of ADH3 alleles and genotypes differs between Caucasians and Asians. The factors that protect against alcoholism and CAP pathology in the Azerbaijani population play a different role in other races and populations.

H. Cichoz˙-Lach et al. [27] determined the allele and genotype of ADH2, ADH3, ALDH2, and CYP2E1 in 141 people from the Polish population. Among them, 44 were patients with CAP, 43 were healthy people with alcohol dependence and, as a control group, 54 healthy people who did not drink alcohol. Alle whether ADH2 * 1, ADH3 * 1 and genotypes ADH2 * 1 / * 1, ADH3 * 1 / * 1 were statistically more common among patients with ACP than among the control group. The ADH3*2/*2 genotype was more common among "healthy alcoholics" and in the control group than among patients with CAP. In the study group, only the ALDH2 * 1 allele was detected, all patients were homozygous for ALDH2 * 1 / * 1. Differences in the distribution of CYP2E1 alleles and genotypes in the study groups were not significant. Thus, according to this study, in the surveyed Polish population, the ADH3 * 1 and ADH2 * 1 alleles may be risk factors for the development of alcoholism. ADH3 * 2 / and genotype * 2 may provide protection against CAP. Polymorphism of the CYP2E1 gene is not associated with alcoholism and CAP.

Conclusion.

Our studies show that the ADH3 * 1 allele and the ADH3 * 1 / ADH3 * 1 genotype are less common in patients with ACP and alcohol abusers in the Azerbaijani population. The heterozygous ADH3*1/ADH3*2 genotype predominated in patients with CAP and “practically healthy” alcohol abusers. Among patients who consume excessive amounts of alcohol and in people with chronic pancreatitis, the ADH3*2/ADH3*2 genotype was extremely rare; so, it is likely to be a protective factor for this disease.

However, conclusions should be drawn carefully; It should be borne in mind that the role of the ADH3 genetic polymorphism in the development of alcoholic nutritional injury differs in different populations, in which other stimulating or protective factors of alcoholism may be present. These factors are likely to coexist with genetic polymorphisms of other genes encoding enzymes involved in ethanol metabolism.

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ГЕН АЛКОГОЛЬДЕГИДРОГЕНАЗЫ (ADH3) И АЛКОГОЛЬНЫЙ ХРОНИЧЕСКИЙ ПАНКРЕАТИТ СРЕДИ НАСЕЛЕНИЯ АЗЕРБАЙДЖАНА

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Цель: Определение ответственности генотипов ADH3 в Азербайджанской популяции на развитие хронического алкогольного панкреатита.

Материал и методы: генотип ADH3 и частоты аллелей ADH3*1 и ADH3*2 обследовали у 70 больных (51 с хроническим алкогольным панкреатитом 19 с хроническим панкреатитом неалкогольного генеза) и 90 «практически здоровых» добровольцев (55 употребляющие и 35 не употребляющих алкоголь). Генотипирование ADH3 проводили с использованием с помощью ПЦР-ПДРФ (полимеразная цепная реакция - полиморфизм длины рестрикционного фрагмента) на ДНК лейкоцитов. Продукты анализировали с помощью гель-электрофореза.

Результаты: Для изучения специфичности полиморфизма ADH3 гена у алкогользависимых людей сравнивали генотипы и аллели у пациентов с алкогольным хроническим панкреатитом и «практически здоровых», злоупотребляющих алкоголь. Было обнаружено, что в обеих группах у преобладает ADH3*1/ADH3*2 генотип. Также было установлено, что в азербайджанской популяции частота аллелей ADH3*1 и ADH3*2 разделена поровну. Из полученных данных можно четко сказать, что корреляция аллеля ADH3*1 полиморфизма rs698 ADH3 гена с повышенным риском заболевания не обнаруживается (p=0,876). При сравнении генотипов и аллелей у пациентов с хроническим панкретитом неалькогольного генеза и у людей не употребляющих алкоголь также выявлялось преобладание гетерозиготного ADH3*1 гена в обеих группах без статистической достоверностью (p= 0.777).

Заключение: В азербайджанской популяции ассоциация между полиморфизмом генотипов ADH3 гена и развитием хронического алкогольного панкреатита не выявилась. Преобладание ADH3*1/ADH3*2 генотипа дает объяснение низкой частоте встречаемости как хронического алкогольного панкреатита, так и алкогользависимых людей в азербайджанской популяции.

Ключевые слова: хронический панкреатит, генетический полиморфизм, алкогольдегидрогеназа.