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THE INCIDENCE AND PREVALENCE OF UVEAL MELANOMA IN THE REPUBLIC OF KAZAKHSTAN

Abstract. Uveal melanoma is the most common intraocular tumor, which threatens not only to the eyesight, but the patient life as well. In spite of this, uveal melanoma is rare and the portion of uveal melanoma is small (3.7%) in the structure of general oncopathology, it occurs in 75-94% among malignant intraocular neoplasms.

In this study we obtained the results on the frequency and prevalence of uveal melanomas in the Republic of Kazakhstan.

Thus, the incidence of uveal melanoma in Kazakhstan on average over the study period was 0,16^{0/0000}, and morbidity trends to increase. Women prevailed in 1.6 times the number of men. The incidence rates of the urban population remain stable, while the incidence rate of the rural population is increasing. The incidence of uveal melanomas among people of Asian nationality has doubled, and among European ethnic groups this indicator has remained stable and quite high over the past 5 years. Trends in the incidence of spindle-cell type melanoma in the second five-year period have significantly decreased in 2 times; however, the more aggressive forms (epithelioid and mixed cell) tend to increase.

Key words: uveal melanoma, intraocular tumors, morbidity trends, frequency, prevalence, oncoepidemiology.

Introduction. Over the last years the increasing trend of ocular melanoma is observed. According to the world data, the rate of patients with ocular neoplasms seeking medical assistance accounts for 110-120 people per 1 000000 population every year [1-3].

Intra ocular tumors account for up to 30% of all eye neoplasms.

Uveal melanoma is the most frequently occurring intraocular tumor threatening not only to eyesight but also to the life of the patient. Despite the fact that uveal melanoma is quite rare and its share in the overall oncopathology is insignificant (3.7%), it represents 75% - 94% of all malignant eye neoplasms, while the part of this tumor in the death rate from metastasis in all types of cancer is 15% [4-6].

The relevancy of choroidal melanoma is defined by a high relative density of this pathology in the structure of primary intraocular neoplasms (80-90%) [3, 7, 8].

Annual incidence of choroidal melanoma in different parts of the world comprises 7-12 people per 1 million population [1]. However, according to other authors, the total rate of choroidal melanoma around the world varies between 2 to 10 people per 1 million population [1, 9-11].

According to Pane A.R., the annual rate of disease in the USA and Europe is 4-6 people per 1 million population. In Russia, the rate of uveal melanoma based on patient applications in different regions varies from 6,23 to 8 people per 1 million adult population [9, 12]. According to Buiko A.S. and Vit V.V., the rate of patient applications for uveal melanoma in Ukraine accounts for about 3,2 people per 1 million population [13]. In the Republic Belarus, in the last decade, the incidence of uveal melanoma is 7-8 people per 1 million adult population (70-90 people annually) [14]. In Central Asia, the rate was considerably lower (2 persons per 1 million population) [1, 15]. In Tajikistan, the rate of ocular melanoma is 0,08 per 100 thousand population [20]. On average in the USA [16], Russia [17], Beloruss [18] and Kazakhstan [19, 20] an ocular melanoma occurs with incidence of 6 cases per 1 million people, while skin melanoma occurs more frequently and comprises 153,5 cases per 1 million [21, 22].

All of the above necessitates the study of incidence and prevalence of uveal melanoma in the last decades in the Republic of Kazakhstan.

The purpose of this search was the study of incidence and prevalence of uveal melanoma in the Republic of Kazakhstan.

The material is based on the data of 259 patients with uveal melanoma for 2006-2015, which were on hospital treatment in Kazakh Scientific Research Institute of Eye Diseases and Kazakh Institute of Oncology and Radiology (verified diagnosis). The main method in study in of uveal melanoma was a retrospective study with descriptive and analytical methods in contemporary oncoepidemiology. The extensive and intensive morbidity rates were defined by generally accepted methodology in modern statistics. The morbidity trends were defined by the method of the least quadrant method ($y=a+bx$). We used average intensive morbidity rates for 10 years (2006-2015) to make a map of the prevalence of uveal melanoma.

Methods. For the period in study (2006 - 2015) 259 cases of uveal melanoma are registered in the Republic. There were 100 ($38,6 \pm 5,0\%$) men and 159 ($61,4 \pm 4,0\%$) women. The number of women was 1.6 times higher than men, and 95% amplitude of relative density of the patients does not overlap, the differences are statistically significant ($t=4,03$; $p<0,001$). Therefore, the factors affecting occurrence of malignant eye tumors are not ambiguous. Average intensive morbidity rates for uveal melanomas of both genders of Kazakhstan population for the study period (since 2006 to 2015) are $0,16^0/_{0000}$, i.e. 1,6 per 1 million population and the morbidity rate has a trend for increase. Intensive morbidity rates for uveal melanoma depending on gender show that annual rate for men is $0,13^0/_{0000}$, and for women is $0,19^0/_{0000}$. That being said, the rate for men is decreasing, while rate for women has a tendency for growth. Such changes in trends of uveal melanoma confirm once again that female morbidity rates for these forms of tumors are comparably higher than male ones, have a tendency for growth in dynamics, especially for the last 5 years.

Territorial prevalence of the patients revealed that the share of urban residents was $54,1 \pm 4,2\%$ (140 patients) and rural – $45,9 \pm 4,6\%$ (119 patients), and 95% amplitude of relative density of patients between urban and rural residents intersect and the statistical differences are insignificant ($t=1,32$; $p>0,05$). Annual mean of intensive morbidity rates for uveal melanoma in urban residents for the last 10 years are $0,143^0/_{0000}$, in rural – $0,171^0/_{0000}$. That being said, morbidity rate in urban residents has a tendency for slight decrease, these trends are insignificant and remain stable for the study period, while rural morbidity rate has a growing tendency, and its growth is quite significant.

The share of patients with uveal melanoma in Asian population equals $9,3 \pm 1,84\%$ (24 patients), European – $90,7 \pm 1,9\%$ (233 patients), statistical differences are significant ($t=3,07$; $p<0,001$), and 95% amplitude of relative density of patients in the specified ethnic groups does not overlap. Therefore, the factors affecting occurrence of malignant pigment eye neoplasm are different. The morbidity rates for uveal melanoma in Asians have increased from $0,03 \pm 0,02^0/_{0000}$ in 2006 to $0,06 \pm 0,03^0/_{0000}$ in 2015, while in European ethnic groups this indicator remains stable and high ($0,51 \pm 0,11^0/_{0000}$) in the last 5 years (2011-2015), and the differences are statistically significant ($t=3,75$; $p<0,01$).

Annual mean of intensive morbidity rates for uveal melanoma of spindle cell type is $0,06 \pm 0,06^0/_{0000}$, epithelium cell type – $0,05 \pm 0,05^0/_{0000}$ and mixed cell type – $0,05 \pm 0,02^0/_{0000}$. Moreover, the rate for spindle cell type have decreased double in the last five years, while epithelium cell type and mixed cell type have a tendency for growth.

Annual mean of grouped prevalence of patients with malignant ocular melanoma by degree of process development has been presented as follows. The number of registered patients with ocular melanoma in periods (2006-2010 and 2011-2015) is relatively similar, 133 (51,4%) and 126 (48,6%) patients respectively, however, advanced forms of the stage IV ocular melanoma in the second 5-year period (19,1%) was almost 4 times higher than in the first 5-year period (5,2%). In overall, the share of advanced forms of tumor of vascular tract for the period in study was 12,0%. At the same time, the relative density of tumor in the I stage was only 9,2%. The majority of patients with malignant ocular pigment tumors were in stages II (41,3%) and III (37,5%), and the share of these patients in the last 5 years had a tendency for decrease. That being said, patients with early stages of uveal tract tumor (I-II stages) accounted for 50,5%, while the rest had stages III – IV of tumor process.

The epidemiological research of prevalence of uveal melanoma on the territory of Republic Kazakhstan for 10 years (since 2006 to 2015) revealed that the incidence of the studied malignant pigment ocular tumors has its peculiarities, which are characterized by the fact that extensive and intensive as well as aligned rates of morbidity vary depending on gender, ethnic composition of population, cell type, as well as place of residency of patients. Rank-abundant prevalence of stages of malignant tumor of eye vascular tract were also revealed. It was identified that the share of patients with early stages of tumor (I-II) is still low, the relative density of advanced stages in the last 5 years has a tendency for growth.

The uveal melanoma prevalence map was designed for separate regions of Kazakhstan. We recalculated incidence rates by estimation of the average annual indicators for 10 years.

In compiling cartograms of prevalence of intraocular melanomas, we used the mapping method suggested by S. I. Igissinov, based on the determination of the standard square deviation from the average level of incidence rates, which clearly gives the distribution of the incidence rate on a scale of cartograms of the prevalence of different forms of cancer. The morbidity stage scale clearly defines the level of disease as low, medium and high.

Prevalence map of ocular melanoma in regions of Republic Kazakhstan for 100000 population (2006-2015)

No	Morbidity level	Morbidity scale	City & Regions
1	Low	Up to 0,07	Aktobe (0.013) South Kazakhstan (0.02) Mangystau (0.032) Kyzylorda (0.049) Atyrau (0.067)
2	Middle	0,07-0,1	Karaganda (0.072) West Kazakhstan (0.076) Zhambyl (0.087) North Kazakhstan (0.091) Pavlodar (0.101)
3	High	Over 0,1	Akmola (0.141) Kostanay (0.219) East Kazakhstan (0.245) Astana (0.47) Almaty (0.616) Almaty region (0.645)

Hence, the designed uveal melanoma prevalence map enables to define space-time prevalence of the disease in separate administrative territorial regions of Kazakhstan, which must be considered in development of programs for oncological assistance to population, setting-up of anti-cancer activities in separate regions of the Republic.

Conclusion. The morbidity rate for uveal melanoma of both genders of population of Kazakhstan in average for the period in study was accounted for $0,16^0/_{0000}$, i.e. 1,6 per 1 million population, and the trend has a tendency for growth. With that, the number of women was 1,6 higher than men, which can be explained by the impact of female endocrine profile on formation of pigment neoplasms. The male morbidity trends are decreasing; while female have a tendency for growth. The morbidity rates in urban population have a tendency for a slight decrease, these trends are insignificant and remain stable, while the same rate for rural population is growing, and its growth is significant. The rate of morbidity among Asians have doubled, and among Europeans this rate remains stable and relatively high $0,51\pm 0,11^0/_{0000}$ within the last 5 years. The rate of morbidity in spindle cell types of melanoma in the second 5-year period have decreased double, however, the more aggressive form types (epithelium cell type and mixed cell type) have a trend for growth.

The highest rates of uveal melanoma prevalence defined by the morbidity scale are in Almaty region, Almaty city, Astana city, which is probably connected with availability of advanced diagnostics during screening examinations, as well as oncological awareness of ophthalmologists.

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ҚАЗАҚСТАН РЕСПУБЛИКАСЫНДА УВЕАЛЬДІ МЕЛАНОМАНЫҢ ЖИІЛІГІ МЕН ТАРАЛУЫ

Аннотация. Увеальді меланомасы – ең көп кездесетін көз іші ісігі, бұл тек көру мүшелеріне қауіп төндірмей қоймай, сонымен бірге науқастың өміріне қауіп төндіреді. Увеальді меланомасы сирек кездесетініне қарамастан және жалпы онкопатология құрылымында оның үлесі үлкен емес (3,7%), қатерлі ісік аурулары арасында 75-94% жағдайларда кездеседі.

Аталмыш зерттеу жұмыста Қазақстандағы увеальді меланомдардың жиілігі мен таралуы үшін нәтижелер алдық.

Осылайша, Қазақстанда увеальді меланоманың орташа зерттеу кезеңінде орташа есеппен 0,16%₀₀₀₀, құрады және бұл көрсеткіштің есү үрдісі байқалады. Сонымен қатар, ерлердің саны бойынша эйелдер 1,6 есе көп болды. Қалалық тұрғындардың сырқаттанушылық деңгейі тұрақты қалпынта, ал ауыл халқының ауру көрсеткіштері артып келуде. Азиялық ұлт өкілдері арасында увеальді меланомалардың пайда болуы екі есе өсті, ал европалық этникалық топтар арасында бұл көрсеткіш соңғы 5 жылда тұрақты және жоғары болып қалды. Екінші бесжылдықта меланоманың шпиндель жасушаларының түріне шалдығу үрдістері 2 есеге азайған, алайда түрінің пішіні (эпителиялы жасуша және арапас жасуша) анағұрлым агрессивті болып келеді.

Увеальді меланом ауруларының таралуы жағынан, ең жоғары көрсеткіш бойынша Алматы облысы, Алматы қаласы және Астана қаласы анықталып отыр, мұндай көрсеткіш болу себебі скринингтік зерттеу әдістері кезінде диагностиканың жақсаруымен, сонымен қатар офтальмолог дәрігерлерінің онкологиялық сақтылықтарының жақсаруымен байланысты.

Түйін сөздер: увеальді меланома, көз іші ісік аурулары, аурудың таралу трендтері, жиілігі, таралуы, онкоэпидемиология.

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ЧАСТОТА И РАСПРОСТРАНЕННОСТЬ УВЕАЛЬНЫХ МЕЛНОМ В РЕСПУБЛИКЕ КАЗАХСТАН

Аннотация. Увеальная меланома – наиболее часто встречающаяся внутриглазная опухоль, представляющая угрозу не только зрению, но и жизни пациента. Несмотря на то, увеальная меланома встречается редко и в структуре общей онкопатологии доля ее невелика (3,7%), среди злокачественных внутриглазных новообразований она встречается в 75-94 % случаев.

В данном исследовании нами получены результаты по частоте и распространенности увеальных меланом по Республике Казахстан.

Так, заболеваемость увеальными меланомами Казахстана в среднем за изучаемый период составили 0,16%₀₀₀₀, и тренды заболеваемости имеют тенденции к росту. При этом женщины преобладали в 1,6 раза над числом мужчин. Показатели заболеваемости городского населения остаются стойкими, в тоже время показатель заболеваемости сельского населения растет. Заболеваемость увеальными меланомами среди лиц азиатской национальности увеличилась в два раза, а среди европейских этнических групп этот показатель остается стабильным и достаточно высоким в течение последних 5 лет. Тренды заболеваемости веретено-клеточного типа меланомы во втором пятилетии значительно уменьшились в 2 раза, однако, более агрессивные по типу формы (эпителиоидноклеточный и смешанноклеточный) имеют тенденцию к увеличению.

По распространенности увеальными меланомами заболеваемость определяется как наиболее высокая в Алматинской области, г.Алматы, г.Астане, что вероятно связано с улучшением диагностики при скрининговых методах обследования, а также онкологической настороженностью врачей офтальмологов.

Ключевые слова: увеальная меланома, внутриглазные опухоли, тренды заболеваемости, частота, распространенность, онкоэпидемиология.

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