

THE BENEFITS OF PRIMARY PREVENTION OF COLORECTAL CANCER AROUND THE AGE OF 20 COMPARED TO SECONDARY PREVENTION AFTER THE AGE OF 50

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The major advantages of primary prevention of colorectal cancer in young adults (around 20 years) compared with secondary prevention in adults (after 50 years). Primary prevention is aimed at screening and eliminating one of the major proven risk factors for colon cancer – chronic constipation and its predecessor – colorectal bradyarrhythmia – as slower circadian rhythm of defecation. The main advantages of primary prevention of colorectal cancer are: non-invasiveness, safety, efficiency and timeliness. Screening of colorectal bradyarrhythmia at 2501 operating physician is allowed to diagnose this arrhythmia in 44% of the surveyed entities. There is discovered the new fundamental dependence between the regularity of circadian rhythm of defecation and an acrophase of this rhythm. The implementation of the morning acrophase of the circadian rhythm of defecation is the key mechanism of the regularity of this rhythm. Repeated screening of colorectal bradyarrhythmia in individuals around the age of 20 years (a month after informing students about the law of circadian rhythm in the brain and intestine) showed that 53% of the students began to observe the morning routine of bowel movements. This led to a transition of moderate stage of colorectal bradyarrhythmia severity (3-4 times a week) in an easy stage (5-6 times a week). It's proved the possibility of primary (behavioral) prevention of colorectal bradyarrhythmia (colorectal coprostasis) as a risk factor for colorectal cancer. Secondary prevention of colon cancer is associated with the invasiveness of colonoscopy, its possible complications (bleeding, perforation of bowel and fatal outcomes), the high cost of special equipment and late in the approach to screening for colorectal cancer (after the appearance of blood in the stool or after 50 years).

Keywords: primary secondary prevention; colorectal bradyarrhythmia; regular circadian rhythm; irregular bowel habit; complications of colonoscopy.

ПРЕИМУЩЕСТВА ПЕРВИЧНОЙ ПРОФИЛАКТИКИ КОЛОРЕКТАЛЬНОГО РАКА В ВОЗРАСТЕ ОКОЛО 20 ЛЕТ ПО СРАВНЕНИЮ С ЕГО ВТОРИЧНОЙ ПРОФИЛАКТИКОЙ В ВОЗРАСТЕ ПОСЛЕ 50 ЛЕТ

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Представлены основные преимущества первичной профилактики колоректального рака у молодых лиц (около 20 лет) по сравнению с его вторичной профилактикой у взрослых (после 50 лет). Первичная профилактика направлена на скри-

нинг и устранение одного из основных доказанных факторов риска рака толстой кишки — хронического запора и его предшественника — брадиэнтерии — замедления циркадианного ритма дефекации. Скрининг колоректальной брадиаритмии у 2501 работающего медика позволил диагностировать эту аритмию у 44 % обследованных лиц. Обнаружена новая фундаментальная зависимость регулярности циркадианного ритма дефекации от акрофазы этого ритма. Реализация утренней акрофазы околосуточного ритма дефекации оказалась ключевым механизмом регулярности этого ритма. Повторный скрининг колоректальной брадиаритмии у лиц в возрасте около 20 лет (через месяц после информирования студентов о законе циркадианного ритма мозга и кишечника) показал, что 53 % студентов стали соблюдать утренний режим дефекации. Это привело к переходу умеренной стадии тяжести колоректальной брадиаритмии (3–4 раза в неделю) в легкую стадию (5–6 раз в неделю). Доказана возможность первичной (поведенческой) профилактики колоректальной брадиаритмии (колоректального копростоза) как фактора риска колоректального рака. Главными преимуществами первичной профилактики колоректального рака являются: неинвазивность, безопасность, экономичность и своевременность. Вторичная профилактика рака толстой кишки сопряжена с инвазивностью колоноскопии, возможными ее осложнениями (кровотечения, перфорации кишки и летальные исходы), высокой стоимостью специальной аппаратуры и поздним подходом к скринингу колоректального рака (после появления крови в стуле или после 50 лет).

Ключевые слова: первичная профилактика; скрининг брадиэнтерии; регулярный циркадианный ритм; нерегулярная дефекация; вторичная профилактика; осложнения колоноскопии.

INTRODUCTION

Colorectal cancer is a predominant cause of cancer morbidity in St. Petersburg, Russia. In 2015, the incidence of colon cancer increased by 34% with 3,654 newly diagnosed cases compared with the reported incidence in 2010 [2]. It has been established that colorectal coprostasis, accompanied by chronic constipation, is a risk factor for the development of colorectal cancer (2.5-fold increase in risk) [5, 11, 14, 15].

Inducers of colorectal cancer, namely, animal proteins, and red meat fats (particularly barbecue processed with open fire, grill, or shashlik), overweight, hypodynamia, excessive consumption of alcohol, and tobacco smoking are known to promote colorectal coprostasis [7, 14]. In contrast, protective risk factors for colorectal cancer stimulating the evacuation function of the intestine include vegetables, fruits, dietary fiber, fish, chicken meat, calcium, folates, vitamin D, antioxidants, biologically active food components, sufficient physical activity, and a normal level of sex hormones.

Recently, it was demonstrated that certain widely used laxatives (currently not produced in numerous Western countries) and unapproved medications (e. g., polyphenol laxatives and senna preparations) are considered risk factors for the development of colorectal cancer [6]. Chronic constipation accompanied by colorectal coprostasis increases the risk of colon carcinoma from 1.36 to 4.4 times [15].

Modern approaches to the prevention of colorectal cancer is secondary (screening), mainly focusing on late manifestations of colon pathology, detection of blood in the feces, and the endoscopic removal of adenomatous polyps (precancerous colon formations) [1, 14]. It is recommended that screening should be initiated at the age >50 years, with colonoscopy and

sigmoidoscopy performed once every 10 and 5 years, respectively [1].

According to colon cancer studies conducted in the USA and UK [6], the average age of colon cancer detection is approximately 63 and 68 years in women and men, respectively. In 2008, 55,719 newly diagnosed cases of colorectal cancer were recorded in Russia, with the mortality rate amounting to 37,901 cases [3]. In the Northwestern Federal District, pediatricians have reported that nearly half (48%) of the children suffer from the earliest stages of constipation, a known risk factor for the development of colorectal cancer [14].

Academician N.N. Petrov in the clinical manual “Malignant tumors” emphasized the importance of habitual constipation in the occurrence of colon cancer, stating that “prevention of colon cancer is the prevention of constipation” [8].

Primary prevention of colorectal cancer should be aimed at diagnosing and eliminating the earliest stages of circadian rhythm disruption in the evacuation function of the intestine. Such prevention should be functional, non-invasive, and implemented as early as possible in the life of the patient.

The purpose of the current study was to describe the benefits of primary prevention of colorectal cancer in the form of prevention of early disruptions of the circadian rhythm of the intestine.

MATERIALS AND METHODS

The chronoenterography method involves weekly monitoring of the frequency and acrophase of the circadian rhythm of enteric evacuation activity of the colon [10]. A total of 2,501 medical workers, aged between 24 and 75 years, were examined.

Screening for bradyenteria (slowing and disturbance in the regularity of the circadian rhythm of defecation) was performed. This disorder, indicating

a tendency toward constipation, is one of the earliest manifestations of colorectal coprostasis. The severity of bradyenteria was defined on the basis of the defecation frequency, i. e., mild (5–6 times per week), moderate (3–4 times per week), and severe (1–2 times per week).

For early primary prevention of colorectal cancer, we screened for bradyenteria (slowing the circadian rhythm of defecation to <7 times a week). It was conducted as weekly monitoring of frequency and acrophase (the moment of implementation of the function in the diurnal period) of the circadian rhythm of defecation among medical institution students aged 19–20 (50 men and 81 women). For screening, a specially developed questionnaire was used to assess the frequency of the evacuation function of the intestine (number of days per week with acts of defecation), the number of bowel evacuations per day (number of acts of defecation within 24 h), and the acrophase of the circadian rhythm of defecation (the time of bowel evacuation in each of the four following periods of the daily 24-h cycle: 06:00–12:00, 12:00–18:00, 18:00–24:00, and 24:00–06:00). In addition, quality of life was investigated using the health, activity, and mood system [9].

RESULTS

Screening for bradyenteria showed that in individuals with a regular (daily) rhythm of defecation, morning (06:00–12:00) acrophase was observed more frequently (3.6-fold difference) than the evening (18:00–00:00) acrophase of the circadian rhythm of bowel evacuation (1,098 vs. 301 cases, respectively) (Table 1).

In contrast, among those with an irregular rhythm of defecation, the evening acrophase was observed more frequently (1.5-fold difference) than the morning acrophase (667 vs. 435 cases, respectively). These findings showed that the acrophase of the circadian rhythm of the evacuation function of the intestine is a key mechanism for the regulation of the rhythm of defecation.

The predominance of the morning acrophase and evening acrophase was associated with the regular and irregular rhythm of It was revealed that 34% of young male doctors had irregular bowel rhythm, whereas 86% of the interviewed students did not have a physiologically optimal habit for morning bowel evacuation (Table 2).

Irregular enteral rhythm in the form of bradyenteria was diagnosed in 34% and 45% of male and female doctors, respectively. Moreover, only 14% and 20% of the male and female students were shown to have a physiologically optimal habit for morning bowel evacuation, 86% of the interviewed students do not have a physiologically optimal habit for morning bowel evacuation (Table 2).

The level of quality of life in individuals with a regular morning intestinal rhythm (94% of the optimal) was 8% higher than that in individuals with an irregular evening rhythm of the intestine (86% of the optimal).

Morning defecation (acrophasia of the defecation rhythm) was observed 6 times more often in male doctors with a regular bowel rhythm than those with an irregular bowel rhythm (bradyenteria with a defecation frequency of 1–6 times a week). Morning defecation in female students with a regular rhythm of the in-

Table 1 (Таблица 1)

Frequency and acrophase of circadian intestinal rhythm in working persons ($n = 2501$)

Частота и акрофаза циркадианного ритма кишечника у работающих лиц ($n = 2501$)

| Frequency of defecation (once per week) | Morning acrophase | Evening acrophase | Total surveyed |
|---|-------------------|-------------------|----------------|
| 7 (regular rate) | 1098 | 301 | 1399 |
| 1–6 (irregular rate) | 435 | 667 | 1102 |
| Total | 1533 | 968 | 2051 |

Table 2 (Таблица 2)

Frequency and acrophase of circadian intestinal rhythm in medical students ($n = 131$)

Частота и акрофаза циркадианного ритма кишечника у студентов-медиков ($n = 131$)

| Frequency of defecation (once per week) | Men | | | Women | | |
|---|-------------------|-------------------|----------------|-------------------|-------------------|----------------|
| | Morning acrophase | Evening acrophase | Total surveyed | Morning acrophase | Evening acrophase | Total surveyed |
| 7 (regular rate) | 6 (12%) | 27 (54%) | 33 (66%) | 15 (19%) | 29 (36%) | 44 (55%) |
| 1–6 (irregular rate) | 1 (2%) | 16 (32%) | 17 (34%) | 1 (1%) | 36 (44%) | 37 (45%) |
| Total | 7 (14%) | 43 (86%) | 50 (100%) | 16 (20%) | 65 (80%) | 81 (100%) |

Table 3 (Таблица 3)

Advantages of functional over organic prevention of colorectal cancer

Преимущества функциональной профилактики над органической профилактикой колоректального рака

| Aspects of benefits | Functional prevention | Organic prevention |
|---------------------|--|--|
| Mode of application | Non-invasive | Invasive |
| Hazard | Non-hazardous | Hazardous for life |
| Approach | Elimination of functional risk factors | Elimination of organic precancerous polyps |
| Complications | None | Contact bleeding, gut perforation, fecal peritonitis, and death |
| Purpose | <ul style="list-style-type: none"> • Primary prevention • Prenosological prevention • Prevention of the transition of functional disorders in organic pathology • Prevention of diseases | <ul style="list-style-type: none"> • Secondary prevention: after the emergence of blood in the feces, after the detection of polyps • Prevention of transition from precancer to cancer • Prevention of mortality |
| Age | 15–20 years Timely | 50–75 years Late, with a delay of almost 30 years |
| Cost | Low | High |
| Result | Improvement in health | Disease and death |

testine was noted 15 times more often than in those with irregular rhythm.

The habit of morning defecation contributes to its regularity and a higher level of quality of life.

In total, 45% of young female medical students have irregular bowel rhythm, whereas 80% of the students surveyed did not have a physiologically optimal habit of morning bowel evacuation.

The level of quality of life (87% of optimal) in women with regular intestinal rhythm was 11% higher than that in women with irregular bowel rhythm (76% of optimal).

Repeated screening for bradyenteria (a month after acquaintance with the principle of circadian regularity of the brain and intestines) revealed that 53% of the individuals with moderate bradyenteria, determined during the first screening, strived to implement the circadian rhythm of defecation predominantly in the morning. This change in behavior led to improvement in the stage of bradyenteria severity from moderate (frequency of defecation, 3–4 times per week) to mild (frequency of defecation, 5–6 times per week) in more than half (53%) of the participants. This reduction in the severity of bradyenteria indicates that the regularity of the circadian rhythm of enteral activity may be improved through behavioral adjustments.

Two approaches for prevention of the risk of colorectal cancer should be compared, namely the primary functional prevention aimed at screening and elimination of bradyenteria (as a proven functional risk factor for colon cancer) and secondary organic prevention aimed at screening and endoscopic removal

of adenomatous polyps (as a potential precancerous condition of the colon).

Studies involving screening and endoscopic prevention of colorectal cancer showed that complications occurring during colonoscopy include bleeding, colon perforations, and death (three deaths per 30,000 colonoscopies and seven deaths per 97,000 colonoscopies reported in two studies) [12, 13]. The total risk of complications during colonoscopy (gut examination without biopsy) and surgical colonoscopy (biopsy and removal of adenomatous polyps) is approximately 1% and 3%, respectively.

The new clinical recommendations established by the Russian Gastroenterological Association, headed by academician V.T. Ivashkin, are aimed at optimizing the diagnosis and treatment of patients with irritable bowel syndrome, and those with chronic constipation using drugs such as trimebutine and lactitol [4].

CONCLUSION

The main advantages of the primary prevention of colon cancer are non-invasiveness, harmlessness, absence of complications, and cost-effective. These advantages are based on the timely detection and elimination of known risk factors (such as chronic constipation). It is particularly important to identify the predecessor of constipation, bradyarrhythmia of the intestine, which is a disruption in the regularity

According to the clinical recommendations [5] of the Russian Gastroenterological Association, a physiologically optimal habit of bowel evacuation in the morning, especially after breakfast, is essential from

early childhood and throughout the life of the individual.

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