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BIOLOGICAL RHYTHMS AS MARKERS OF THE GASTROINTESTINAL TRACT FUNCTION

SUMMARY

Circadian (daily) rhythm in GIT activity provides the optimal organism's function. Generally, motor and secretory activity of the GIT organs is higher in the active phase of the day (during the day time). Physiological rhythmicity is the significant indicator of the absence of the pathological processes in this system and in organism in general. In pathogenesis of the GIT organs' diseases the disturbance of the normal rhythmicity parameters as well as formation of desynchronosis occure – the state that accompanies all the diseases. An important role in prescribing medicines should be given to the rhythmic activity of the liver as to the main metabolic center of the organism. The significance of standards and also the ability to determine their violations (desynchronosis) is very important in optimization of gastroenterological diseases' diagnostics and in development of efficient and safe regiments of chronotherapeutic treatment based on it.

Key words: gastrointestinal tract; cyclical change; vibration; rhythm; treatment.

INTRODUCTION.

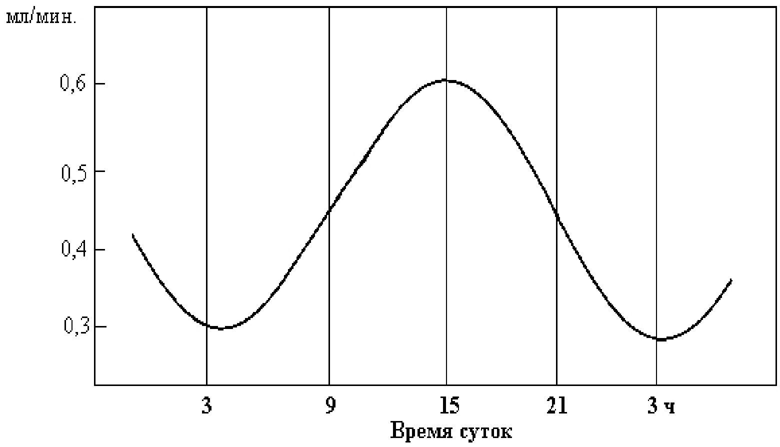
The presence of rhythmic activity in the digestive tract is responsible for optimum functioning of the body. This is due to the activation and regulation of the intensity of metabolic, neuroendocrine, and immune processes in accordance with the biorhythms of the body. From the digestive tract organs the most studied one is circadian (daily) rhythm. For humans and animals that are active during the light phase of the day, the intensity of the metabolic processes that are directly related to the gastrointestinal tract, is higher during the day. Despite the high activity of people working in the night shift, the efficiency of digestion is lower at night than during the day. The common feature of rhythms of secretory and motor activity of the digestive system is the high variability of adaptation: homeostasis support, adaptation processes, ensuring dynamic equilibrium. [4, 7]

The rhythmic activity of smooth muscles, that are responsible for the tonus and motor activity of all hollow organs of the gastrointestinal tract, is coordinated: stomach contractions occure at the same time with contracting of the lower esophagus and upper small intestine. Common rhythm of these organs has particular frequency and is coordinated by the central nervous system. All gastrointestinal smooth muscle organs work at even faster rhythms. They differ depending on the organ: the rhythm of gastric motility is in a 3:1 ratio to the minute rhythm, rhythm of duodenum peristalsis is in the ratio of 4:1 to the rhythm of gastric motility. It results in a balanced range of vibrations that correlate with each other. There are also slow oscillations of the tonus with a period of one hour. [3]

It has been found that the rate of solid food evacuation from the stomach in the evening (8 p.m.) is almost 20% lower than in the morning (8 a.m.). 31 reduction of the stomach in 1 hour was observed on healthy people when they are awake and 26 at bedtime, i.e. motor activity has decreased by 16%. [2]

Circadian rhythmicity of resorptive intestine activity has been studied. The concentration of substances (including drugs) in the blood depends on its level. The resorption in the intestine fluctuates depending on the volatility in the state of the mucous membrane epithelium, pH, evacuation gastric activity, the nature of the blood flow in the gastrointestinal tract. Blood flow velocity in the intake stage in its turn is directly related to the phase of the circadian cycle.

Fluctuations in time is subject to periodontal condition: the daily amount of fluid secreted by the gum, progressively increases from morning to evening hours. (Pic. 1). The content of epithelial cells in the gingival grooves peaks between 11 a.m. and 8 p.m., phagocytes - at 2 p.m., the protein - between 5 and 6 p.m. The tonus of vessels of parodentium has maximum acrophase between 11 a.m. and 2 p.m. The curve of gums temperature is characterized by peaks at 8 a.m., 2 p.m. and 8 p.m.

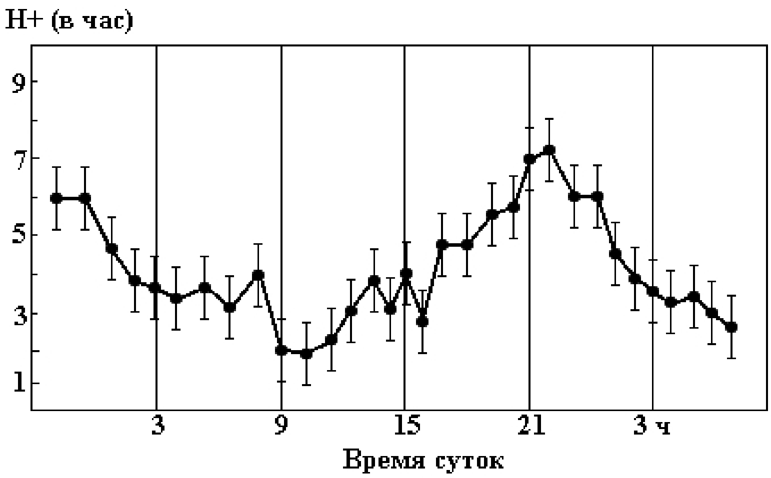


Pic.1 Circadian variations of saliva secretion

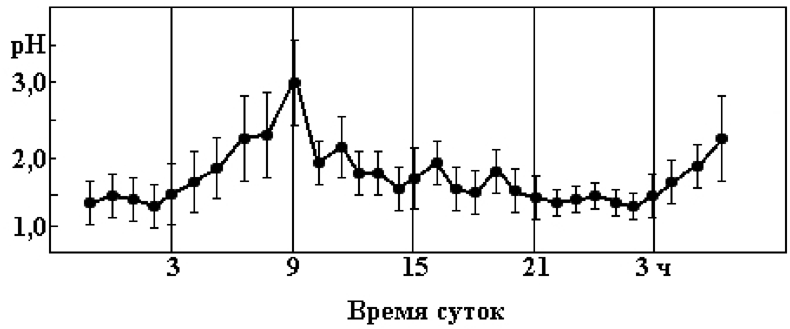
Acrophase of saliva conductivity is achieved during the nighttime (1-5 a.m.), which corresponds to the period of enhanced excretion of sodium and potassium ions. The maximum content of calcium and magnesium ions in saliva is observed in the morning (7-8 a.m.), while reducing the excretion of electrolytes occurs at day time - light hours of the day.

Acrophase of sodium and potassium concentration in the saliva is a few hours ahead of acrophase of rhythms of aldosterone concentration and renin plasma activity, which in turn reflects the natriuretic effect of corticosteroids on the salivary glands as well as the rhythm of aldosterone concentration in the blood. [6]

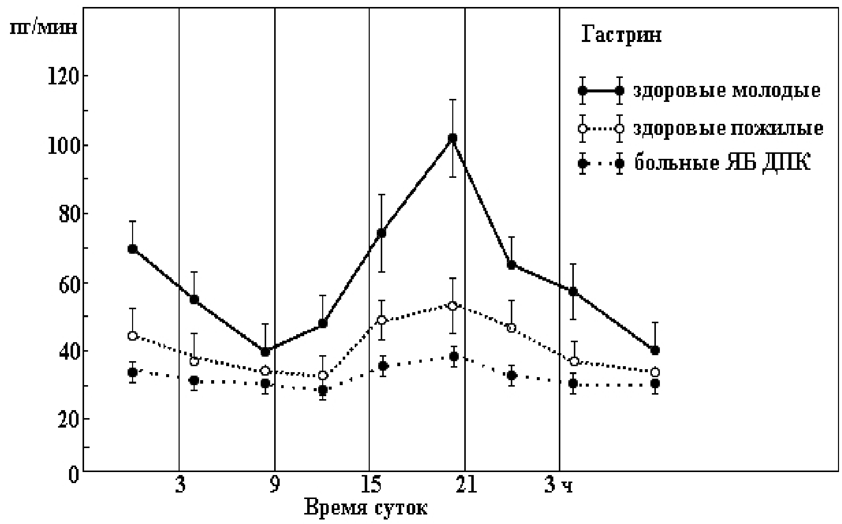
Of undeniable importance to the digestive system are diurnal oscillations of gastric acid secretion (acrophase at 9 p.m.) (Pic. 2), the basal parameters of pH (Pic. 3), and corresponding daily fluctuations of gastrin (acrophase at 8 p.m.) (Pic 4).



Pic. 2 Circadian rhythm of gastric acid secretion in healthy people



Pic.3 Circadian rhythm of basal gastric pH of healthy people



Pic.4 Circadian rhythm of the content of gastrin in the young and the elderly, and in patients with duodenal ulcer

When a healthy person has fallen asleep, gastric secretion dramatically reduces in volume and soon stops almost completely. (Pic. 2) Along with the reduction of secretion, the concentration of free hydrochloric acid and digestive juice strength fall off sharply (Pic. 3). The state of gastric secretion is highly dependent on the particular diet. The maximum acidity in the stomach is recorded a few hours after each meal and at night. Increasing of acidity during food consuming is due to the stimulation of acid formation by food, the evening increase reflects its endogenous rhythm of acid formation. [5]

Diurnal fluctuations of activity of the liver and gall bladder have been determined. In 1928 Forsgren discovered daily rhythm of bile secretion and the glucose accumulation in the liver. The periodicity of the liver activity is dependent on many variables factors, including the food and hormonal status. The activity of liver enzymes is of particular importance for the parameters of chronopharmacokinetics.

The nocturnal animals have a tendency towards reducing in the light time and increasing in the dark time of the average weight of liver, glutathione content in hepatocytes, glycogen and nucleic acids, the activity of some microsomal enzymes, such as cytochrome P-450. This leads to the increased metabolism of many drugs in the dark phase of the day, including anesthetic agents. The maximum of the glycogen in the liver is reached at 3 a.m., its minimum at 3 p.m., because glycogen from liver is primarily used by the body from 3 a.m. to 3 p.m., and accumulates in the liver from 3 p.m. to 3 a.m. Glucose-6-phosphate dehydrogenase, 6-phosphogluconate dehydrogenase and transcetolaze of rat liver act according to circadian rhythm of activity with a maximum between 10 p.m. and 6 a.m. and a minimum in the early light period. Inverse relation of these indicators is typical for animals living daily lives. [1, 4]

Data on the rhythm of the liver activity are very important for the selection of a rational scheme of chronopharmacokinetics, as the rate of metabolism of drugs at a particular time and, therefore, the severity of their actions depends on the activity of hepatocyte enzyme systems. This is a universal law, and thus it is obvious to expect the maximum attenuation of drugs effects in the daytime for people and diurnal animals, and in the dark - for nocturnal animals.

The maximum proliferative activity in rat liver is observed from 8 p.m. to 4 a.m.: the content of pyrimidine nucleotides is at its peak from 8 p.m. to 4 a.m., whereas the content of adenine and guanine derivatives in this period is minimal. This rhythmic relation is the basis of self-regulation processes in the liver and its functioning.

It is known that catecholamines are involved in the regulation of many metabolic processes in hepatocytes. The maximum concentration of adrenaline in the liver is observed at 8 a.m. The acrophase of DOPA content in the liver is observed from 2 to 4 a.m. , earlier than adrenaline and noradrenaline one. [3; 4]

Gallbladder filling in dormant state and its contraction in response to stimulation and subsequent dilation displays distinct diurnal vibrations.

The intensity of the bile secretion in the liver of rats is higher in the morning than in the evening by 3-10%, and the total amount of bile acids is higher in the evening than in the morning by 10-48%. In the evening the concentration and the total amount of secreted bilirubin is also higher in the morning by 13-81%, and of cholesterol - by 13-59%. There are seasonal peculiarities of bile secretion in rats: this process is most intense in spring and winter. At this time the content of cholates in bile is at the highest level.

By the hungry state there is reliable rhythm of periodic activities of the duodenum: sequential alternation of the periods of simultaneous motor and secretory activity with pauses of complete rest. The average duration of activity is about an hour (64.2 minutes). During this time about 70 ml of pancreatic juice is secreted into the duodenum. Rest periods last on average less than an hour (23.8 min). The phase characteristic of the ultradian rhythm of duodenum periodic activity is one of the criteria of the gastrointestinal tract normal functioning.

The functional state of the pancreas (RV) is characterized by alternating periods of activation and inhibition of its exocrine function, which is a manifestation of the ultradian rhythm of activity. At daytime there is a lower functional activity in exocrine tissue of the gland compared with the night time. In the active period of the pancreas there is 4-5-time-increase in hydrocarbons products, the activity of enzymes (lipase, amylase, trypsin) and the glycoprotein synthesis, in comparison with the rest period. The circadian rhythmicity of pancreatic enzymes activity has been determined: the amylase activity acrophase accounts for 6 a.m., trypsin – 10 p.m., the decline phase of amylase activity - between 6 a. m. and 12 p.m., of lipase between 5 a.m. and 6 p.m. 5 types of circadian rhythms of amylase, lipase and trypsin activity have been distinguished. Quantitative relation of particular types is changed in case of pancreatic pathology.

Seasonal variations are typical for exocrine pancreatic activity - the maximum increase in the concentration of trypsin and lipase in the blood is observed in February and August, also the level of protease inhibitors decreases. These changes preceded the spring-autumn recurrence of chronic pancreatitis. [7]

Daily fluctuations are typical for defecation. The most often frequency of intestine movements is once a day, which is observed in the morning.

Therefore, at present we have chronobiological features of work of various anatomical and functional structures of the digestive system have been determined. (Table 1)

Table 1

Standards of GIT

Parameter	Circadian rhythm
Motor and secretory activity of the gastrointestinal tract	***Max:*** daytime ***Min:*** nighttime
The intensity of the digestive and metabolic processes *	***Max:*** daytime ***Min:*** nighttime
Amount of gingival fluid	***Max:*** morning-evening ***Min:*** nighttime
The protein content of saliva	***Max:*** 5-6 p.m. ***Min:*** 6 a.m.
The content of epithelial cells in the gingival grooves	***Max:*** 11 a.m. and 8 p.m.
The content of phagocytes in the gingival grooves	***Max:*** 2 p.m.
Vascular tone of periodontium	***Max:*** 11 a.m. and 2 p.m.
Gums temperature	***Max:*** 8 a.m. and 2,8 p.m.
Electrical conductivity of saliva (the content of sodium and potassium)	***Max:*** 1-5 a.m. ***Min:***daytime
The content of calcium and magnesium in saliva	***Max:*** 7-8 a.m. ***Min:*** daytime
Stomach activity	***Max:*** 7-9 a.m.
Gastric acidity	***Max:*** вечер и после каждого приёма пищи
The content of gastrin	***Max:*** 8 p.m. ***Min:*** 8 a.m.
The rate of evacuation of solid food from the stomach	***Max:*** morning ***Min:*** evening-nighttime
Liver activity**	***Max:*** morning-daytime
Adrenaline content in the liver (mice)	***Max:*** 8 a.m.
DOPA content in the liver (mice)	***Max:*** 4-6 a.m.
Gallbladder volume	***Max:*** 9 a.m. ***Min:*** 9 p.m.
The intensity of bile secretion *** (rats)	***Max:*** morning

The total amount of bile acids, bilirubin, cholesterol (rats)	***Max:*** evening ***Min:*** morning
Pancreas and spleen activity ****	***Max:*** 9-11 a.m.
Pancreatic acinar cell size	***Max:*** morning ***Min:*** daytime-nighttime
Pancreatic amylase	***Max:*** 6 a.m. ***Min:*** 6 a.m. -12 p.m.
Pancreatic trypsin activity	***Max:*** 10 p.m.
Pancreatic lipase activity	***Min:*** 5 a.m. -6 p.m.
Activity of the small intestine	***Max:*** 1-3 p.m.
Activity of the large intestine	***Max:*** 5-7 a.m.
The frequency of bowel movements	***Max:*** morning

* - ***Max*** the intensity of digestion and metabolism - spring and summer;

** - the activity of microsomal liver enzymes, liver weight, the content of glutathione in hepatocytes, glycogen, nucleic acids is implied;

*** - ***Max*** bile production and cholates content - spring-winter;

**** - ***Max*** exocrine function of pancreas - February and August;

Thus, circadian rhythmicity is typical for most of the physiological processes in the gastrointestinal tract. In general, the motor and secretory activity of the gastrointestinal tract is higher in the active phase of the day (in the daytime). Physiological rhythmicity is an important marker of the lack of pathological processes in this system and in the body as a whole. In the process of development of the gastrointestinal tract diseases occures a violation of their normal rhythm parameters and desynchronosis developmet – the condition that accompanies all diseases. Knowing the standards and the ability to notice their violation (desynchronosis) is very important to optimize the diagnosis of gastrointestinal diseases, and to develop effective and safe therapeutic chronotreatment schemes on its basis.

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