Monitoring the action of drugs in patients in the early recovery period cerebral infarction as the basis of corrective therapy

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RESUME

The paper presents the results of treatment of patients in the early rehabilitation period of ischemic stroke and their evaluation by different methods; it was shown that the differential thermometry BAT can be used to correct the treatment of cerebral infarction.

Keywords: cerebral infarction, treatment adjustment, differential thermometry.

SUMMARY

The paper presents the results of treatment of patients in the early recovery period of ischemic stroke and their assessment by various methods; it was shown that the method of differential thermometry BAP can be used to correct the treatment of cerebral infarction.

Key words: cerebral infarction, treatment correction, differential thermometry.

Introduction

Personalized medicine, combined with predictive, preventive and partner components, is currently the basic strategy for the development of medical science in the Russian Federation until 2025 [1]. Personalized treatment based on monitoring the action of drugs can be especially justified in the rehabilitation treatment and medical rehabilitation of patients after acute cerebrovascular accident. The interest in this disease is not accidental: according to the National Stroke Association, 31% of stroke patients require constant outside help, of which 20% cannot walk on their own. Stroke places a heavy socio-economic burden on society as a whole [2, 3, 4]. Since the 60s of the last century, there has been a clear tendency towards “rejuvenation” of the contingent of patients with multifactorial vascular diseases of the brain [5]. At the same time, statistical data indicate that the incidence and prevalence of stroke increase with age: age is one of the unmodifiable risk factors regardless of the type of stroke, although about 80% of strokes occur after age 65 [6]. In this regard, the modern treatment of ischemic stroke involves not only the development of new directions for the treatment of acute cerebrovascular accident (ACVA), but also the personification of the treatment of cerebral infarction with the possibility of its correction based on taking into account all the characteristics of the patient and risk factors for the disease.

Purpose of the study: to evaluate the effectiveness of the application of the method of differential thermometry BAP as a basis for correction of treatment of patients in the early recovery period of cerebral infarction.

Materials and methods

We have proposed a method for predicting the effectiveness of treatment of patients with ischemic stroke, based on measuring the temperature difference between biologically active points and the intact area of the skin and allowing to completely eliminate the influence of environmental factors on temperature indicators. The method involves recording not the absolute temperature of the BAP, but the temperature difference between the BAP and the intact area of the skin, where the second thermocouple sensor is installed, for at least 2 minutes. At the same time, there are no negative effects on

acupuncture point; The proposed method has a high resolution, effective, inexpensive, atraumatic, non-invasive, convenient and easy to use.

In the work of Fedorov B.A. [7] for the first time revealed the dependence of the change in the signal on the position of the sensors, the age of the patients, the pathological state, taking into account one or another BAP. In particular, the dependence of thermograms on the position of the sensors for point P7 of the lung canal was established; also studied the dynamics of changes in ΔT BAP depending on the localization of the second sensor at point Gi4 of the colon canal, at point E36 of the gastric canal, at point V60 of the bladder canal. As a result of the study, the most stable graphs of all examined patients were selected, temperature fluctuations were noted depending on the time of day in the daytime and at night.

A device for measuring the temperature difference between a biologically active point and an intact skin area consists of a signal formation unit connected to a registration and analysis unit based on an analog-to-digital converter, a single-chip micro-computer and an indicator, characterized in that a memory unit is inserted into it and a serial interface for communication with a personal computer. The device is approved for clinical trials by the Scientific and Technical Medical Council [protocol No. 15 of March 25, 1999], and also has a certificate of compliance with hygienic standards in accordance with the "Requirements for medical devices and medical equipment" [laboratory research protocol No. 2205 of May 16, 2012 .] and a patent for a useful model No. 134028 "Device for recording biopotentials and temperatures of biologically active points." For a quantitative assessment of thermogram indicators, a computer program was developed (certificate of state registration of computer programs No. 2011611929), which allows calculating 14 digital indicators reflecting the regulatory characteristics of BAP thermograms. The following indicators were analyzed, their physiological significance and the results of changes were determined (Table 1).

To assess the effect of drugs in real time, studies of thermograms ΔT BAP at point C7 were carried out in patients of all groups for 1 (before treatment), 7 and 14 days of hospitalization [8]. Point C7 Shen - the smaller of the heart canal is located at the medial end of the wrist fold lateral to the flexor ulnar tendon. Its functions: sedative point, YUAN - point, point of the element "earth". Registration of ΔT BAP was carried out every second for 2 minutes and was reflected on the computer screen. Then, using a computer program, 14 thermogram indicators were calculated.

The study involved 78 patients: 47 men (60%) and 31 women (40%) aged 45 to 61 years. Informed consent was obtained from all subjects. All the data obtained were registered in a special individual registration card, executed in accordance with the recommendations of M.V. Leonova. and Asetskaya I.L. [9]. The criteria for enrolling patients in the study were: the presence of a confirmed ischemic stroke, the absence of hemorrhagic syndrome of any localization and etiology, trauma, operations in the last 3 months before the stroke. The exclusion criteria were: pregnancy, severe liver and kidney pathology, mental illness, therapy-resistant arterial hypertension with blood pressure above 180/110 mm. rt. Art., as well as the unwillingness of patients to participate in the study. During the entire observation period, the patients received standard pharmacotherapy (SFT), which is used to treat the early recovery period of ischemic stroke, but during the course of treatment it underwent drug correction depending on the dynamics of ΔT changes recorded in the BAP on the 1st and 7th day of the study. On the 7th day of observation, the patients were divided into 3 subgroups. For each of these subgroups, the correction of treatment was carried out with a certain drug (Actovegin, Cortexin or Cerebrolysin), which the patient received over the next week until the end of the course of rehabilitation treatment. registered in the BAP, on the 1st and 7th days of the study. On the 7th day of observation, the patients were divided into 3 subgroups. For each of these subgroups, the correction of treatment was carried out with a certain drug (Actovegin, Cortexin or Cerebrolysin), which the patient received over the next week until the end of the course of rehabilitation treatment. registered in the BAP, on the 1st and 7th days of the study. On the 7th day of observation, the patients were divided into 3 subgroups. For each of these subgroups, the correction of treatment was carried out with a certain drug (Actovegin, Cortexin or Cerebrolysin), which the patient received over the next week until the end of the course of rehabilitation treatment.

To confirm the results of the study obtained using the method of differential BAP thermometry, the dynamics of the neurological status was assessed in patients using neurological scales (NiHSS and Original [10, 11]), the dynamics of the psychoemotional state - using the SAN method [12], the dynamics of the level quality of life - using the Bartel scale [13] and the dynamics of the functional state of the vascular system - using the method of R. Voll [14].

Table 1

No. p-la	Indicator content	Physiological value of the indicator	Results (interpretation)
one	Total positive and negative fluctuations	It makes it possible to evaluate 2 opposite processes of the state of the meridian function.	An increase in the indicator corresponds to an increase in intensity regulatory processes.
2	The number of positive and negative fluctuations in 1 minute	It makes it possible to evaluate 2 opposite processes of the state of the meridian function within 1 minute.	An increase in the indicator corresponds to an increase in intensity regulatory processes in 1 minute.
3	Number of positive fluctuations per minute (frequency)	It characterizes the unidirectionality of the process of the state of the meridian function, conventionally designated by the "+" sign.	The increase in the indicator characterizes the activation of regulatory processes in one direction.
4	Number of negative fluctuations per minute (frequency)	It characterizes the unidirectionality of the process of the state of the meridian function, conventionally designated by the "-" sign.	An increase in the indicator characterizes the activation of regulatory processes in another, opposite direction.
5	The ratio of positive and negative fluctuations in 1 minute in frequency (the difference between indicators 3 and 4)	It makes it possible to assess the prevalence of unidirectional processes in accordance with the frequency.	The increase in the indicator characterizes the relationship of regulatory processes associated with frequency.
6	Duration of positive fluctuations in 1 minute	Determines the stability of the unidirectional process of functioning of the meridian for 1 minute, conventionally indicated by the "+" sign.	An increase in the indicator characterizes the constancy of regulatory influences in one direction.
7	Duration of negative fluctuations in 1 minute	Determines the stability of the unidirectional process of functioning of the meridian for 1 minute, conventionally indicated by the sign "-".	An increase in the indicator characterizes the constancy of regulatory influences in the other, opposite direction.
eight	The ratio of positive and negative fluctuations in 1 minute in duration (difference between indicators 6 and 7)	Determines the stability of the prevailing unidirectional process in 1 minute.	The increase in the indicator characterizes the relationship of regulatory processes associated with duration.
9	Frequency regulation index (quotient of indicators 3 and 4)	It makes it possible to determine the coefficient characterizing the ratio of two opposite changes in the functioning of the meridian.	It characterizes the severity of regulatory processes in terms of frequency.
10	Regulation index for duration (quotient indicators 6 and 7)	Determines the coefficient characterizing the stability of the ratio of two opposite changes in the functioning of the meridian.	Characterizes the degree of stability of regulatory processes by duration.
eleven	average value positive transitions of fluctuations in amplitude in 2 minutes	Reflects the intensity unidirectional regulatory process, conventionally designated by the "+" sign.	An increase in the indicator corresponds to an increase in the amplitude of regulatory processes in one direction
12	Average value of negative transitions of fluctuations in amplitude in 2 minutes	Reflects the intensity unidirectional regulatory process, conventionally designated by the sign "-".	An increase in the indicator corresponds to an increase amplitudes regulatory processes v another, opposite side.
thirteen	Horizontal frequency segments in 1 minute	Indicates no change in frequency fluctuation.	It characterizes the state of the organism in the absence of regulatory changes in frequency fluctuations.
14	Duration of horizontal segments in 1 minute	Indicates no change in duration fluctuations.	It characterizes the duration of the absence of regulatory influences.

The use in our work of quantitative indicators of methods characterizing the processes of restoring the functions of patients makes it necessary to perform mathematical processing of data, which is implemented in accordance with the recommendations of Sidorenko E.V. [15]. We used parametric and nonparametric criteria [16, 17]. Paired two-sample Student's t-test was used to test the hypothesis about the difference in means for two data samples. It does not assume that the variances of the populations from which the data are sampled are equal. The paired test was used when

there was a natural pairing of observations in the samples, for example, when the general population was tested twice, as was the case in most of our studies. In other cases, to prove the reliability of changes in one or another parameter, a nonparametric test was used: Wilcoxon's T test Statistical analysis of the research results was carried out using the Statistica 6.1 software.

Research results

According to the data obtained (Table 2) at point C7 on the 7th day of the study, the results obtained indicate an increase in the severity of fluctuations with a "+" sign (n5) and an increase in the stability of fluctuations with a "-" sign (n8) in the functioning of the heart meridian, which indicates a moderate stimulation of regulatory processes.

table 2

Dynamics of changes in ΔT BAP C7 (p.u., M ± m) in patients with ischemic stroke in early recovery period (n = 78)

Показатели	Сроки (сутки)				
	1 сутки n = 78	7 сутки n = 78	14 сутки Актовегин n = 26	14 сутки Кортексин, n = 27	14 сутки Церебролизин, n = 25
1	36,2 ± 1,41	39,1 ± 1,48*	36,5 ± 1,50	36,9 ± 1,45	36,5 ± 1,42
2	18,0 ± 0,75	19,6 ± 0,79*	18,4 ± 0,69	18,5 ± 0,71	18,4 ± 0,70
3	9,38 ± 0,42	10,5 ± 0,51*	9,66 ± 0,44	9,76 ± 0,47	9,68 ± 0,45
4	8,62 ± 0,38	9,57 ± 0,47*	8,52 ± 0,51	9,16 ± 0,44	8,71 ± 0,39
5	0,76 ± 0,04	0,93 ± 0,04*	1,14 ± 0,06*	0,60 ± 0,03*	0,97 ± 0,04*
6	10,8 ± 0,59	11,9 ± 0,61	10,9 ± 0,56	11,2 ± 0,57	12,7 ± 0,55
7	11,6 ± 0,62	12,9 ± 0,65*	11,9 ± 0,58	10,0 ± 0,59	11,7 ± 0,60
8	0,80 ± 0,03	1,00 ± 0,04*	1,06 ± 0,02*	1,02 ± 0,02*	1,05 ± 0,05*
9	1,08 ± 0,04	1,09 ± 0,04	1,13 ± 0,06	1,07 ± 0,05	1,09 ± 0,04
10	0,93 ± 0,05	0,92 ± 0,04	1,06 ± 0,06*	0,92 ± 0,03	0,94 ± 0,06
11	1,25 ± 0,06	1,35 ± 0,02*	1,24 ± 0,03	1,28 ± 0,02	1,26 ± 0,03
12	-1,26 ± 0,05	-1,35 ± 0,03*	-1,27 ± 0,03	-1,31 ± 0,04	-1,29 ± 0,03
13	12,2 ± 0,42	13,3 ± 0,45*	12,2 ± 0,38	12,4 ± 0,43	12,3 ± 0,39
14	37,1 ± 1,43	35,6 ± 1,34	38,2 ± 1,30	38,9 ± 1,41	37,8 ± 1,35

* – p < 0,05 1–14 – см. расшифровку показателей выше.

In addition, according to the patent for invention RU 2467680 C1 "A method for predicting the effectiveness of treatment of patients with ischemic stroke" dated November 27, 2012, since indicators 3 and 6 increased by the middle of the course of rehabilitation treatment by less than 20% of the indicators at the time of initiation of therapy, we can assume a slight improvement in the patients' condition by the 14th day. Therefore, the patients underwent treatment correction with one of three drugs: Actovegin, Cortexin or Cerebrolysin. On the 14th day of observation, the ΔT BAP values significantly changed in terms of indicators 5 and 8 in three subgroups, however, the degree of change was different. Thus, in patients receiving Actovegin, the indicator (5) increased by 50% (p <0.05); indicator (8) increased by 32.5% (p <0.05), which indicates an increase in the severity of fluctuations with a "+" sign in the functioning of the heart meridian and an increase in the stability of fluctuations with a "-" sign, which indicates a moderate stimulation of regulatory processes. In the subgroup of patients taking Cortexin, the indicator (5) decreased by 21% (p <0.05); indicator (8) increased by 28% (p <0.05), which indicates a decrease in the severity of fluctuations with a "+" sign in the functioning of the meridian and an increase in their stability, and also corresponds to a moderate stimulation of regulatory processes. In the subgroup of patients who were added to the treatment on the 7th day with cerebrolysin, the indicator (5) significantly increased by 28% (p <0.05) and the indicator (8) significantly increased by 31% (p <0.05),

Thus, changes in indicators (5) and (8) at point C7 on the 7th day of the study indicate a moderate stimulation of regulatory processes; on the 14th day of observation in the subgroups of patients taking Actovegin and Cortexin, one can also note a moderate stimulation of the regulatory processes, and in patients receiving Cerebrolysin, these processes are more pronounced.

As you can see from the table. 3, significant changes in the dynamics of neurological status are noted on the 14th day of the study in patients who received Actovegin from the 7th day of the study, according to the NiHSS scale (indicators decreased by 40%; p <0.05) and according to the Original scale (indicators increased by 11.8%; p <0.05). When assessing the psycho-emotional state in the same subgroup of patients,

significant changes in activity indicators (increased by 12.8%; p <0.05), well-being (increased by 21.9%; p <0.05) and mood (increased by 15.2%; p <0.05) ... Indicators of the quality of life also significantly increased by 18.4% compared with the beginning of treatment (p <0.05); indicators according to R. Voll's method significantly increased by 47.6% (p <0.001). In the subgroup of patients taking Cortexin, significant changes in the dynamics of neurological status were noted on the NiHSS scale (indicators decreased by 41.5%; p <0.05) and on the Original scale (indicators increased by 12%; p <0.05). When assessing the psychoemotional state, the same patients showed significant changes in activity indicators (increased by 14.3%; p <0.05), well-being (increased by 22.1%; p <0.05) and mood (increased by 21, 6%; p <0.05).

Table 3

Dynamics of neurological deficit, psychoemotional status and quality of life (points, M ± m) in patients with ischemic stroke in the early recovery period

when correcting treatment (n = 78)

SCALES	1st day n = 78	14th day Actovegin, n = 26	14 days Cortexin, n = 27	14 days Cerebrolysin, n = 25
NiHSS	14.0 ± 2.42	8.44 ± 1.68 *	8.19 ± 1.35 *	7.98 ± 1.19 *
Original	34.0 ± 1.62	38.0 ± 1.28 *	38.1 ± 1.33 *	38.2 ± 1.38 *
Wellbeing	2.92 ± 0.21	3.56 ± 0.22 *	3.57 ± 0.23 *	3.59 ± 0.24 *
Activity	3.12 ± 0.18	3.52 ± 0.24 *	3.57 ± 0.25 *	3.59 ± 0.27 *
Mood	3.22 ± 0.25	3.71 ± 0.20 *	3.92 ± 0.22 *	4.04 ± 0.25 *
BARTEL	75.1 ± 3.77	88.9 ± 4.47 *	89.0 ± 4.50 *	89.4 ± 4.52 *
Indicators by method R. Voll	43.3 ± 4.93	63.9 ± 3.89 **	60.7 ± 3.51 **	62.9 ± 3.68 **

* - p <0.05, ** - p <0.001

Indicators of the quality of life also significantly increased by 18.5% compared with the beginning of treatment (p <0.05); indicators according to R. Voll's method significantly increased by 40.1% (p <0.001). In the subgroup of patients who received Cerebrolysin from the 7th day of treatment, significant changes in the dynamics of neurological status were noted according to the NiHSS scale (indicators decreased by 43%; p <0.05) and according to the Original scale (indicators increased by 12.3%; p <0.05). When assessing the psychoemotional state, these patients showed significant changes in activity indicators (increased by 15.2%; p <0.05), well-being (increased by 23%; p <0.05) and mood (increased by 25.5%; p <0.05). The indicators of the quality of life also significantly increased by 19% compared with the beginning of treatment (p <0.05); indicators according to the method of R.

Thus, in patients with the correction of rehabilitation treatment, one can note the parallelism between the ΔT BAP indicators and the data of the neurological status, psychoemotional state and the level of quality of life. The best recovery of neurological deficit, mental state and social adaptation of patients is observed when Cerebrolysin is used from the 7th day of treatment, which is accompanied by significant stimulation of regulatory processes at point C7 of the heart channel and is confirmed by the maximum positive dynamics on two neurological scales, the SAN and Bartel scale. Changes in indicators by the method of R. Voll on the 14th day of observation significantly exceed the percentage of the results of other research methods and, therefore, cannot objectively reflect the depth and intensity of recovery processes in the patient's body.

conclusions

1. As a result of the study, it was found that the best treatment results are observed with an increase in the severity of fluctuations with the "+" sign and their stability, and a decrease in the severity of fluctuations with the "-" sign and their stability.

2. Established parallelism between changes in ΔT BAP and the dynamics of recovery neurological deficit, psychoemotional state and quality of life in patients in the early recovery period of ischemic stroke. It is noted that the dynamics of changes in the functional state of the cardiovascular system, determined using the R. Voll method, does not always correspond to the dynamics of these other research methods and, therefore, cannot fully reflect the processes of regulation and recovery occurring in the body.

3. The method of differential thermometry BAP is effective and can be recommended for

correction of treatment of patients in the early recovery period of cerebral infarction.

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