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Original Article

Possibilities of antianginal therapy in improvement of quality of life of patients with stable angina of effort

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ABSTRACT

Objective: High prevalence of ischemic heart disease (IHD) is currently both of medical and social concern, thus requiring treatment with drugs capable of influencing not only the prognosis of the disease but also quality of life of patients. This study was undertaken to investigate the possibilities of antianginal therapy with nicorandil and isosorbide dinitrate in order to improve quality of life of patients with stable angina pectoris.

Method: The authors carried out a comprehensive examination of a total of eighty-four 44-to-76-year-old patients suffering from IHD with functional class 2-3 stable angina of effort and followed up in ambulatory settings. The patients were randomized into two groups of treatment to receive either nicorandil or isosorbide dinitrate as antianginal agents added to basic therapy. The groups of patients did not significantly differ by anamnestic and demographic characteristics. The duration of follow up amounted to 24 months. We determined the physical and mental components of health-related quality of life and their dynamics on the background of antianginal therapy with nicorandil and isosorbide dinitrate. The parameters of quality of life were evaluated by the findings of two screening tools: the General Health Questionnaire (GHQ-28) and Seattle Angina Questionnaire (SAQ).

Results: The findings obtained within the timeframe of the study demonstrated that patients suffering from FC 2-3 stable angina of effort and taking standard therapy with beta-adrenoblokers, calcium antagonists, and antiplatelet drugs were found to have a decrease in their quality of life. The lowest scores were observed by the scales reflecting the psychological component of health, whereas the scores of physical limitation, angina stability, and angina frequency were considerably better. After 24 weeks of treatment with nicorandil and isosorbide dinitrate, the patients of both groups were found to have significantly improved scores for quality of life assessed by the SAQ on all scales. Initially high scores by the GHQ characterizing the patient's psychological discomfort were revealed in both groups of patients, with no statistically significant differences between the groups. The highest score was revealed by the scales of somatic symptoms and social dysfunction in both the nicorandil group (11.8 and 13.2 points, respectively) and isosorbide dinitrate group (12.1 and 13.5 points, respectively). The mentioned alterations underline the significance of such disease as IHD in adaptation of the patient to the social environment. Angina attacks, physical limitations lead to deterioration of the emotional state and interfere with daily activity. High scores by the scales of anxiety and depression suggested a low level of mental health of IHD patients with stable angina pectoris. After 24 months of treatment, manifestations of anxiety and depression in patients of both groups significantly decreased (with the results comparable in both groups), with clear advantage in the nicorandil group.

Conclusion: Nicorandil turned out to be superior to isosorbide dinitrate in improvement of physical and psychological components of quality of life of patients with stable angina of effort.

Keywords: cognitive quality of life, stable angina pectoris, antianginal therapy, nicorandil

INTRODUCTION

Present-day assessment of efficacy of pharmacotherapy for socially significant diseases can no longer be limited to only influencing the pathogenesis, clinical course or prognosis of a disease. One on the main trends in both medicamentous and drug-free interventions is the influence on quality of life of patients. Quality of life is an extremely multifarious notion which with equal success may be used in various spheres of life of a society since the final goal of any social activity is human well-being (1). That is why health-related quality of life may be regarded as a social characteristic of physical, psychological and social functioning of both healthy and diseased people, which is based on their subjective perception (2, 3).

In modern practical medicine, IHD was one of the first nosological entities subjected to studying the patients' quality of life (4-7). As antianginal therapy in patients with stable angina pectoris widely used are traditional therapeutic agents

to which nitrates belong (8, 9, 10). However, nitrates often induce side effects, with headache being most commonly encountered. Another cause of limiting prescription of nitrates is the development of tolerance thereto. The degree of the development of habituation to nitrates is quite different in different people (11, 12).

This dictates the necessity of further search for and improvement of antianginal therapy. In this connection, of particular interest is studying antianginal efficacy of potassium channel modulator nicorandil. The findings of clinical trials are suggestive of high antianginal and anti-ischaemic efficacy of nicorandil, as well as of its several advantages over nitrates (13, 14). Thus, no development of tolerance to nicorandil has been revealed. The drug was shown to improve delivery and increase the amount of oxygen supplied to the heart without increasing the requirements of the heart therein (15). Nicorandil, unlike b-adrenoreceptor blockers, calcium antagonists and nitrates, exerts virtually no influence on the heart rate (HR), the conductivity system and contractility of the myocardium.

Our own experience in studying comparative antianginal efficiency of using nicorandil and isosorbide dinitrate for preventing and relieving attacks of stable angina pectoris in patients with IHD demonstrated that nicorandil at a dose of 20 mg twice daily resulted in a significant decrease in the number of angina attacks, increasing tolerance to physical load and may be used both for prevention of angina attacks and rapid relief of them (16, 17).

The effect of nicorandil on parameters of quality of life has been studied in a series of foreign and Russian randomized trials (18, 19). However, of considerable interest is comparing the effect of nicorandil and conventional antianginal therapy on indices of quality of life in patients with stable angina pectoris.

MATERIALS AND METHODS

We followed up a total of eighty-four patients with IHD (28 (33.3%) men and 56 (66.7%) women, mean age 59.2±9.8 years) with FC 2-3 stable angina of effort. The functional class of angina pectoris was distributed as follows: FC 2 was diagnosed in 58 (69%) patients, FC 3 – in 26 (31%) patients, with the average FC of angina pectoris amounting to 2.14±0.24. Forty-one (31%) patients were found to have a history of endured myocardial infarction. In order to attain the goal of this study the following groups of patients were formed: Group One (taking nicorandil) comprised 43 patients (15 (34.9%) men and 28 (65.1%) women, mean age 56.3±7.6 years) and Group Two (taking isosorbide dinitrate) was composed of 41 patients (13 (31.7%) men and 28 (68.3%) women, mean age 60.2±6.1 years). The groups of patients were comparable by the main demographic and clinical-anamnestic characteristics.

The patients' quality of life was assessed by means of two screening tools: the General Health Questionnaire (GHQ-28) and Seattle Angina Questionnaire (SAQ).

The GHQ-28 inventory is designed for diagnosis of psychological well-being and emotional stability. Originally, the inventory had three versions consisting of 60, 30 and 12 questions, respectively, with the answers to be given by the patient according to a 4-point scale: 0 – «certainly not», 1 – «perhaps not», 2 – «perhaps yes», 3 – «certainly yes». High scores characterizing the pole of psychological discomfort correspond to affirmative answers to the questions which disclose manifestations of psychological ill-being, emotional instability and to negative answers to the questions which are associated with displaying positive emotion, psychological stability (they are assessed in the reverse order). However, in 1979 D Goldberg and V. Hiller suggested a new version of the inventory consisting of 28 questions (GHQ-28) and considering, in the opinion of the authors, psychological well-being as an element of a more general notion – "quality of life". The GHQ-28 consists of 4 scales: somatic symptoms, anxiety/insomnia, social dysfunction and depression. The mentioned version of the questionnaire has been widely used in both the Russian Federation and abroad, being highly valid and reliable.

The SAQ inventory was developed by Spertus et al. and first reported in the literature in 1992. The authors suggested that quality of life of patients with angina pectoris be evaluated by 5 scales: PL (Physical Limitation), AS (Angina Stability), AF (Angina Frequency), TS (Treatment Satisfaction) and DP (Disease Perception). Quality of life by all 5 scales of the SAQ is measured and expressed as percentage, with higher scores indicating better quality of life The questionnaires were intended to be self-administered by the patients, with a deviation of a score of any SAQ scale by ≥ 10 points (%) considered clinically significant (20-23).

Statistical Processing

The data was statistically processed on a personal computer by means of the "STATISTICA" software (version 6.1). The quantitative variables in two independent groups were compared by a nonparametric method with the help of the Mann-Witney U-test. Significance (p) of differences of independent groups by qualitative signs was compared by a nonparametric method using the chi-squared test. Results were regarded as statistically significant if $p < 0.05$.

Table 1: *Quality-of-life scores in IHD patients with FC 2-3 stable angina of effort according to the SAQ before and 24 weeks after treatment with nicorandil and isosorbide dinitrate*

SAQ scale (%)	Group One (n = 43)			Group Two (n = 41)		
	At baseline	After 24 weeks	Change of the score, Δ%	At baseline	After 24 weeks	Change of the score, Δ%
Physical Limitation	44.6±8.9	78.6±5.9ΨΨ	76.2	45.8±7.4	71±5.4ΨΨ	55.0**
Angina Stability	55.6±9.5	88.7±4.7ΨΨ	59.5	54.5±8.1	84.5±5.1ΨΨ	55.0
Angina Frequency	61.2±3.4	90.6±4.2ΨΨ	48.0	59.8±5.9	86.8±3.9ΨΨ	45.2
Treatment Satisfaction	39.7±7.2	79.2±8.8ΨΨ	99.4	41.8±5.8	77.5±7.2ΨΨ	85.4*
Disease Perception	42.3±7.8	80.5±5.8ΨΨ′	90.3	39.5±9.1	71.8±6.1ΨΨ	81.8*

Note: Ψ′ - significance of differences between the baseline scores and those 24 weeks after treatment;
* - significance of differences between the scores of Group One and Group Two;
* - p <0.05; ΨΨ, ** - p<0.01.

RESULTS

Quality of life of patients with IHD was evaluated using the patients' subjective assessment of their condition, with the information obtained by means of questionnaires acquiring a standardized pattern (24, 25).
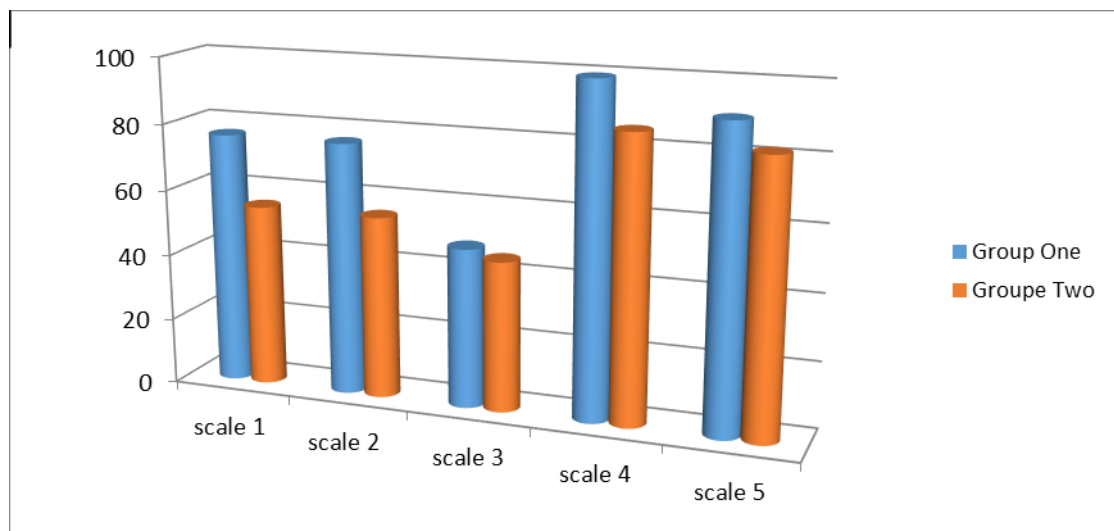
In the course of the study it was determined that assessing physical and psychological status of the patients by the SAQ the patients of both groups suffering FC 2-3 stable angina of effort and taking standard therapy including beta-adrenoblockers, calcium antagonists, statins, aspirin had a decrease in their quality of life (**Table 1**). The results of assessing the scores by all five scales in both groups of patients prior to the beginning of treatment of stable angina pectoris with nicorandil and isosorbide dinitrate were comparable.

A detailed analysis of the initial quality-of-life scores assessed by the SAQ showed that the lowest scores in both groups were observed for the scales reflecting the psychological component of health (the scale of Treatment Satisfaction and the Disease Perception scale), being, however significantly considerably better by the scales of Physical Limitation, Angina Stability and Angina Frequency scales. This circumstance once again proves the fact that the level of psychological comfort for a patient with a chronic disease is extremely important. The way a patient co-exists with his/her illness, perceives disease-related limitations and understands the sense of medicamentous interventions being performed to a large extent determines further prognosis for each particular patient involved concerned.

Patients of both groups at 24 weeks of treatment were found to have significant improvement in the quality-of-life scores assessed by the SAQ on all scales (**Table 1**). Analysing the dynamics of the quality-of-life scores 24 weeks after treatment demonstrated an interesting peculiarity: with a relatively equivalent increment of the parameters assessed by the scales of Angina Stability and Angina Frequency (with a slight preponderance in Group One), a significant increase in the scores by the Physical Limitation scale was noted in the group of patients taking nicorandil (Group One). Thus, by the Angina Stability scale the increase in the quality-of-life scores in Group One amounted to 59.5% versus 55% in Group Two (without significant difference). A similar situation was observed in accretion of the scores for the Angina Frequency – 48% vs. 45.2% in Group One and Two, respectively, either without significant differences. The increment of quality-of-life scores by the Physical Limitation scale in Group One patients amounted to 76.2%, being in Group Two patients significantly lower amounting to 55% (p<0.01).

The highest increment of the quality-of-life scores in both groups of patients was registered by the scales reflecting the psychological component of the disease – the Treatment Satisfaction scale and Disease Perception scale (**Figure 1**). The group of nicorandil patients demonstrated a significantly higher increment both by the Treatment Satisfaction scale (99.4% vs. 85.4%, p<0.05) and by the disease perception scale (90.3% vs. 81.8%, p<0.05) compared with the isosorbide nitrate group.

Hence, with relatively equal antianginal and anti-ischaemic effects of both drugs, confirmed by the results of assessing by the scales of angina stability and angina frequency, having resulting in an increase of treatment satisfaction and change in disease perception, nevertheless, such factor as physical limitation on the background of treatment with nicorandil and isosorbide dinitrate was judged by the patients differently. Apparently, control over angina attacks alone is not enough for physical and psychological comfort of the patient with IHD.

scale 1 – physical limitation   scale 4 – treatment satisfaction   * - $p<0.05$ ** - $p<0.01$

scale 2 – angina stability   scale 5 – disease perception

scale 3 – angina frequency

Figure 1: *Dynamics of quality-of-life scores in IHD patients with FC 2-3 stable angina of effort according to the results of the SAQ at 24 weeks after treatment with nicorandil and isosorbide dinitrate*

Table 2: *Quality-of-life scores in IHD patients with FC 2-3 stable angina of effort according to the results of the GHQ inventory before and at 24 weeks after treatment with nicorandil and isosorbide dinitrate*

GHQ scale	Group One (n = 43)			Group Two (n = 41)		
	At baseline	After 24 weeks	Change of the score, Δ%	At baseline	After 24 weeks	Change of the score, Δ%
Somatic symptoms	11.8	6.9$^{⹋}$	-41.5	12.1	9.7$^{⹋}$	-19.8**
Anxiety	11.3	8.6$^{⹋}$	-23.9	11.1	8.4$^{⹋}$	-24.3
Social dysfunction	13.2	9.2$^{⹋}$	-30.3	13.5	11.3$^{⹋}$	-16.3**
Depression	10.7	7.2$^{⹋}$	-32.7	11.0	8.2$^{⹋}$	-25.5
Total score	47.0	31.9$^{⹋}$	-32.1	47.7	37.6$^{⹋}$	-21.2*

Note: $^{⹋}$- significance of differences between the baseline scores and those 24 weeks after treatment;

* - significance of differences between the scores of Group One and Group Two;
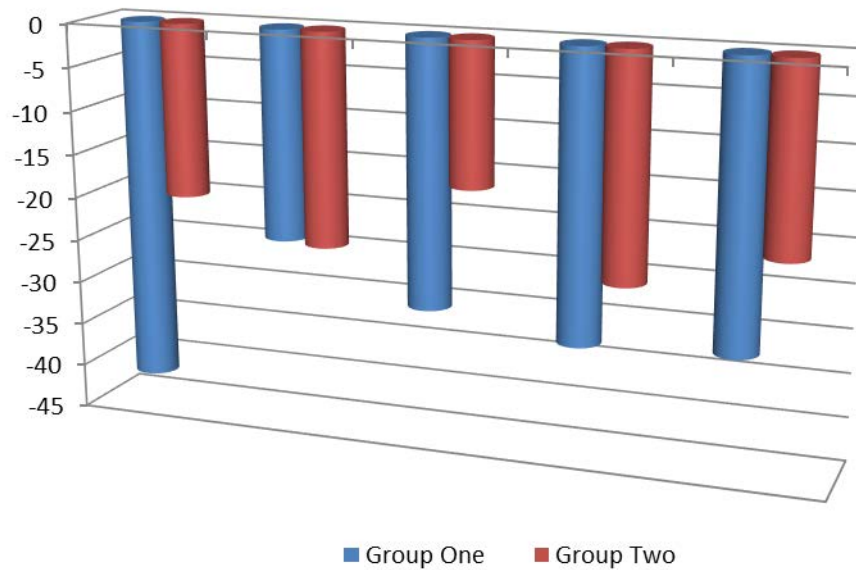
* - p <0.05; ** - p<0.01.

Psychological well-being, as an element of quality of life, was assessed by 4 scales of the GHQ inventory (**Table 2**).

Initially high scores characterising psychological discomfort of the patient were revealed in both groups of patients, without statistically significant differences between the groups. The highest score was observed by the scales of somatic symptoms and social dysfunction both in Group One (11.8 and 13.2 points) and in Group Two (12.1 and 13.5 points).

The observed changes are completely complying with the significance of such disease as IHD in adaptation of the patient to the social environment. Angina attacks, physical limitations induced by angina pectoris attacks lead to deterioration of the emotional state and, consequently, to limitation of performing daily life activities, a decrease of life activity of patients. High scores by the scales of anxiety and depression suggest a low level of mental health of IHD patients with stable angina pectoris.

Analysing the results of the GHQ inventory in both groups of patients after 24 weeks of treatment showed statistically significant improvement of all scores (**Figure 2**).

Mention, however, should be made that the maximal improvement was revealed by the scale of somatisation: a decrease of the level of somatisation by 41.5% in Group One and by 19.8% in Group Two (with the statistically significant intergroup differences, i.e., p<0.01), which was expectedly related to the manifestation of both antianginal and anti-ischaemic efficacy of nicorandil and isosorbide dinitrate. Improvement of the physical component of health resulted in a decrease of manifestations of social dysfunction, which was most apparently manifested in Group One. Manifestations of anxiety and depressive conditions in patients of both groups also decreased, with the results being comparable in both groups. On the whole, the psychological stability (the summary score of the GHQ) in IHD patients with FC 2-3 stable angina pectoris strengthened under the influence of treatment by isosorbide dinitrate, as well as by nicorandil, with a significantly more considerable influence on this parameter exerted by nicorandil.

* - p<0.05   ** - p<0.01

Figure 2: *Dynamics of quality-of-life scores in IHD patients with FC 2-3 angina of effort according to the results of the GHQ inventory at 24 weeks after treatment with nicorandil and isosorbide dinitrate*

CONCLUSIONS

Hence, the results of studying the effect of medicamentous therapy of IHD patients with FC 2-3 stable angina of effort by means of potassium channel activator nicorandil compared with traditional conventional therapy with isosorbide dinitrate on the quality-of-life scores demonstrated that:

1. IHD with FC 2-3 stable angina of effort leads to a significant decrease of the physical and psychological components of the patients' quality of life.
2. The use of potassium channel activator nicorandil and isosorbide dinitrate for treatment of stable angina pectoris exerts a significant positive effect on quality-of-life indices.
3. Improvement of quality of life indices is determined predominantly by direct effect on the physical component of health and associated therewith psychological component of quality of life.
4. Administration of nicorandil for treatment of FC 2-3 stable angina pectoris has statistically significant advantages over conventional therapy with isosorbide dinitrate as to the effect on the physical and psychological components of patients' quality of life.

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