Most patients with shingles complain of severe pain. Within the affected dermatomes, sensation disorders often appear, such as hypersensitivity to touch and dysesthesia. Pain associated with shingles usually subsides spontaneously, however in some patients chronic pain syndrome may persist or recur. Postherpetic neuralgia is defined as pain lasting more than three months after skin lesion appears. It develops in 10-15% of patients who have had zoster, and in up to 50% of patients aged ≥ 60 years (1-3). Neuralgia is usually unilateral and limited to one or several spinal dermatomes. It is described as pain that is spontaneous, stinging, stabbing, burning, shooting or throbbing. It can be continuous or spasmodic in character. The affected area manifests as altered sensitivity to mechanical and thermal stimuli (allodynia, hyperalgesia) significantly limiting the patient’s ability to perform self-care on a daily basis. Neuralgia is exacerbated by cold, rainy weather and stress.

The treatment of postherpetic neuralgia is difficult. The mechanisms involved in neuropathic pain are not clear, possibly complex and show individual differences. In postherpetic neuralgia simple analgesics are usually ineffective. American Academy of Neurology guidelines suggest use of tricyclic antidepressants (amitriptyline, desypramine or clomipramine) – in monotherapy or in conjunction with other drugs, such as gabapentine, pregabaline or opioids (Evidence Based Medicine-EBM level A class I and II) (4).

The aim of this study was to evaluate the usefulness of fentanyl (skin) patches in the combined treatment of postherpetic neuropathic pain according to the above guidelines.
process within the central nervous system; 5) treated for liver or kidney failure; 6) with unstable respiratory and cardiovascular diseases and 7) a history of sensitivity to opioids. The disqualified group also included pregnant women or women capable of conceiving during the observation period and patients who had undergone invasive treatment for postherpetic neuralgia (peripheral blockades, neurosurgical techniques etc.).

The following assessment tools were used in order to evaluate quality of life for patients with chronic postherpetic neuropathic pain:

1. SF-36 questionnaire (short-form health survey with 36 questions) measuring the patient’s health status, the pain experienced, general well-being and the degree to which the disease limits the patient’s ability to perform daily activities (5).

2. The Zung Depression Scale made up of 20 statements divided into two groups. The first one comprises the symptoms of the depressive syndrome. The items in this group rate psychomotor retardation. The second group comprises questions rating depressive symptoms not directly linked to axial depressive symptoms. This scale score can be treated as an index of emotional disturbances and low mood (6).

3. Numeric rating scale (NRS) of pain intensity. On a 10 cm section of the scale the patient circles a number, which corresponds to the current pain intensity (7).

The study was begun after the patients had been informed about its purpose and methods and after any doubts related to the assessment tools had been clarified. The assessment was performed at the first visit. Subsequent assessment was performed once a week over three months after the start of treatment.

Treatment of chronic neuropathic pain syndrome involved use of pharmacotherapy. For each patient the treatment was started with a single 10 mg dose of amitriptyline (Amitriptylinum VP®) taken in the evening, gabapentine (Gabapentin TEVA 100 mg®) 200 mg/24 h orally in two divided doses and fentanyl (skin) patches (Durogesic ®) in the dose of 12.5 µg/hour (one-half of a 25 µg/hour patch).

Statistical analysis was performed with Simstat (Provalis Research 1998) and StatDirect (CamCode 2000) software. The analysis of the obtained results contained the arithmetic mean, standard deviation, minimal and maximal values, as well as assessment of statistical significance of the differences by means of student’s t-test, ANOVA and Wilcoxon. In all the calculations the value p=0.05 was chosen as the threshold for statistical significance.

To assess the treatment results, the Wilcoxon signed-rank test was used, and - where there was little variation of measurements - the sign test. The Spearman’s rank correlation coefficient was applied in order to assess the correlation of the changes in the mental and physical condition of patients with the quantitative effects of pain management (expressed as a difference in pain intensity measured by means of numerical scale at the start of the study and after its completion).

To assess the treatment results, unilateral tests were used, as it seemed plausible to expect positive (or at worst neutral) impact of the treatment on the patients’ condition. The probability values for the type I error in unilateral tests are marked with an asterisk (p*). All other tests are bilateral.

RESULTS

Thirty four patients were qualified for the study - 27 women (79.4%) and 7 men (20.6%) aged 40-94 years (mean 55.5). Most of the patients in this group were aged 60-75 years (Fig. 1).

Nineteen patients (55.9%) were in permanent relationships, the remaining 15 (44.1%) - were single. Nineteen patients had completed secondary or higher education (55.9%). For all the patients in the study group postherpetic neuralgia was the cause of pain. Patients, before they sought treatment, had complained of pain from 6 months to 1 year - 12 patients (35.3%), from 1 year to 3 years - 13 patients (38.2%), more than 3 years - 4 patients (11.8%).

In the twelve weeks of the study the amitriptyline dose was not changed, whereas the amount of gabapentine was in the 200-900 mg/24 h range and was adjusted to the ongoing pain control and patient tolerance. The appropriate fentanyl dose for pain management was found by means of titration, increasing the dose by 12.5 µg/hour every 72 hours. This was conditioned by the frequency of patch replacement in conjunction with observing possible adverse effects. The mean time necessary to determine the effective fentanyl dose producing no adverse effects was approximately 4 weeks (from 2 to 6 weeks). Effective fentanyl dose range was 12.5-100 µg/hour (mean - 62.5 µg/hour).

Subjective feelings of patients - pain intensity and self-perception of health.

Comparison of pain intensity measured using NRS scale before the start and after three months of treatment showed
that all the subjects in the study experienced relief (Fig. 2, Fig. 3).

The median of differences of pain intensity was 3 units (95% confidence interval: 2-3.75) and was significantly different from zero. (Wilcoxon signed-rank test: N=34, p*<0.0001). Taking into account that the NRS scale has a 10-unit range, the obtained result suggests that the mean pain intensity after a 3 month treatment was reduced by 30% compared to the values at entry.

In item 7 of the SF-36 questionnaire the patients assessed pain intensity on a 6-point scale. Comparison of the assessment values before and after three months of treatment suggests that it gave positive results. The median of the differences in the assessment was 1 point (95% confidence interval: 1-1.5; N=34) and this difference was statistically significant (Wilcoxon signed-rank test: p*<0.0001).

Similar results were obtained in the analysis of point 8 of the questionnaire, in which the subjects were to assess on a 5-point scale the degree to which the pain interferes with their work or daily activities. On average, the assessment by patients after a 3 month treatment was higher by 1 point in comparison with the value at the start of treatment (95% confidence interval:1-1.5; N=34; Wilcoxon signed-rank test: p*<0.0001).

There is a slight, but statistically significant trend in the self-perception of health (point 1 SF-36) in the study group. Only three persons (8.8%; N=34) reported that their health status had worsened. On average, on a 5-point scale, patients assessed their health status after three months of treatment by half a point higher (95% confidence interval for the median: 0-0.5; N=34; sign test: p*<0.006). The analysis of the questions in point 10 F-36, probing the patients’ feelings more thoroughly, yielded similar results: slight, but statistically significant trend to assess health status as better after 3 months of treatment (median of differences: 0.5 point on 16-point scale, 95% confidence interval: 0-0.5; N=34; Wilcoxon signed-rank test: p*<0.044).

**Domain of physical functioning**

In general, the 3-month treatment improved the physical functioning of patients. The positive effects of treatment were seen in the analysis of changes in functional capacity of patients (answers to 10 questions in point 3 SF-36). Most patients in the study (72.7%; N=34) reported that their ability to perform activities which required physical effort (climbing the stairs, a long walk) improved (patients scored 1.5 points higher; 95% confidence interval for the median: 1-2.5; N=34), compared to the start of treatment. The difference was not great (considering the 20-point scale of measurement), but the results of the statistical test suggest that this was not accidental. The pain experienced by the

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**Fig. 2.** Pain intensity measured in consecutive patients on NRS scale before the start of treatment and after 3 months of treatment continuation.

**Fig. 3.** Pain intensity measured on NRS scale before the start of treatment and after 3 months of treatment continuation (x, SD) (data average for all patients).
patients after three months of treatment limited and interfered less with daily activity (work, household duties) than before the treatment (Wilcoxon signed-rank test: $p^*<0.0005$; N=34). In point 4 SF-36 on a 4-point scale, the patients rated their activity after a 3-month treatment by 1 point higher than before the start of treatment (95% confidence interval for the median: 0.5-1; N=34).

**Domain of mental functioning**

In point 5 of the questionnaire (SF-36), the subjects in the study group were asked to answer three questions, which made it possible to assess the degree to which emotional difficulties associated with the pain impacted on their everyday activity. Comparing the answers before and after 3 months of treatment suggests that the therapy improved mental functioning of the patients (the median of differences: 0.5 points on a 3-point scale; 95% confidence interval: 0-0.5; N=34; Wilcoxon signed-rank test: $p^*<0.0001$). The changes in the general well-being of patients were strongly correlated. Increase in physical activity was accompanied by positive changes in the mental condition (point 6 of the questionnaire). There was little improvement in the physical domain in the SF-36 questionnaire (Wilcoxon signed-rank test: $p<0.0001$).

**Domain of social functioning**

In point 6 of the SF-36 questionnaire the patients rated on a 5-point scale the impact of their own health status on interactions with other people (relatives, friends, colleagues). After 3 months of treatment self-perception of social functioning in the study group was on average 1 point higher than before treatment (95% confidence interval: 0.5-1; N=34). The test results show that this difference was not accidental. (Wilcoxon signed-rank test: $p^*<0.0001$).

The effects of pain management in the physical, mental and social domains - comparative analysis

The comparison of pain management effects on the physical and mental condition as well as on the quality of patients’ social interactions is difficult by virtue of different range measurement scales. Thus, for example, the average improvement in patients’ functioning by 1 point has a totally different meaning on a 5-point scale than when there are ten points. This effect can be eliminated by standardizing the differences. Such standardization was performed by denoting the difference in measurements at the first and second assessment as a percentage of the measurement scale (Table 1).

The treatment markedly (by 25%) lessens the limitations that severe pain places upon physical activity of the patients (point 4 questionnaire SF-36). Significant, on average 20% improvement, can be observed in the social interactions domain (point 6 of the questionnaire). There was little improvement in general physical capacity and mental condition (e.g., on the Zung scale – practically insignificant), although statistically significant. The analysis of codependence between the changes in quality of life in the emotional (point 9 of questionnaire), physical (point 3) and social (point 6) domains indicates that they were strongly correlated. Increase in physical activity was accompanied by positive changes in the mental condition (Spearman coefficient: $r_s=0.404$; N=34; $p=0.020$), better mental condition was correlated to increased social activity of the patients ($r_s=0.460$; N=34; $p=0.006$) and increased activity in the social domain was accompanied by better physical condition ($r_s=0.400$; N=34; $p=0.021$).

**Table 1. Effects of pain management. The table shows standardized medians of measurement differences of the physical and mental condition and the quality of social interactions in the study at the start of treatment and after three months (N=34; question numbers from SF-36 in the square brackets).**

<table>
<thead>
<tr>
<th>Patients’ life domain</th>
<th>Average % improvement (median of differences)</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical domain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daily activity [3]</td>
<td>7.5</td>
<td>5 - 12.5</td>
</tr>
<tr>
<td>Pain as a factor limiting and worsening activity [4]</td>
<td>25.0</td>
<td>12.5 - 25.0</td>
</tr>
<tr>
<td>Mental domain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emotional difficulties [5]</td>
<td>0</td>
<td>0 - 16.7</td>
</tr>
<tr>
<td>General wellbeing [9]</td>
<td>10</td>
<td>5.6 - 15.6</td>
</tr>
<tr>
<td>The Zung depression scale</td>
<td>3.8</td>
<td>1.3 - 6.3</td>
</tr>
<tr>
<td>Social domain</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Table 2. Analysis of correlation between change in pain intensity measured on VAS scale in the three months of treatment and changes in the physical, mental and social life domains of patients (N=34; question numbers from SF-36 in the square brackets). Spearman’s rank correlation coefficients are given (rs) and bilateral probability values of type I errors.**

<table>
<thead>
<tr>
<th>Change in pain intensity VAS:</th>
<th>rs</th>
<th>$p$</th>
<th>Interpretation: where pain intensity decreases:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in daily physical activity [3]</td>
<td>0.409</td>
<td>0.018</td>
<td>...physical activity increases</td>
</tr>
<tr>
<td>Change in general wellbeing [9]</td>
<td>0.520</td>
<td>0.002</td>
<td>...general wellbeing improves</td>
</tr>
<tr>
<td>Result changes on the Zung scale</td>
<td>0.515</td>
<td>0.002</td>
<td>…depression symptoms decrease</td>
</tr>
<tr>
<td>Change in social activity [6]</td>
<td>0.564</td>
<td>0.001</td>
<td>...social activity increases</td>
</tr>
</tbody>
</table>

The comparison of pain management effects on the physical and mental condition and the quality of social interactions is difficult by virtue of different range measurement scales. Thus, for example, the average improvement in patients’ functioning by 1 point has a totally different meaning on a 5-point scale than when there are ten points. This effect can be eliminated by standardizing the differences. Such standardization was performed by denoting the difference in measurements at the first and second assessment as a percentage of the measurement scale (Table 1).
The effect of pain management and positive changes in patients' quality of life

The correlation of analysis makes it possible to see how a decrease in pain intensity following treatment relates to positive changes in the mental domain. The more effective the treatment (i.e. the more the pain intensity over three months of treatment decreased), the better was the patients’ quality of life in the physical, social and mental domains (Table 2).

DISCUSSION

The use of opioids in the neuropathic pain has the unquestioned advantages of pain reduction, which significantly improves quality of life, and at the same time - better daily functioning.

It is important that the decision about the treatment be made collaboratively with the patient after defining his expectations and considering his social and family situation. The factors calling for inclusion of opioids in the treatment are: chronic, severe pain resistant to treatment, limiting the patient’s functioning, lowering quality of life, causing depression, insomnia and impossibility to use another form of therapy (8, 9).

The first stage of the opioid treatment is a trial period, lasting from 1 to 6 weeks, designed to determine the optimal drug dose, minimizing side effects and monitoring the following treatment parameters: pain intensity, functioning in daily activities (10). It is important that the patient be given the opportunity to contact the doctor frequently in order to clarify any treatment related issues (11). The length of treatment is mostly dependent on the patient’s needs, their acceptance and ability to cope with adverse effects (12, 13).

Fentanyl is a very strong analgesic from the opioid antagonist receptor group (strong antagonist of μ receptor, weak antagonist of delta and kappa receptors). It has very little effect on the cardiovascular system. In the long-term treatment, it is used in the form of patches. The (skin) patch applied to the skin is first absorbed after about 15 hours and then the appropriate dose gets into the blood. After a period of initial dose adjustment in blood serum, transdermal fentanyl is titrated over 6 weeks, based on the individual patient requirements and possible adverse effects which would prevent further dose escalation.

The extension of drug titration period is dependent on the frequency of patch replacement (72 hours). It is of utmost importance in the long-term treatment as the convenience of taking drugs means no discomfort in attaining the principal goal - quality of life (14).

There are many ways of assessing quality of life, however it appears that the questionnaire is the most useful type. As the assessment of quality of life is based on the data collected from the patient, it is largely subjective. Patients should know that they do not have to suffer and they have the full right to demand it from the doctor. Chronic pain is devastating to the body, making the patient suffer unnecessarily. If the pain lasts a long time, it can compromise not only the patient’s mental condition, but also physical, causing irreversible changes. Neuropathic pain is the cause of much suffering and has a negative impact on the patient’s social and mental functioning. High prevalence of neuropathic pain, its multifactorial etiology, recurrent character and persistence in chronic cases suggest that simple clinical solutions are inadequate (15). Assessment of quality of life can aid in the treatment optimization.

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