Hydromorphone in elderly patients with polypathia and with severe pain

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Summary

There continue to exist serious deficiencies in the analgesic therapy of elderly patients and patients with polypathia and severe pain. Orally administered controlled-release hydromorphone (see Note 1) appears to be particularly suitable for this patient group due to its pharmacological and metabolic benefits. The aim of the present prospective, multicentre study was to analyse the effects of hydromorphone therapy on quality of analgesia and potential side effects.

Patients and methods. 567 elderly patients with severe, predominantly tumour-related or musculoskeletal pain were included in this study. The majority of these patients had received prior analgesic therapy. The following parameters were measured before initiating treatment with orally administered controlled-release hydromorphone and at three further assessments during the therapy: the daily dose required, intensity of pain (measured on the Numeric Rating Scale: 0 = no pain to 10 = worst pain imaginable); typical opioid-related side effects such as tiredness, nausea, vomiting, constipation, pruritus; and severe adverse events, e.g. hospitalisation due to tumour therapy, dyspnoea, urinary retention. Pain-related interferences were assessed in seven spheres of life: general activity, mobility, social relationships, enjoyment of life, mood, resilience, sleep. Furthermore, the quality of life was assessed by means of the 'Brief Pain Inventory' developed by Cleeland as well as in diaries. A differentiated final assessment with regard to efficacy, tolerability and compliance was performed by the physician on completion of the study using a 5-point scale.

Results. Within three weeks of therapy with controlled-release hydromorphone, intensity of pain was reduced by 65.7% on average, from 7.0 at the beginning to 2.4 at the final assessment. Typical opioid-related side effects frequently present at the beginning of the study decreased during therapy with hydromorphone by 88.6% on average. Therapy resulted in a reduction in pain-related interference by 50.7% and thus in a marked improvement in quality of life. In the final assessment by the physician both, efficacy and tolerability, as well as compliance were rated as 'very good' or 'good' in more than 80% of patients.

Conclusion. The advantages of controlled-release hydromorphone offer an appropriate analgesic therapy even for elderly patients and patients with polypathia in the clinical and outpatient setting. Hydromorphone was well tolerated and effective in the treatment of severe pain. Quality of life improves substantially as a result of a marked decrease in opioid-related side effects and interferences in daily life. Prior to inclusion in this study, only a few patients with severe pain were treated with WHO-level III opioids indicating that blatant inadequacies in tumour pain therapy continue to exist.

Key words: Elderly patients; polypathia; inpatient and outpatient treatment; severe pain of different genesis; controlled-release hydromorphone; opioids; quality of life.

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introduction There continue to exist serious inadequacies in the pain therapy of elderly patients. Polypathia frequently associated with elderly patients appears to be an obstacle to adequate pain therapy. The most frequent causes of severe and persistent pain in elderly patients are tumours and diseases of the musculoskeletal system. Statistics indicate that the elderly experience pain significantly more frequently in comparison with younger patients and achieve higher scores for physical discomfort on the subjective complaints list. Results of representative surveys of the elderly German population using the Giessen Subjective Complaints List revealed that over 90% of patients aged more than 75 years complain of pain in the region of the body axis and joints. Moreover, apart from their chronic pain in the region of the musculoskeletal system, elderly patients have at least one further diagnosis. On average they have diagnoses in five other organ systems. According to a study based on the Swedish population about one-third of very elderly patients suffered from severe and very severe persistent pain. Up to 80% of all patients with advanced tumour diseases suffer from severe pain and thus their quality of life is markedly impaired. Thirty to forty percent of patients continue to experience pain even during treatment.

Polypathia is associated with multiple medication, so potential drug interactions complicate the therapy of chronic pain and requires the physician's full attention. In Germany, the number of deaths related to drug-induced adverse events and side effects is estimated to be 57,000. Among other causes, these can be attributed to drug interactions. About 28,000 of these cases (>50%) can be classified as avoidable (Scholz database). Thus, there is an increasing need for the use of effective and easily administered analgesics with a favorable safety and interaction profile. To date morphine has been the gold standard in the treatment of severe and most severe pain, which all other analgesics had to equal. Sufficient analgesia, however, cannot be achieved in all patients with morphine. Moreover, many patients experience the known side effects of morphine. In this context modern opioids, such as hydromorphone, are an alternative. Hydromorphone as a WHO level III opioid is available in a controlled-release formulation. Its analgesic potency is 7.5 times higher than that of morphine and it exhibits no ceiling effect. In contrast to morphine, hydromorphone therapy is associated with fewer opioid-induced side effects. Particularly in the elderly and in patients with polypathia, the safety of therapy with controlled-release hydromorphone has been demonstrated. Low plasma protein binding (only 8%), which is an important decision criterion in therapy of patients with polypathia, contributes to its safety. Usually, elderly and patients with polypathia are given a high number of other pharmaceuticals, which frequently have high plasma protein binding and compete, in case of concomitant administration, for plasma protein binding sites. This can result in variations in free concentrations of active ingredient and thus provoke adverse drug interactions. There are no indications that hydromorphone does impair the action of concomitant medications, which are frequently required in these patients, or that its own action is impaired. This could be attributed to its very low plasma protein binding.

Approximately 95% of hydromorphone is metabolised by glucuronidation in the liver to hydromorphone-3-glucuronide. In contrast, morphine is metabolised predominantly to morphine-6-glucuronide, which has equal analgesic activity and which can accumulate at excessive levels in patients with renal impairment. Experience to date indicates that hydromorphone is not associated with the accumulation of active metabolites. This implicates that there is no risk of overdose or excessive sedation even in these patients.
It is particularly important that the metabolism of hydromorphone does not involve cytochrome P450 and thus no interactions occur with medications which inhibit or activate this system.

The aim of the present study was to gain clinical experience of the analgesic efficacy, frequency of opioid-induced side effects and quality of life in elderly patients with polyopathia and with tumour diseases and diseases of the musculoskeletal system after changing to oral controlled-release hydromorphone.

Patients with severe pain of different genesis were treated and monitored in this prospective, multicentre study performed over three weeks in an outpatient or clinical setting. Prior to the study with oral hydromorphone therapy and at the three following assessments, daily hydromorphone doses, intensity of pain, side effects and adverse events as well as concomitant symptoms and pain-related interference, in accordance with the Brief Pain Inventory developed by Cleeland, were assessed in the context of standardised patient interviews and examinations. In addition, intensity of pain, measured on a Numerical Rating Scale (NRS) from 0 (no pain) to 10 (worst pain imaginable) were recorded in standardised pain questionnaires. Moreover, pain-related interference in seven spheres of life such as general activity, mood, mobility, resilience, social relationships, sleep and enjoyment of life were measured using a NRS. Individual parameters were summarised as a sum score in order to determine quality of life (0 = no interferences, 70 = worst interferences). At the end of the observational study a final assessment of efficacy, tolerability and compliance was completed by the physician using a 5-point scale (very good, good, moderate, bad, not specified).

The initial daily dose of controlled-release hydromorphone was generally 2 × 4 mg. In case of high baseline doses of level III opioids, dosage was selected in accordance with the recommendations for changing medication. If pain relief did not last for 12 hours the single dose could be increased to 8 mg.

The statistical analysis was performed using descriptive statistical comparisons. Location and scatter parameters (mean, variance, minimum, 1st quartile, median, 3rd quartile, maximum) were given for continuous variables. For categorical variables absolute and relative frequencies were given. Side effects were recorded in accordance with the requirements of the German Federal Institute for Drugs and Medical Devices, notified regularly to the sponsor and in summary presented and analysed. Patients were included in the efficacy analysis only if the date specifications were within the designated range, which means that the difference between entry date and the 2nd assessment date or between the 2nd and 3rd assessment date was 1–7 days and the difference between the 3rd and final assessment was 3–28 days. Data consistency was checked by performing a plausibility test.

Demographic data (Table I)
A total of 567 patients were enrolled in the study: 300 of the patients were female and the remainder male. Mean age was 63.5 years (range: 26 to 95 years), just over half of whom were between 60 to 79 years (51.0%). About two-thirds of the patients were more than 60 years old. In most instances data from more than four weeks' therapy (maximum: 135 days) were available. Mean duration of therapy was 22.5 days, but 75% of patients were treated for 30 days. In the majority of patients (449 = 79.2%) dosage was adjusted in an outpatient setting and further treatment was also given there. Patients were predominantly treated by general practitioners (47.8%).
Table I.
Demographics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. of patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total no. of patients</td>
<td>567</td>
<td>100</td>
</tr>
<tr>
<td>Female</td>
<td>300</td>
<td>52.9</td>
</tr>
<tr>
<td>Male</td>
<td>265</td>
<td>53.8</td>
</tr>
<tr>
<td>Gender unknown</td>
<td>2</td>
<td>0.4</td>
</tr>
<tr>
<td>Age (yrs, range)</td>
<td>63.5 (26–95)</td>
<td>–</td>
</tr>
<tr>
<td>Age &gt; 65 yrs</td>
<td>211</td>
<td>37.2</td>
</tr>
<tr>
<td>Outpatient</td>
<td>449</td>
<td>79.2</td>
</tr>
<tr>
<td>Inpatient</td>
<td>74</td>
<td>13.1</td>
</tr>
<tr>
<td>Outpatient and inpatient</td>
<td>36</td>
<td>6.4</td>
</tr>
</tbody>
</table>

Body Mass Index classified in:

- Normal weight: 264 patients (46.6%)
- Overweight: 203 patients (35.8%)
- Obesity: 54 patients (9.5%)
- Underweight: 28 patients (4.9%)
- Not available: 18 patients (3.2%)

Table II.
Most frequent underlying disease*  

<table>
<thead>
<tr>
<th>Disease</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neoplasms</td>
<td>303</td>
<td>53.4</td>
</tr>
<tr>
<td>Musculoskeletal disease</td>
<td>251</td>
<td>53.1</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>196</td>
<td>34.9</td>
</tr>
<tr>
<td>Diseases of the nervous system</td>
<td>74</td>
<td>13.1</td>
</tr>
</tbody>
</table>

* Multiply entry possible.

pain therapists (19.6%) or specialists in internal medicine (15.7%); in the clinic they were generally treated by oncologists (34.6%) and specialists in internal medicine (10.9%).

The most frequent diseases that caused pain were tumour diseases (53.4%), generally at an advanced stage, diseases of the musculoskeletal system (53.1%) and of the nervous system (13.1%). Multiple entries were frequent in these patients often with polypathia. Thus 70.5% of patients had at least two and possibly as many as nine different diseases. The most frequent underlying diseases included neoplasms (53.4%), cardiovascular disorders (34.9%) and diseases of the muscle, skeleton and connective tissue (53.1%) (Table II). Non-tumour patients suffer most frequently from diseases of the muscle, skeleton and connective tissue (79.54%), cardiovascular disorders (40.9%) and endocrine, nutritional and metabolic diseases (16.6%). Concomitant medication for these diseases was not recorded. In 46% of patients pain had been present for more than one year at the start of study, in 21.3% for more than 5 years. 19.4% suffered from pain for less than one month. 91.5% of patients had an analgesic pre-treatment with substances other than hydromorphone. The highest level of analgesic pre-treatment according to the WHO classification consisted of analgesics of level I for 308 patients (54.3%), level II for 158 patients (27.9%) and level III for 61 patients (10.8%). 30 patients (5.3%) had received no analgesic pre-treatment. 455 of the 567 patients (80.2%) were included in the efficacy analysis.

Medication
At the beginning of the study 509 patients (89.6%) were taking 4 or 8 mg hydromorphone b.i.d. At the end of the study this figure had dropped to
441 patients (= 79.0%). The initial mean daily dose of hydromorphone was 12.4 ± 12.9 mg. The mean daily dose increased to 16.7 ± 68.5 at the 2nd assessment and to 21.8 ± 73.9 mg at the end of the observation period (Table III). Mean dose differed according to prior therapy (Table IV). Patients who had been given prior analgesic therapy at WHO level I received a mean dose of 11.2 mg hydromorphone on the inclusion date. By completion of the study, the dose doubled to 22.7 mg. In patients who had received prior treatment at WHO levels II and III, mean dose increased from 10.5 to 14.8 mg or from 22.2 to 36.8 mg, respectively.

In parallel to the increase in hydromorphone dose, the proportion of patients who needed further analgesics (predominantly at WHO level I) in addition to controlled-release hydromorphone decreased during the study. Whereas 59.3% of patients were taking further analgesics at the start of treatment with hydromorphone, this proportion was only 36.6% at the final examination (Table V). Likewise the total number of additional analgesics taken dropped during treatment. At the start of the study 45.2% of patients took more than one and up to four additional analgesics. By the end this proportion was reduced to 6%. At this point in time 63.4% of patients were taking hydromorphone as the only analgesic.

Three hundred and thirty-seven patients were treated with concomitant systemic medication, such as laxatives, antiemetics, tranquilisers and neuroleptics, on the inclusion date. The number of patients who supplied this kind of information remained nearly constant up to completion of the study (n = 326). Between the inclusion date and the final assessment, intake of laxatives dropped from 61.7% to 0.3%, that of antiemetics from 38% to 15.6%.

Table III.
Mean daily dose of hydromorphone during treatment

<table>
<thead>
<tr>
<th></th>
<th>mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial assessment</td>
<td>12.4 ± 12.9</td>
</tr>
<tr>
<td>2nd assessment</td>
<td>16.7 ± 68.5</td>
</tr>
<tr>
<td>3rd assessment</td>
<td>19.9 ± 71.2</td>
</tr>
<tr>
<td>Final assessment</td>
<td>21.8 ± 73.9</td>
</tr>
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</table>

Table IV.
Mean hydromorphone doses related to pre-treatment

<table>
<thead>
<tr>
<th>Pre-treatment/WHO-level</th>
<th>N</th>
<th>Daily dose in mg Initial assessment</th>
<th>Daily dose in mg Final assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>WHO I</td>
<td>307/304**</td>
<td>11.2 ± 7.0</td>
<td>22.7 ± 9.6</td>
</tr>
<tr>
<td>WHO II</td>
<td>158/155</td>
<td>10.5 ± 7.6</td>
<td>14.8 ± 11.0</td>
</tr>
<tr>
<td>WHO III</td>
<td>61</td>
<td>22.2 ± 31.9</td>
<td>36.8 ± 65.3</td>
</tr>
</tbody>
</table>

* One patient not specified.
** Initial/final.

Table V.
Additional analgesics during treatment

<table>
<thead>
<tr>
<th>Date</th>
<th>% of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-treatment</td>
<td>91.5</td>
</tr>
<tr>
<td>Initial assessment</td>
<td>59.3</td>
</tr>
<tr>
<td>2nd assessment</td>
<td>43.2</td>
</tr>
<tr>
<td>3rd assessment</td>
<td>39.0</td>
</tr>
<tr>
<td>Final assessment</td>
<td>36.6</td>
</tr>
</tbody>
</table>
and that of tranquillisers and neuroleptics from 4.5% to 3.4%. Reduction of all named concomitant medications had already commenced at the 2nd assessment, at which time only 2% of patients were taking laxatives, 18.8% antiemetics and 2% tranquillizers and neuroleptic agents.

**Efficacy**

Within 21 days the intensity of pain recorded by the physician from 7.0 ± 1.5 at the inclusion date to 4.4 ± 2 at the 2nd assessment. At the 3rd and final assessment the scores decreased to 3.2 ± 1.9 and 2.4 ± 1.8, respectively (Fig. 1). Intensity of pain was hence reduced during therapy with hydromorphone by 65.7% on average within three weeks.

In parallel to this, the 24 h mean pain intensity recorded on the pain questionnaire was reduced by 54.1% from 6.1 ± 1.2 to 2.8 ± 1.9. Even the most severe pain within the last 24 hours decreased from an average of 7.4 ± 1.7 (maximum: 10) in the first pain questionnaire to 3.6 ± 2.2 in the last pain questionnaire, corresponding to a decrease of 51.3%. In the final assessment by the physician, the efficacy of pain therapy with hydromorphone was assessed to be good to very good in 87% of cases (Table VI).

Two hundred and fifty-seven patients mentioned pain-related interference in the seven spheres of life surveyed in the pain questionnaire. The greatest improvements were seen in enjoyment of life (interference decreased by 4 scores on average), mood (−3.7) and sleep (−3.6). Sum scores obtained from all parameters reduced from 45.4 ± 13.0 at the beginning to 22.4 ± 14.4 at the final examination (Fig. 2). Thus, therapy induced 50.7% improvement of quality of life.

**Pain intensity (NRS) n = 567 patients**

![Image of bar chart showing pain intensity over time](image)

**Figure 1.** Mean pain intensity assessed by using the Numerical Rating Scale (NRS).

**Table VI.**

Final assessment by the physician, data in % (n = 455)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Good/very good</th>
<th>Satisfactory</th>
<th>Bad</th>
<th>Not available</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efficacy</td>
<td>87.03</td>
<td>6.59</td>
<td>2.42</td>
<td>3.96</td>
</tr>
<tr>
<td>Safety</td>
<td>87.96</td>
<td>5.27</td>
<td>1.98</td>
<td>5.05</td>
</tr>
<tr>
<td>Compliance</td>
<td>88.27</td>
<td>4.62</td>
<td>1.32</td>
<td>5.49</td>
</tr>
</tbody>
</table>
Hydromorphone in elderly patients

Degree of impairment
Brief Pain Inventory, n = 257 (56.5% of all patients)

Figure 2. Mean extent of pain-related interferences in different spheres of life.

Tolerability
The typical opioid-related symptoms of tiredness, nausea, vomiting and constipation, which were actively enquired, were markedly reduced in most patients by changing from other analgesics to hydromorphone. At the inclusion date, 361 (63.7%) of patients were affected by one of these symptoms; at the end of therapy this number was reduced to 41 (7.2%). Related to the number of patients this is equivalent to a reduction in typical opioid side effects of 88.6%. Only in 26 patients (4.6%) symptoms (predominantly constipation) increased during therapy. In detail, mentions of tiredness/fatigue reduced from 241 cases (42.5%) to 17 cases (3.0%), those of nausea from 198 (34.9%) to 10 (1.8%), those of constipation from 162 (28.6%) to 20 (3.5%) and those of vomiting from 80 (14.1%) to 7 (1.2%) (Fig. 3).

Thirteen cases of death occurred, 9 during the observation phase and 3 after it had ended. In one patient, time of death was unclear. A causal relation with hydromorphone therapy could not be established in any of these patients. All 13 patients involved were carcinoma patients.

Serious adverse events e.g. hospitalisation due to tumour therapy, dyspnoea, urinary retention, were recorded in seven patients with malignant diseases, two patients with polypathia and one with herpes zoster. A positive causal connection with therapy was recorded for only one patient with urinary retention, in which catheterisation was necessary. A total of 74 patients discontinued hydromorphone therapy, 3.2% of whom (n = 18) did so because their pain was alleviated, 2.1% (n = 12) because of inadequate efficacy and 4.1% (n = 23) because of adverse events such as pruritus or urinating difficulties.

In the final assessment by the physician, tolerability and compliance were assessed as good to very good in 88.0% and 88.3%, respectively. Only in 1.3% of cases was compliance assessed as poor.

discussion
The results of the present prospective study provide striking confirmation of the results of the available clinical studies, in which hydromorphone was proved to be an exceptionally effective analgesic with a favourable side effect profile in tumour patients with severe to most severe pain.10,11,13–15,17 In the present study as well, the patients treated with twice-daily hydromorphone experienced significant relief from severe pain. Opioid-induced side effects also decreased significantly. Consequently, the optimisation of analgesia and
reduction of side effects resulted in a significant improvement in quality of life in elderly patients with polypathia: 53.4% of patients were suffering from tumour pain and 53.1% of pain related to the musculoskeletal system. In addition, a high percentage of patients (70.5%) had at least two and possibly up to nine different diseases that were treated with appropriate medication. Already at the 2nd assessment after administration of controlled-release hydromorphone, intensity of pain, degree of interference and number of side effects had decreased significantly. This demonstrates that in the majority of patients, despite prior analgesic therapy (91.5%), management of pain was less than optimal. It is noteworthy that only 10.8% of patients were stabilised by a WHO level III analgesic. This is telling evidence that in Germany analgesic treatment regime for tumour patients and patients with pain related to the musculoskeletal system is quite clearly inadequate.

During treatment with hydromorphone intensity of pain had decreased by 65.7%. This significant reduction applied to all indications in the patient group. The favourable results were supported in the final assessment by the physicians, who assessed the efficacy of pain therapy with hydromorphone as good to very good in 87% of cases.

The efficacy of the pain therapy studied was clearly evident, particularly in the reduction in use of rescue medication. In parallel to the reduction in additional analgesic medication, as expected, the mean daily dose of hydromorphone increased continuously during the three-week treatment period. This can be explained by the fact that the dose of hydromorphone had to be titrated over three weeks in order to find the ideal dose for analgesic efficacy. A further important reason is the course of the disease. The significant reduction in additional analgesics in this study constitutes a clear benefit of controlled-release hydromorphone in elderly patients with polypathia. Multiple medication conceals the risk of adverse interactions, a risk on which the beneficial pharmacological and metabolic profile of hydromorphone has no negative impact. In addition, reduced hepatic and renal blood flow is to be assumed in elderly patients due to impairments in metabolism and synthesis. In tumour patients in particular, renal function decreases as the disease progresses, and active metabolites such as the 6-glucuronide of morphine accumulate and cause side effects. In these patients, therefore, it is unfavourable to use several analgesics, particularly those with active metabolites, in addition to the high number of other medications which are already being taken. According to the results presented in this study, pain therapy with hydromorphone, which does not lead to an accu-
Hydromorphone in elderly patients

Hydromorphone in elderly patients has a high value in the treatment of tumour patients and in particular in elderly patients.

The special pharmacological and metabolic properties of hydromorphone were revealed by the low frequency of opioid-induced side effects. At the beginning of the observational study over 60% of patients had typical opioid-related symptoms such as tiredness, nausea, vomiting and constipation, which were related to prior analgesic medication. After changing to an appropriate hydromorphone dose and continuing suitable concomitant medication, the typical opioid-related symptoms could be markedly reduced already within three days. At the end of the study typical opioid-related symptoms were observed in less than 10% of patients. Once again this clearly indicates that patients previously treated with other opioids with their typical side effects clearly benefit from changing therapy to hydromorphone. Although only 10.8% of patients were pre-treated with highly effective opioids, opioid-induced side effects also occurred with WHO level II agents and adjuvants. Recent clinical studies suggest that not only the intensity of pain but also opioid-induced side effects, such as perceptual disorders, hallucinations, nausea and vomiting could be markedly reduced by changing the opioid to hydromorphone. Particularly, in palliative care, patients with impaired renal function switching from other opioids to hydromorphone because of intolerable side effects results in significant improvement. Lee et al. were able to demonstrate that both intensity of pain and frequency/quality of side effects markedly improved in tumour pain patients with renal insufficiency after changing to hydromorphone. The results of the present study provide an impressive confirmation of their results. The symptoms of tiredness, nausea and constipation, which interfere with quality of life, were those to be most markedly improved. As already known hydromorphone causes constipation less frequently than morphine. This is also apparent in the present study. It was possible to reduce laxative use within a few days after the beginning of therapy with controlled-release hydromorphone. A similar reduction was observed in all systemic concomitant medications, but was particularly striking with the laxatives. This is unequivocal clinical evidence that hydromorphone causes constipation less frequently than level II and other level III analgesics. In this context it is important to refer to the fact that co-analgesics and WHO level I preparations may also lead to constipation. Thus, before the start of the study, 28.6% had constipation; at the end this number was reduced to 3.5%. Besides laxatives, a significant reduction in the use of tranquilizers, antiemetics and neuroleptics could be demonstrated and was still evident at the end of the study. Again, this clearly shows that hydromorphone therapy leads to a marked reduction of concomitant medications, which is a great advantage in elderly patients with polypathia.

Concomitantly with the reduction in pain intensity and side effects, quality of life (general activity, mobility, social relationships, enjoyment of life, mood, resilience, sleep) improved markedly. This was also shown by the fact that 80% of patients could be treated with controlled-release hydromorphone on an outpatient basis, preventing them from hospitalisation. At the final examination, compliance was recorded as good to very good in almost 90% of cases. This means that even in elderly and patients with polypathia, whose compliance may be altered due to multiple medications frequently necessary and to cognitive impairments, therapy with oral hydromorphone in a controlled-release formulation can be successfully used.
Hydromorphone offers a high degree of safety and a favourable side effect profile in tumour pain therapy and in treatment of chronic pain. Thereby, an improvement in quality of life can be achieved in elderly patients and those with polypathia studied here. The results of the present study clearly demonstrate that controlled-release hydromorphone provides an excellent treatment option for patients with severe pain. Because of its pharmacological and metabolic benefits it can be used appropriately and without problems in the home environment, which is especially important for the quality of life experienced by tumour pain patients.

**References**
