Rapid discontinuation of hypnotics in terminal cancer patients: A prospective study

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Summary

Purpose: To determine the proportion of patients receiving hypnotics upon admission to a palliative care unit, the frequency and intensity of withdrawal symptoms after rapid hypnotic discontinuation, and the effect of discontinuation on insomnia and cognitive failure.

Patients and methods: 120 consecutive admitted patients. Rapid hypnotic discontinuation (1-4 days) was attempted. Insomnia (visual analogue 0 = best, 100 = worst for insomnia, restedness during the morning and difficulty falling asleep), cognition (Mini-Mental State Questionnaire), and withdrawal signs were monitored.

Results: Upon admission, 92/120 patients (77%) had been receiving hypnotics for a mean of 11 (standard deviation = 8) weeks. 4/92 patients (4%) refused hypnotic discontinuation. Acute mild withdrawal was observed in 2/88 patients (2%). The intensity of insomnia was not significantly different, while cognition significantly improved after hypnotic discontinuation.

Conclusion: A large proportion of terminal cancer patients receives hypnotic drugs chronically. These drugs are probably not useful for the treatment of their insomnia, and rapid discontinuation can be safely achieved in most patients.

Key words: cancer, cognitive function, hypnotic, visual analogue scales

Introduction

Hypnotic drugs are considered useful in the treatment of transient (2-3 days) insomnia. These drugs may also be used on an intermittent basis and as adjunctive treatment in both short-term (<3 weeks) and chronic (>3 weeks) insomnia [1]. Long term use of hypnotics is frequently associated with excessive sedation and cognitive failure [2, 3]. These effects are more common among elderly patients (PTS) [4]. Advanced cancer PTS frequently develop cognitive failure even when they are not receiving hypnotics [5]. The purpose of this prospective open study was to determine the proportion of PTS receiving hypnotics upon admission to a palliative care unit, the number of PTS and families who accepted hypnotic discontinuation, the frequency and intensity of withdrawal symptoms, and the effect of rapid discontinuation on insomnia and cognitive function.

Patients and methods

One hundred and twenty consecutive PTS (mean age 62; standard deviation, SD = 12; 62 females) with terminal cancer (defined as locally recurrent or metastatic cancer showing no response to anti-neoplastic therapy) were admitted to the Palliative Care Unit, Edmonton General Hospital between April 1990 and February 1991. PTS were admitted to this tertiary referral unit for the management of different symptoms associated with advanced cancer. One hundred and twelve PTS were admitted from acute care hospitals (93%) and 8 PTS from home (7%). All PTS were receiving opioid analgesics for cancer pain and were considered to be alert and able to communicate with the admitting physician. Upon admission, all PTS and available family were assessed by one of the investigators and were provided information on the management of chronic insomnia. They were told that unless they refused, we would attempt to discontinue all hypnotic therapy rapidly. The mean equivalent hypnotic starting dose per night was calculated for all hypnotics according to the Canadian Pharmaceutical Manual [6]. If a patient was receiving up to the equivalent starting daily dose of a certain hypnotic, the hypnotic was discontinued. If the dose was higher than the one proposed by the Canadian Pharmaceutical Manual, the dose was reduced by 50% every 24-48 hours attempting to complete discontinuation of the drug in approximately 4 days. If a patient refused to reduce or discontinue hypnotics he/she was maintained at the same dose they were receiving upon admission. PTS were assessed daily for signs of withdrawal. Mild withdrawal was defined as the presence of increased restlessness, anxiety, profuse sweating, tremors, increased sensitivity to taste, smell or light, or nightmares. Severe withdrawal was diagnosed as severe agitation, delirium, hyperthermia, or grand mal seizures. If withdrawal was detected, hypnotic dose was re-increased and an attempt for slower discontinuation was made.

A complete assessment of the severity of insomnia was performed during days 1, 4 and 7. This included visual analogue scales (0 = best symptom control, 100 = worst symptom control) for intensity of insomnia, restedness during the morning and difficulty falling asleep. In addition, a global rating of the intensity of insomnia was completed by the patient (0 = no importance; 1 = slight importance; 2 = some importance, consistent problem; 3 = moderate importance, consistent problem; 4 = much importance, good deal of a problem; 5 = very important; 6 = great importance.)
All PTS underwent the assessment of cognitive function using the Mini-Mental State Questionnaire during day 1, 4 and 7. Values of 80% or higher are considered normal [7]. The daily dose of opioid analgesics were expressed as the mean equivalent daily dose of parenteral morphine [8]. The results of the insomnia and cognitive assessments in PTS who received hypnotics versus those who did not receive hypnotics were analyzed using two-tailed non-paired ‘t’ test. Changes in the results of different assessments over time in the same group of PTS were analyzed using two-tailed paired ‘t’ tests. Proportions were compared using chi-square test. Data were analyzed according to the Statistical Package for the Social Sciences [9].

Ninety-two/one hundred and twenty PTS (77%) had been receiving hypnotics for an average of 11 ± 8 days upon admission. The hypnotics were lorazepam (35 PTS), triazolam (22 PTS), chloral hydrate (11 PTS), temazepam (11 PTS), flurazepam (7 PTS), clonazepam (3 PTS) and diazepam (3 PTS), respectively. The mean equivalent hypnotic dose per night was 1.6 (SD ± 1). Four/ninety-two PTS (4%) receiving hypnotics refused to discontinue or reduce their daily dose. Two/eighty-eight PTS (2%) in whom discontinuation was attempted presented with mild acute withdrawal symptoms that required a re-increase in the dose of hypnotic; both of these PTS could ultimately discontinue benzodiazepines. No PTS developed severe withdrawal.

There was no significant difference in the visual analogue scale or global rating for insomnia between the 92 PTS receiving hypnotics and the 28 PTS who were not receiving hypnotics upon admission. The 88 PTS in whom hypnotics were discontinued presented no significant change by day 4 and a decrease by day 7 in the intensity of insomnia, and showed a significant improvement in cognition during days 4 and 7 as compared to day 1, respectively (Table 1). Before hypnotic discontinuation, 13/88 PTS rated their insomnia as ‘very important’ or ‘of great importance’ (15%). After the discontinuation of hypnotics, 11/88 PTS scored insomnia as ‘very important’ or of ‘great importance’ (13%).

Table 1. Change in insomnia and cognition over time during discontinuation of hypnotics.

<table>
<thead>
<tr>
<th></th>
<th>Day 1</th>
<th>Day 4</th>
<th>Day 7</th>
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</thead>
<tbody>
<tr>
<td>Number of PTS</td>
<td>88</td>
<td>88</td>
<td>87*</td>
</tr>
<tr>
<td>Restedness during the morninga (0–100 mm)</td>
<td>35 ± 19</td>
<td>32 ± 20</td>
<td>33 ± 19</td>
</tr>
<tr>
<td>Difficulty falling asleepb (0–100 mm)</td>
<td>38 ± 21</td>
<td>35 ± 19</td>
<td>33 ± 21</td>
</tr>
<tr>
<td>Insomnia (0–100 mm)</td>
<td>28 ± 26</td>
<td>26 ± 23</td>
<td>20 ± 18c</td>
</tr>
<tr>
<td>Global rating of insomnia (0–6)</td>
<td>2.3 ± 1.5</td>
<td>2.1 ± 1.7</td>
<td>2.2 ± 1.7</td>
</tr>
<tr>
<td>Mini-Mental State Questionnaire (0–100 mm)</td>
<td>74 ± 11</td>
<td>79 ± 11</td>
<td>87 ± 10d</td>
</tr>
<tr>
<td>Median equivalent dosee of morphine (mg/day)</td>
<td>195 ± 78</td>
<td>210 ± 85</td>
<td>225 ± 115</td>
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</table>

* One patient died before the day 7 assessment.

Data expressed as mean ± standard deviation.

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References


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