Effects of On-Demand Versus Fixed-Interval Schedules in the Treatment of Chronic Pain With Analgesic Compounds

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The effects of fixed-interval and on-demand administration of analgesic medication in chronic pain patients were compared in a cross-over design. It was hypothesized that each analgesic schedule would have a different effect on subjective pain experience, mood experience, and physical activity. A fixed-interval analgesic schedule was found more effective than an on-demand analgesic schedule in reducing subjective pain and elevating mood. No differences were found between the two conditions on measures of physical activity.

The medical approach to the treatment of pain assumes that pain is a specific sensation, with pain intensity directly proportional to nociceptive sensory input or extent of tissue damage. This assumption of a simple one-to-one relation between a stimulus and a sensation (one cause, one pain) has led to the expectation that if the cause of the pain is eliminated, the pain itself will vanish (Sanders, 1979). This strategy works well enough in some situations; however, it is frequently observed that intensive medical and surgical approaches to chronic pain neither reveal the cause of the pain nor reduce the subjective experience of pain. For instance, Beecher (1959) noted that morphine, a potent narcotic analgesic drug, is only effective in about 70% of the cases. It also appears that morphine, when effective, mainly acts to reduce anxiety, fear, worry, and other emotions that are usually intermingled with pain.

During the last decade, pain research has distinguished between respondent and operant pain. Fordyce (1976) defined respondent pain as pain resulting from stimuli arising from body damage. Operant pain may or may not be associated with body damage. The most important characteristic of operant pain is that pain behavior may be reinforced either through social attention and medication (attention and induced euphoria provide positive reinforcement) or through reduction of tension, anxiety, or fear (negative reinforcement). In a recent analogue study, Linton and Gøtestam (1985) showed that pain responses could be operantly reinforced and that responses remained after relief of the nociceptive stimulus.

Fordyce (1976) argued that medication positively reinforces pain behavior and that pain patients learn that medication will reduce their distress. The reinforcing properties of drugs administered for operant pain seem to increase drug use and to create a vicious cycle, where increased medication leads to increased pain behavior. In animal research, drugs have been shown to have both positive reinforcing and discriminative properties (Haug & Gøtestam, 1980). Such discriminative properties may be of importance when a drug is given on-demand (pro re nata [PRN] or pain-contingent schedule) in the treatment of chronic pain patients. Sternbach (1974a) pointed out that analgesics taken on demand may do more harm than good in chronic benign pain. One strategy to break this vicious cycle is to give analgesics on a time-contingent rather than a pain-contingent basis and to then progressively reduce the dose (Fordyce, 1976; Linton & Gøtestam, 1984). The rationale for administering analgesics on a fixed-interval schedule is that it will not reinforce pain behavior and may even lead to the extinction of pain responses by breaking of the contingency between response and reinforcing stimulus (the drug).

The clinical assumption is that analgesics taken on demand strengthen or reinforce rather than reduce pain behavior in chronic pain populations. This is supported in the only published study to our knowledge that concerns medication intake schedules (White & Sanders, 1985).

In the present study we tested two different schedules of medication administration: (a) on demand (or pain contingent) and (b) fixed interval (or time contingent). It was hypothesized that chronic pain patients would experience less pain relief while taking their medication on demand than while taking it at fixed intervals. Consequently, it was further hypothesized that analgesics given on demand would result in lower mood level than those given at fixed intervals. Finally, it was hypothesized that chronic pain patients who experienced less pain and a higher mood level while taking their medication on a fixed-interval schedule would be more physically active than patients taking their medication on demand. It was assumed that these characteristics of pain behavior could be studied within the patient's repertoire of behavior in response to different schedules of medication.
counters, and patients were instructed to wear the step counter all day with each patient.

scale was superior to a visual analogue scale. Expected difficulties, such as how to remember rating pain intensity each hour or what to do when falling out the card is forgotten for one or more periods, were discussed as how to remember rating pain intensity each hour or what to do when falling out the card is forgotten for one or more periods, were discussed with the patients and families methods to prevent taking medication at other times and what to do if this became too difficult. Each patient was first given a 2-day adjustment period. The total amount of drug given was equal to or slightly above baseline level. All other medicine was held constant. The fixed-interval medication procedure was discussed with each patient and with his or her family or support system. Patients were advised to arrange medication reminders in their homes. Some patients used alarm wrist-watches to give signals at the appropriate medication times. We also discussed with the patients and families the importance of accurate reports for the collection of reliable data and explained that accurate reports would not be used against the patient in any way, despite the possible overconsumption of drugs. Because the patients were using other kinds of analgesics rather than narcotic drugs, the problem of falsified or inaccurate reports was minimized (Ready, Sarkis, & Turner, 1982).

Future medication schedule. At the cross-over point and after the second treatment phase, patients were asked whether they wanted future medication on the specific schedule used. They were asked to answer in one of five categories (0 = no wish, 1 = weak wish, 2 = wish, 3 = strong wish, and 4 = very strong wish).

Mood level Patients were asked to rate their average mood level at the end of the day. The mood level was to be rated on a 6-point scale similar to the scale used to assess pain (e.g., 0 = depressed, 5 = happy or elevated mood).

Method

Ten (6 men and 4 women) chronic pain patients participated in the study. Eight patients were treated on an outpatient level and two (Patients 7 and 8) were institutionalized. Seven more patients were entered in the study but were excluded because of intermittent pain and variable medication schedules (n = 5) or because they did not attend appointments (n = 2). Patient characteristics are shown in Table 1. In addition to excessive use of prescribed analgesics (codeine, paracetamol, and buprenorphine), the patients used benzodiazepines in moderate doses. Patients participated voluntarily and were naive to the intention of the study.

Design

All patients went through 1 week of baseline registration before they were randomly assigned to (a) analgesics on demand or (b) analgesics at fixed intervals. After 1 week the patients were crossed over to the other medication schedule. Half of the patients were assigned to the on-demand schedule first and the fixed-interval schedule second, and half assigned to the opposite sequence.

Dependent Measures

Pain perception. Patients rated their experienced pain at the end of each hour during the day (Turk, Meichenbaum, & Genest, 1983) on a pain intensity rating card. (A rating of 5 = excruciating pain, rest in bed is necessary; of 4 = severe pain, disrupts all behavior except behavior essential to life [eating, etc.]; of 3 = pain cannot be ignored, concentration is difficult; of 2 = pain cannot be ignored but does not interrupt undemanding tasks; of 1 = low level pain can easily be ignored; and of 0 = no pain.) Linton and Götestam (1983) found that such a verbal scale was superior to a visual analogue scale. Expected difficulties, such as how to remember rating pain intensity each hour or what to do when filling out the card is forgotten for one or more periods, were discussed with each patient.

Physical activity. Patients daily activity was measured with step counters, and patients were instructed to wear the step counter all day and to record the number of steps on the physical activity card. They were told to reset the counter watch at bedtime.

Medicine intake. Patients were asked to record type, quantity, and time of analgesic used. All other medication was also registered. This registration was done on the patient's physical activity card.

One problem with this approach is that patients may not accurately report their medicine use, especially if they use large quantities (Taylor, Zlutnick, Carley, & Flora, 1980). To avoid this problem, we emphasized the importance of accurate reports for the collection of reliable data and explained that accurate reports would not be used against the patient in any way, despite the possible overconsumption of drugs. Because the patients were using other kinds of analgesics rather than narcotic drugs, the problem of falsified or inaccurate reports was minimized (Ready, Sarkis, & Turner, 1982).

Procedure

The study was carried out over 18 months. Patients were referred to the program through the Department for Rehabilitation at the university hospital. Each patient and family (or significant other) met for three-five pretreatment sessions before being included in the program. During these sessions, problems concerning pain intensity ratings (duration and frequency), mood and physical activity recordings, accurate medication registration, and so forth were discussed. The patients were informed that we wanted to study the relations between medicine use, pain intensity, mood, and physical activity. Much time was also spent discussing each patient's pain problem within a learning theoretical framework (Fordyce, 1976).

After the baseline condition, patients were assigned randomly to either a fixed-interval medication schedule or an on-demand medication schedule. Analgesic consumption during the fixed-interval condition was divided into four equal doses and administered at 7:00 a.m., noon, 5:00 p.m., and 10:00 p.m. Each day for Patient 7, the analgesic consumption was divided into two equal parts and administered at noon and 10:00 p.m. The total amount of drug given was equal to or slightly above baseline level. All other medicine was held constant. The fixed-interval medication procedure was discussed with each patient and with his or her family or support system. Patients were advised to arrange medication reminders in their homes. Some patients used alarm wrist-watches to give signals at the appropriate medication times. We also discussed with the patients and families the importance of accurate reports for the collection of reliable data and explained that accurate reports would not be used against the patient in any way, despite the possible overconsumption of drugs. Because the patients were using other kinds of analgesics rather than narcotic drugs, the problem of falsified or inaccurate reports was minimized (Ready, Sarkis, & Turner, 1982).

During the on-demand condition, patients were given exactly the same amount of medicine as was given in the fixed-interval condition but were told to take their medicine contingent on pain. Each patient was first given a 2-day adjustment period.

During the baseline condition all other medicine consumption was registered, and this consumption was held constant throughout the program. Nonanalgesic medication was administered on a time schedule similar to that for analgesics.
Discussion

The results presented in this study suggest that a fixed-interval medication schedule is more effective for reducing subjective pain and elevating mood level than an on-demand medication schedule. The two medication schedules did not produce any significant differences in physical activity. This lack of effect does not, however, indicate that there were no differences in such activities as standing, sitting, or reclining. In the present study, walking was the only activity measured.

The results show increased pain ratings for the on-demand condition as compared with the baseline condition. One explanation for this effect might be found in the difference in medication schedules between baseline and the on-demand condition. Even though patients reported that the usual amount of medicine had been taken during the on-demand schedule, patients were instructed to take their medicine contingent on pain. This focus on pain may also explain the small difference in reports of pain between baseline and the fixed-interval schedule, the higher level of mood on the fixed-interval schedule than the on-demand schedule, and the nonsignificant differences between baseline and the on-demand schedule. Calculations of both subjective pain and mood differences when the fixed schedule was compared with baseline were nonsignificant. When these calculations were made on the last 3 days of each period, significant differences were found. These effects may be attributed to the patients’ need for time to adjust to the fixed-interval schedule and can also be understood in the light of extinction theory.

Our data showing a higher level of mood on the fixed-interval medication schedule may be a concurrent effect of the reinforcement schedule or may be due to the mediating effects of mood on pain. Patients on this schedule received their medication noncontingent on pain; according to extinction theory, this

Addendum

Figure 1. Mean pain and mood change scores in the two drug schedules.

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\caption{Mean pain and mood change scores in the two drug schedules.}
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Results

Subjective Pain

Results were analyzed in two-way analyses (Medication Schedule × Order) of variance (ANOVAs) with repeated measures to identify main effects (Kirk, 1968). To detect significant differences between the medication schedules, dependent t tests were performed.

Differences between fixed-interval and on-demand medication schedules as measured by subjective pain experiences are shown in Figure 1. Individual data on each medication schedule for each patient are shown in Figure 2. The two-way ANOVA showed a significant main treatment-type effect in subjective pain, F(2, 16) = 12.47, p < .001, and an order effect, F(1, 8) = 8.26, p < .05, but no interaction (F < 1). There was a significant decrease in subjective pain in the fixed-time medication schedule as compared with the on-demand schedule, t(9) = 5.26, p < .001, and a significant increase in pain in the on-demand schedule as compared with the baseline condition, t(9) = 4.14, p < .01. No significant difference was found between baseline and the fixed-interval medication schedule, t(9) = 2.02, p > .05. The level seemed to stabilize more after some days, especially in the fixed schedule, and if analyses were made on only the last 3 days in each period, the difference between baseline and the fixed schedule also became significant, t(9) = 4.58, p < .01. The fixed schedule always produced less pain than the on-demand schedule, regardless of preceding condition; whereas the on-demand schedule always increased pain, regardless of preceding condition.

Mood Level

Differences between medication schedules as measured by mood are also shown in Figures 1 and 2. The two-way ANOVA showed a significant main treatment-type effect in mood, F(2, 16) = 10.16, p < .005, but no order effect (F < 1) or interaction (F < 1). There was a significantly higher level of mood on the fixed-interval schedule than the on-demand schedule, t(9) = 4.02, p < .01, but not between the baseline and the fixed-time condition, t(9) = 1.73, p > .05, or the on-demand condition, t(9) = 0.31, p > .05. Calculated on the last 3 days in each period, the difference between baseline and the fixed schedule also became significant, t(9) = 2.54, p < .01.

Physical Activity

No obvious changes in activity were shown, and the two-way ANOVA showed no significant main treatment-type effect in activity, F(1, 18) = 3.55, p > .05, no order effect (F < 1), and no interaction (F < 1).

Future Medication Schedule

All patients were asked to rate both schedules. Two patients expressed wishes for a future fixed-medication schedule, and 7 patients expressed wishes for a future on-demand medication schedule. One patient expressed equal wishes for both future medication schedules. Only 1 patient had very strong wishes (Score 4) for a future fixed-medication schedule and no desire for an on-demand medication schedule. Mean ratings were 1.0 for the fixed schedule and 1.9 for the on-demand schedule. This difference was significant (Fisher exact probability p = .013).
Figure 2. Daily pain and mood scores for each patient during different drug administration schedules. (Patients on the left began with the fixed-interval schedule; patients on the right with the on-demand schedule.)
would lead first to an increase and later to a decrease in problem behavior. Calculations made on the last 3 days in each period support this view.

One might assume that this study did not fully control all the patients' medication because the program was mostly conducted with outpatients. Yet, this assumption cannot explain the differences in subjective pain and mood detected in patients on the two schedules of medication.

Furthermore, it is not likely that the results obtained with the different schedules were affected by demand characteristics or other nonspecific variables because the patients were naive to the real intention of the study and because patients later expressed a wish for future on-demand medication, which was the least effective schedule. However, therapists treating the patients were not blind to our hypothesis, and this variable could be controlled for in future research.

Our results do indicate that differences between the two conditions in pain and mood could be produced by different schedules of medication. In addition, the fact that the order variable had a significant effect on the pain variable underlines the importance of medication history. This importance is further supported by the clinical assumption that long-term use of analgesics for chronic pain will result in addiction and will increase reported pain intensity (Sternbach, 1974a). Recently, White and Sanders (1985) found the time-contingent schedule of medication on pain patients under detoxification to be significantly more effective in reducing pain and elevating mood than a pain-contingent schedule. Thus, patients who, to a significant degree, wanted the on-demand schedule in the future may have responded to a euphoric drug effect on that schedule, which may demonstrate the higher dependence-producing potential of on-demand schedules.

One important clinical implication of the present study is that fixed-time schedules appear to be preferable to on-demand schedules for chronic pain patients because of (a) better effect on pain, (b) positive effect on mood, and (c) lower drug-dependence potential. In assessing this implication it is important to distinguish between operant pain (pain behavior reinforced through medication) and respondent pain. However, the present conclusion, based on a relatively small number of subjects, demands replication in larger scale studies.

References


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