ORIGINAL ARTICLES

Patient Misunderstanding of Dosing Instructions

Nicholas A. Hanchak, MD, Monica B. Patel, Jesse A. Berlin, ScD, Brian L. Strom, MD, MPH

OBJECTIVE: **To compare outpatients' understanding of medication dosing instructions written in terms of daily frequency with patients' understanding of instructions specifying hourly intervals.**

DESIGN: **Prospective cohort study involving patient interviews.**

SETTING: **A university hospital outpatient pharmacy.**

PATIENTS: **Five hundred patients presenting new and refill prescriptions to the hospital outpatient pharmacy.**

INTERVENTION: **Patients were interviewed using a standardized questionnaire.**

MEASUREMENTS AND MAIN RESULTS: **Of the 71 patients with prescriptions specifying dosing instructions in hourly intervals (e.g., q6h), 55 (77%) misinterpreted the recommended frequency of dosage compared with only 4 (0.93%) of the 429 patients with dosing instructions specifying daily frequency (e.g., qid) (relative risk 83; 95% confidence interval 31-200). This difference remained when patient subgroups were evaluated by education level, new versus refill prescriptions, and analgesic versus nonanalgesic medications.**

CONCLUSIONS: **This study indicates that the intended dosing regimen is frequently misunderstood when the physician writes outpatient prescriptions in hourly intervals. To promote optimal patient compliance, the outpatient prescription label should state the number of times a day a medication is to be taken.**

KEY WORDS: **prescription drugs; patient compliance; dosage.**
J GEN INTERN MED 1996;11:325–328.

Received from the Hospital of the University of Pennsylvania, Philadelphia (NAH); University of Pennsylvania, Philadelphia (MBP); Center for Clinical Epidemiology and Biostatistics, Department of Biostatistics and Epidemiology, and Division of General Internal Medicine of the Department of Medicine, University of Pennsylvania School of Medicine, Philadelphia (JAB, BLS).

Dr. Hanchak is currently President, U.S. Quality Algorithms, Inc., Blue Bell, Pa.

Presented as a poster at the 17th Annual National Meeting of the Society of General Internal Medicine, Washington, DC, April 29, 1994.

Address correspondence and reprint requests to Dr. Strom: Room 824 Blockley Hall, Center for Clinical Epidemiology and Biostatistics, University of Pennsylvania School of Medicine, Philadelphia, PA 19104-6021.

Patient compliance is important in achieving optimal treatment outcomes. Poor compliance is frequently a cause of suboptimal treatment of medical illness and often results in adverse side effects and dangerous toxicities. Among the many important components of patient compliance are unrealistic expectations by the physician, such as asking a patient to take medication too frequently or in the middle of the night; a patient's lack of understanding of the importance of proper treatment; and a lack of reinforcement over time. The physician must effectively and explicitly communicate the directions for drug therapy to the patient if the patient is expected to follow the intended instructions.

Haynes and coworkers defined compliance as "the extent to which a person's behavior (in terms of taking medications, following diets, or executing lifestyle changes) coincides with medical or health advice."[1] However, several studies have suggested that noncompliance often results from a lack of agreement between what the patient thinks he or she is supposed to do and what the physician actually wants the patient to do.[2–5]

The timing of drug administration may be considered an important aspect of drug therapy, especially when multiple daily doses are required to maintain a therapeutic blood concentration of the drug. Critical to the adherence to an appropriate drug regimen is effective communication of the dosage instructions to the patient. When the patient is taking multiple medicines, it is often difficult for the physician to state the exact time of day when the patient should take each medication. Often the physician assumes patient understanding. However, a patient who does not understand the correct dosage instructions for a medication cannot be expected to comply with those instructions.

In an inpatient setting, it is easy to administer medicines at specified hourly intervals, but such a precise regimen is sometimes impractical for patients to follow in their home environments and usually unnecessary. Given that most physicians have been trained primarily in inpatient settings, this practice of giving dosages by hourly intervals may be common and may often lead to misunderstanding among outpatients. When a prescription is written for an hourly interval, the potential for confusion of interpretation is substantial. For example, a physician may write a prescription as q6h (every 6 hours), intending that the patient take the medication four times a day.

However, the patient may interpret these instructions as every 6 hours while awake and may take the medicine only three times a day, such as on a 10:00 AM, 4:00 PM, and 10:00 PM schedule. This study compares patient understanding of dosage instructions, specifically how many times a day a medication is to be taken, when prescriptions are written in terms of hourly intervals between drug ingestion with that when prescriptions are written in terms of daily frequency.

METHODS

This study was approved by the Hospital of the University of Pennsylvania Outpatient Pharmacy and the Institutional Review Board of the University of Pennsylvania.

Patient Selection

Five hundred patients presenting either new or refill prescriptions at the Outpatient Pharmacy of the Hospital of the University of Pennsylvania were interviewed sequentially while they waited in line to fill their prescriptions. In general, persons using this pharmacy are patients seen in the housestaff clinics or the faculty practices, but they also include some hospital employees. One nonphysician researcher (MBP) interviewed all 500 patients. Interviews were collected over 7 months, on weekdays only. The time of the day of the interviews was varied to ensure a representative sampling of the patient population. A day was divided into morning and afternoon/evening segments, with morning including the hours between 9:00 AM and 12:00 noon and afternoon/evening including the hours between 12:00 noon and 7:00 PM. Interviews were collected during each period of each day of the week between Monday and Friday. All eligible patients who consented and spoke English were enrolled during any given period. Data collection began in August 1993 and was completed in February 1994.

Prescription Selection

Data collection involved only one prescription per patient. In situations in which the patient presented more than one prescription to be filled, a single prescription was selected by arranging the prescriptions that specified hourly intervals in alphabetical order (according to their generic names) and identifying a single prescription at random, utilizing a table of random numbers. If the patient presented no prescriptions written in hourly intervals, then the same procedure was used to select a prescription written in terms of number of times a day. Because of an anticipated low frequency of misunderstanding, prescriptions written as qd (once a day) or q24h, qod (once every other day) or q48h, qhs (once at night) or q24h at night, and qam (once in the morning) or q24h in the morning were excluded from this study. Because of a lack of specific dosing instructions, prescriptions written as prn (take as needed) and tad (take as directed) were excluded as well.

Study Questionnaire

The study questionnaire first obtained demographic information. The main outcome was based on the patient's response to the following question: "How many times a day do you understand that your medication is to be taken?" Specifically, we were interested in whether patients misunderstood the intended frequency of medication. Before asking the patient's understanding of frequency, the interviewer explained to the patient what the instructions on the prescription specified. For example, if a prescription read "q6h," the interviewer would tell the patient that the instructions were to take the medication every 6 hours. Other information obtained from the patient included the total number of prescriptions to be filled at that visit, the total number of medications currently being taken (including those presented to the researcher), patient age, marital status, type of prescription insurance, level of education, gender, and race. Information obtained from the prescription label included the prescription type (new or refill), the dosage type (times a day or hourly intervals), the prescribed frequency of drug administration, the class of medication (analgesic, antibiotic, cardiovascular-renal, dermatologic, endocrinologic and metabolic, gastrointestinal, hematologic, respiratory and antihistamine, vitamin or nutritional supplement, or other), the presence or absence of the indication for the medication on the label or physician's prescription, and agreement of patient understanding of dosing instructions with instructions written on the label. For prescriptions written in hourly intervals, we assumed that the physician's intention was to be interpreted literally on the basis of a 24-hour daily period: e.g., q6h was assumed to mean four times a day.

Statistical Analysis

The patients with prescriptions given in terms of hourly intervals and those with prescriptions specifying number of times a day were first compared with respect to demographic and other characteristics that might affect their level of understanding of prescriptions. For discrete variables χ^2 tests were used. The mean age was compared between groups using the Student's t test for independent samples.

The proportion of patients misunderstanding their dosing instructions was compared between the two prescription groups using the χ^2 test. The relative risk (RR) of misunderstanding and a 95% confidence interval (CI) were calculated using standard methods.[6] Stratified analyses and logistic regression were used to compare the two groups while controlling for potential confounding and to investigate the possibility that the differences were confined to particular subgroups of patients. When any ex-

pected cell counts in 2 × 2 tables were less than 5, Fisher's Exact Test and exact stratified analyses were used.[6]

RESULTS

Of the 500 patient prescriptions evaluated, 71 (14.2%) were written with instructions specifying medication ingestion by hourly intervals while 429 (85.8%) were written specifying the number of times a day the medication was to be taken. There were significant differences ($p < .005$) between the study groups in the distribution of analgesic versus nonanalgesic prescriptions and new versus refill prescriptions (Table 1). No significant differences were found between the two groups for any other characteristics studied.

Overall, 59 (11.8%) of the 500 prescriptions were misinterpreted. Only 4 (0.93%) of the 429 prescriptions written in frequency of dosage were misinterpreted, whereas 55 (77%) of the 71 of those written in hourly intervals were misinterpreted (RR 83; 95% CI 31-200). Of the 59 patients who misinterpreted prescriptions, 40 had prescriptions written as q6h. Of those 40 patients, 31 (78%) interpreted q6h to mean three times per day and 9 (22%) thought the medication was to be taken twice per day.

Although analgesic prescriptions may be written in hourly intervals, analgesic medications could be misinterpreted as having implicit prn instructions. In this study, 83 (16.6%) of the 500 prescriptions were written for analgesics: 27 (87%) of the 31 analgesic prescriptions written in hourly intervals were misinterpreted, while 0 (0%) of the 52 analgesic prescriptions written in frequency per day were misinterpreted ($p < .001$). Nonanalgesic prescriptions showed similar results: 28 (70%) of the 40 prescriptions written in hourly intervals misinterpreted while only 4 (1.06%) of the 377 nonanalgesic prescriptions written in frequency per day were misinterpreted ($p < .001$).

Age, gender, race, insurance, education, marital status, and the absence of medication indication showed no relation to patient understanding of dosage instructions. Adjustment for any of the characteristics listed in Table 1, using either stratified analysis or logistic regression, also had no meaningful effect on our results.

DISCUSSION

Several studies suggest that noncompliance may be caused by a misunderstanding of physicians' intentions regarding drug therapy. Ostrom et al. found disagreements between the patient's interpretation and the instructions on the prescription label for 51 (37%) of 138 patients interviewed who were using prescription drugs.[2] Zuccollo and Liddell found that 37 (60%) of 60 elderly outpatients did not have a clear understanding of prescription dosing instructions,[3] while Fletcher et al. reported that only 77 (58%) of the 133 patients interviewed who received prescriptions knew the correct dosage for all of their medications.[4]

Salako and Adadevoh interviewed patients to determine their reasons for not taking medications as they were prescribed.[5] A frequent cause of noncompliance was misunderstanding of the prescription label, which included taking half or double the dosage or taking the medication in a manner unrelated to the actual prescription instructions.

Lack of patient compliance often leads to therapeutic failure and consequently adverse side effects. Col et al. interviewed 315 elderly patients admitted to the hospital and found that 36 (11.4%) of those admissions were due to medication noncompliance.[7]

Our study demonstrates that an extremely large percentage of dosage instructions are misinterpreted when they are written in hourly intervals. Other studies have

Table 1. Distribution of Characteristics for Patients with Prescriptions Written in Terms of Frequency per Day Versus Those with Prescriptions Written in Terms of Hourly Intervals

Characteristic	Frequency per Day (N = 429)		Hourly Intervals (N = 71)		p Value
	No.	(%)	No.	(%)	
Mean age, years (SD)	41.8	(16.4)	39.7	(14.6)	.31
Male gender	146	(34.0)	23	(32.4)	.79
Black race	244	(56.9)	48	(67.6)	.09
Insured	414	(96.5)	68	(95.8)	.76
College education or higher	95	(22.1)	13	(18.3)	.47
Married	195	(45.5)	28	(39.4)	.35
Indication noted on prescription	20	(4.7)	9	(12.7)	.007
Analgesic	52	(12.1)	31	(43.7)	<.001
No. of prescriptions being filled					
1	205	(47.8)	42	(59.1)	.03
2	122	(28.4)	20	(28.2)	(trend)
3	102	(23.8)	9	(12.7)	
New prescriptions	352	(82.1)	69	(97.2)	.001

also shown that the patient misunderstands instructions when a prescription does not specify the number of times a day a medication is to be taken. When Kendrick and Bayne asked 37 nursing home residents to interpret a prescription written as "take one tablet every 6 hours," only 8 (22%) indicated that they would take four tablets a day, the correct dosage for this medication.[8] Mazzullo et al. found that 17 (25%) of 67 patients interpreting a prescription written as "tetracycline, 250 mg every 6 hours" indicated that they would take the medication only three times a day.[9] The main reason for excluding the fourth dose was that the patients had interpreted a "day" to indicate 18 hours or only hours while awake.[9] Kimminau and Wright suggest that prescriptions written as "take at 7:00 AM, 12 noon, 6:00 PM, and 11:00 PM" are better than "take every 6 hours."[10] However, these studies observed misunderstanding of prescription labels of medications that were not specifically prescribed to the patient interviewed.

Wootton interviewed patients about their prescription instructions and concluded from her data that information on prescription labels is often poorly written.[11] In addition, Morrell et al. found that prescriptions written as "take at 8:00 AM and 8:00 PM" were more often correctly understood than prescriptions written as "take every 12 hours."[12] These studies stress the need for a clear definition of what constitutes a "day."

The strengths of this study include its prospective nature, rigorous study design, and unambiguous results. We analyzed several important patient characteristics including education level and insurance type as possible confounders and possible sources of interaction and found no change in our conclusions. Also, all interviews were conducted using a standardized questionnaire designed to analyze a clearly defined study outcome.

However, this design has a few potential limitations. The study measured patient compliance by evaluating only one prescription per patient. Patient understanding of instructions may not be accurately assessed from one particular prescription label, although the results were clearly not due to random error.

We also assumed that prescriptions written as hourly intervals require an explicit drug administration period of 24 hours. Although it seems unlikely, perhaps physicians who write prescriptions as q6h actually intend drug administration 3 times a day rather than 4 times a day. If so, we misinterpreted physicians' instructions, but patients who interpret q6h as four times a day, as we did, would then be taking more medication than their physicians intended. What is important is not the physician's intent, per se, but that the patient's understanding matches that intent. Even if the physician explains his or her intent to the patient, it would seem crucial to reinforce that information by having explicit instructions written directly on the label.

We cannot rule out the possibility that, in fact, the individual physicians who wrote prescriptions in hourly intervals also took less time to explain the prescriptions to patients. Even if this were true, that lack of time spent with patients makes it still more important for labeling to be extremely explicit.

Another potential limitation is that results from this single university hospital may have limited generalizability to other settings. For example, the proportion of prescriptions already being written in terms of frequency was quite high (85.8%). If this proportion were still higher at other types of hospitals, the absolute number of misunderstood prescriptions would be smaller than expected on the basis of our results. Nevertheless, among patients with prescriptions written in hourly intervals, there was a high level of misunderstanding of daily frequency.

In conclusion, in order to ensure complete patient understanding of outpatient prescription dosing instructions, we recommend that: (1) the prescription label should state the number of times a day a medication should be taken, rather than the hourly intervals, and (2) if around-the-clock administration or the hourly interval or both are clinically important, ambiguity should be avoided, perhaps by specifying the actual times of day when medications should be taken.

REFERENCES

1. Haynes RB, Taylor DW, Sackett DL. Introduction. In: Compliance in Health Care. Baltimore, Md: Johns Hopkins University Press; 1979.
2. Ostrom JR, Hammarlund ER, Christensen DB, Plein JB, Kethley AJ. Medication usage in an elderly population. Med Care. 1985; 23:157–64.
3. Zuccollo G, Liddell H. The elderly and the medication label: doing it better. Age Ageing. 1985;14:371–6.
4. Fletcher SW, Fletcher RH, Thomas DC, et al. Patients' understanding of prescribed drugs. J Community Health. 1979;4:183–9.
5. Salako LA, Adadevoh BK. Patient attitudes, understanding and consumption of prescribed drugs. West Afr J Med. 1972;140–3.
6. Kleinbaum DG, Kupper LL, Morgenstern H. Epidemiologic Research: Principles and Quantitative Methods. Belmont, Calif: Lifetime Learning Publications; 1982.
7. Col N, Fanale JE, Kronholm P. The role of medication noncompliance and adverse drug reactions in hospitalizations of the elderly. Arch Intern Med. 1990;150:841–5.
8. Kendrick R, Bayne JRD. Compliance with prescribed medication by elderly patients. CMA J. 1982;127:961–2.
9. Mazzullo JM, Lasagna L, Griner PF. Variations in interpretation of prescription instructions. JAMA. 1974;227:929–31.
10. Kimminau MD, Wright RJ. The pride and perfection of the prescription label. Am Pharm. 1981;NS21:46–9.
11. Wootton J. Prescription for error. Nurs Times. 1975;884–6.
12. Morrell RW, Park DC, Poon LW. Quality of instructions on prescription drug labels: effects on memory and comprehension in young and old adults. Gerontologist. 1989;29:345–54.