Defining the Proper Role for Self-administered Sublingual Nitroglycerin*

A Survey of Physicians and Patients

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Within a half-year period, we encountered six cases of patients harmed by the adverse effects of self-administered nitroglycerin—syncope, delayed definitive medical care, and the worsening of nonischemic symptoms. We therefore surveyed 112 patients after a remote myocardial infarction, and 121 cardiologists and internists, regarding the use of sublingual nitroglycerin. Of the physicians, 84 percent routinely prescribed nitroglycerin to patients after a myocardial infarction, and 79 percent of the patients had the tablets available (83 percent of these, at all times). Most patients used the tablets less than once per month, and 37 percent of the patients who always carried nitroglycerin had not used it at all during the preceding year. Although 89 percent of the patients claimed to know when to use the drug, 57 percent had used it or would use it for symptoms such as dizziness, rapid heartbeat, or presyncope. All patients having nitroglycerin claimed it relieved their symptoms, even if the relief was only partial, the time elapsed until relief could not be specified, and the symptoms were of a type unlikely to be relieved by the drug. We suggest that the practice of routinely prescribing nitroglycerin to patients after a myocardial infarction should be reassessed. (Chest 1991; 100:34-8)

Sublingual nitroglycerin is commonly prescribed to patients with coronary artery disease, or even only suspected coronary artery disease, for self-administration on an as needed basis. Attention has been called to the morbid side effects of sublingual nitroglycerin, most notably severe hypotension and bradycardia.1 Within a half-year period, the author encountered the following six patients who were affected adversely by the well-intentioned use of sublingual nitroglycerin.

**CASE REPORTS**

**CASE 1**

A 60-year-old man, two years after an inferior myocardial infarction, was attending a family barbecue when he suddenly felt extremely weak, with dyspnea and mild chest discomfort. He took one of the sublingual nitroglycerin tablets which he carried with him since his heart attack, but had never used until then. He immediately felt worse, as if he were about to faint, and was described as looking "as white as chalk." Paramedics were summoned, and an electrocardiographic (ECG) monitor revealed supraventricular tachycardia at a rate of 180/min.

**CASE 2**

An apparently healthy 52-year-old man was seen in the emergency department at 10 P.M. following a 20-minute episode of left-sided chest pain at home. An ECG was normal, and the patient felt well. He was discharged home with a supply of nitroglycerin tablets, with instructions to return to the hospital if the pain recurred and was unrelated by the nitroglycerin. During the night, the patient had intermittent chest pain that seemed to respond transiently to repeated doses of sublingual nitroglycerin. In the morning, the patient returned to the hospital where an ECG demonstrated ST-elevation and Q-waves in the anterior precordial leads. When asked what he would have done when the chest pain recurred at home had he not had nitroglycerin tablets, the patient stated unequivocally that he would have returned to the emergency department immediately.

**CASE 3**

A 49-year-old man was hospitalized with an acute inferior myocardial infarction. Several hours after admission, he mentioned to the nurse that he was having mild chest pain, and he was given a sublingual nitroglycerin tablet. He immediately began to feel faint and became pale. Blood pressure fell to 60 mm Hg systolic, and pulse to 45/min. The patient was placed in the Trendelenburg position and felt better. After 20 minutes he was able to sit up.

Three days later the patient's attending internist ordered the administration of a test dose of sublingual nitroglycerin to make sure the patient would no longer have an adverse reaction to the nitroglycerin tablets that he would be prescribed on discharge for future use as needed. The patient refused the nitroglycerin, and the attending internist was unhappy with the CCU-ruining cardiologist's refusal to convince the patient to try the drug.

**CASE 4**

A 54-year-old woman, two months after an anterior myocardial infarction, was sitting in church when she realized she had changed paces and left her nitroglycerin tablets at home. Although she had never used them, she began to sweat and her heart began to pound. She imagined having a heart attack in church "and they'd have to pick me up right in here."

**CASE 5**

A 74-year-old man, five days after hospital discharge for an acute anterior myocardial infarction, was readmitted to the hospital in severe pulmonary edema requiring intubation. During the time he had been at home, he had had four episodes of severe chest pain at rest, each of which had been relieved within 5 min by sublingual nitroglycerin. When asked what he would have done if he had not had nitroglycerin tablets, he replied, "I probably would have come to the hospital earlier, because it just would have gone on hurting.”
CASE 6

A 55-year-old man was hospitalized because of chest pain and syncope. He had suffered an acute myocardial infarction seven months previously, and had subsequently taken a sublingual nitroglycerin tablet every two to three weeks for chest pain that would subside within 30 to 60 seconds. On the evening of hospital admission, the patient still had chest pain 2 min after taking a nitroglycerin tablet, and he therefore took a second one. Shortly thereafter, he felt dizzy and sweaty, got up to call his mother, and fainted.

These six incidents stimulated the author to undertake the present study which surveyed physician and patient attitudes and practices regarding sublingual nitroglycerin use. In addition, the relevant literature was examined to determine to what extent such attitudes and practices are scientifically justified.

METHODS

Patient Survey

Patients in the waiting room of the outpatient cardiology department of a large health maintenance organization (HMO) in southern California were surveyed regarding their use of nitroglycerin. Patients were requested to fill out a questionnaire if they answered affirmatively when asked by a reception clerk if they had had a heart attack. The responses were anonymous, and no independent means were employed to confirm that a patient had indeed suffered a myocardial infarction beyond his own attestation, his presence in the cardiology department, and his ability to specify on the questionnaire the month and year that his first heart attack occurred. The survey was carried out over a two-month period in late 1989.

Physician Survey

Physicians attending a large American cardiology convention in the spring of 1989 were approached at random between sessions and requested to fill out a brief questionnaire. It surveyed their prescribing habits regarding sublingual nitroglycerin after a myocardial infarction for patients who did not necessarily have a stable anginal syndrome. The physicians were also asked about their opinions regarding the efficacy of nitroglycerin in various situations. A sample of internists from the same HMO as the surveyed patients filled out the same brief questionnaire.

RESULTS

Patient Survey

Of 112 patients surveyed, 87 percent were men; the mean age was 64 years, and the average number of years since the patient's first myocardial infarction was eight.

Eighty-nine patients (79 percent) had nitroglycerin tablets for use as needed, and 83 percent of these patients carried the tablets with them at all times. Only 12 (11 percent) of the patients had ever had an adverse reaction to sublingual nitroglycerin and for 9 of the 12 this consisted of a bad headache. Two patients had experienced dizziness, and one patient had actually fainted.

Perceived Benefits of Nitroglycerin: Patients were asked to select from a list of possible benefits of nitroglycerin those they believed were applicable in their case. The percentage of patients choosing a given response are as follows: 70 percent, it relieves my symptoms; 61 percent, it might save my life in an emergency; 49 percent, if it helps, it shows the symptom is cardiac; 47 percent, having it gives me a feeling of security; and 34 percent, it might prevent a heart attack.

The 79 percent of the sample who had nitroglycerin tablets available were asked if the tablet "generally helps" when taken. Not one patient answered "no," although two patients answered "yes and no," and one answered "sometimes." Patients were asked how soon the tablets helped: 58 percent, within 5 minutes; 15 percent, 10 to 15 minutes; 3 percent, 20 to 30 minutes; and 24 percent, "hard to say."

When asked how completely their symptoms were relieved within the above time period, 59 percent answered "completely" and 41 percent answered "partly." The combination of "complete relief within 5 min" was indicated by 45 percent of the patients who used nitroglycerin.

Anxiety over Being without Nitroglycerin: Patients were asked how anxious they would be if they went out of town for a weekend and discovered they had forgotten their nitroglycerin: 12 percent, not at all; 41 percent, a little; 22 percent, a lot; and 25 percent, extremely.

Frequency of Usage: Patients could be divided into three groups according to the frequency of their usage of nitroglycerin: frequent—29 percent of patients used nitroglycerin on a weekly basis (median, four times/week; range, 1 to 22 times); infrequent—16 percent of patients used nitroglycerin on a monthly basis (median, two times/ month; range, one to four times); and rare—55 percent of patients used nitroglycerin on an annual basis (median, 0 times/year; range, zero to eight times).

A full 37 percent of the patients who had nitroglycerin tablets did not use them at all in the previous year, and an additional 13 percent used them no more than three times. Of the patients who carried nitroglycerin with them at all times, 32 percent had not used the drug at all in the previous year.

Knowledge of Proper Use of Nitroglycerin: Patients were asked how certain they felt about how and when to use nitroglycerin. "Very certain" was chosen by 50 percent, "fairly certain" by 39 percent, while only 11 percent of the sample indicated that they were "not certain at all."

For each of 12 listed symptoms, patients were asked whether they had actually used nitroglycerin; whether they would probably use nitroglycerin if they were to experience the symptom; or if they had never used nitroglycerin and were unlikely to use it in the future for the symptom. For exertional chest pain, 71 percent had used nitroglycerin, and an additional 20 percent said they would use the drug were the symptom to occur. Similarly, 68 percent of the patients who had
nitroglycerin available said they had used it for non-exertional chest pain, and an additional 22 percent said they would use the drug for such chest pain.

However, the following percentages of patients indicated they had used or would use nitroglycerin for other indications: 39 percent, attack of fast or strong heartbeat; 36 percent, feeling that they were about to faint; 38 percent, sudden weakness; 27 percent, attack of dizziness; 51 percent, sudden shortness of breath; 61 percent, weakness or numbness in the left arm; and 29 percent, attack of severe nausea with abdominal discomfort. A full 57 percent of the patients who had sublingual nitroglycerin had used it or would use it for one of the first four (inappropriate) symptoms on the above list.

Patients with Angina vs Those without: Sixty-two percent of the patients said they suffered from exertional chest pain relieved by rest and were considered to have angina. The responses of the patients with and without angina were generally similar, except as follows. Patients with angina used more nitroglycerin, with 41 percent using it at least once per week (median frequency, five times) vs only 15 percent of the group without angina (median dose, two times per week). The patients with angina were somewhat more likely to carry nitroglycerin at all times (88 percent vs 75 percent) and were more likely to claim relief of symptoms as a benefit of nitroglycerin (79 percent vs 54 percent).

Physician Survey

Of a total of 121 physicians sampled, 102 (84 percent) indicated that they routinely prescribed sublingual nitroglycerin to patients after an acute myocardial infarction for use as needed, even in the absence of a recurring anginal syndrome. This was true of 85 percent of the 104 physicians surveyed at the cardiology convention, and of 82 percent of the 17 physician members of the HMO internal medicine department.

The convention group physicians described their professional practice as follows: 62 percent, clinical cardiology; 11 percent, cardiology fellowship; 10 percent, academic cardiology; 10 percent, internal medicine/cardiology; 6 percent, internal medicine; and 1 percent, other. The HMO group was composed of 82 percent internists and 18 percent cardiologists.

The surveyed physicians were asked to select from a list of potential benefits of sublingual nitroglycerin those which they believed were real. The percentages of physicians choosing a particular benefit are as follows: 87 percent, may shorten an attack of unstable angina; 72 percent, may provide diagnostic information; 68 percent, gives the patient a feeling of security; 49 percent, may lessen the pain of an acute myocardial infarction; 38 percent, may decrease the size of an acute myocardial infarction; 32 percent, may prevent sudden death during ischemia; and 29 percent, may abort an acute myocardial infarction. The results were not appreciably different between the convention or the HMO groups, nor between those physicians who do or those who do not routinely prescribe nitroglycerin.

Discussion

Our survey has documented a high prevalence of the use of as needed nitroglycerin, with 84 percent of physicians routinely prescribing it to patients after a myocardial infarction, 79 percent of patients having it available, and 83 percent of these keeping it with them at all times. Only a relatively small 11 percent of the patients had ever had an adverse reaction to nitroglycerin. In most cases this consisted of headache, and only 3 percent of the patients had suffered dizziness or fainting.

We found an extremely high degree of belief in the efficacy of nitroglycerin, with not a single one of the patients having nitroglycerin available stating that the drug did not relieve his symptoms. This, despite the fact that 40 percent of the patients stated that they were only partly relieved, and 24 percent of the patients could not specify, even approximately, how long it took nitroglycerin to provide relief. Considering the variety of symptoms (many clearly not able to be influenced by nitroglycerin) for which the patients took the drug, it is clear that a major part of the claimed efficacy of nitroglycerin is a placebo effect.

Of greater concern is the fact that 57 percent of the patients had taken or would take nitroglycerin for symptoms such as rapid heart beat, dizziness, weakness, or presyncope, for which the drug is clearly contraindicated. This, despite the fact that the patient population is made up overwhelmingly of middle-class, employed individuals, 89 percent of whom described themselves as being "very certain" or "fairly certain" of how to use nitroglycerin.

Sixty-eight percent of the physicians felt that giving the patient a sense of security was a real benefit of nitroglycerin, and 48 percent of the patients claimed that having the drug indeed gave them a sense of security. Yet one must question whether the patients' need for such reassurance may not have been artificially created by their being told by their physicians that they should have nitroglycerin available at all times. In fact, 88 percent of the patients stated that they would be anxious to some extent to be away for a weekend without their nitroglycerin, and in 47 percent the degree of anxiety would be "extreme" or "a lot."

A subgroup of 29 percent of the patients, predominantly consisting of those with angina, used nitroglycerin fairly frequently, on an average of four times per week. On the other hand, the large majority of patients used nitroglycerin infrequently, with 55 percent using
it only several times per year. One-third of the patients who carried  nitroglycerin with them at all times had not used it at all during the preceding year.

Of the patients surveyed, 61 percent felt that nitroglycerin might be lifesaving, and 34 percent thought it might prevent a heart attack. Among the physicians, approximately one third subscribed to the view that sublingual nitroglycerin might abort an acute myocardial infarction or decrease its size or prevent sudden death during ischemia. Although sublingual nitroglycerin is clearly capable of providing symptomatic relief from exertional or rest angina, what evidence is there that it can provide critical, long-lasting benefit by modifying the course of an acute myocardial infarction or preventing sudden death?

Although intravenous nitroglycerin has been recommended of late in the treatment of acute myocardial infarction, and may even reduce mortality, it should be recalled that sublingual nitroglycerin has traditionally been avoided in acute myocardial infarction because of the potentially deleterious effects of tachycardia and hypotension and the danger of syncope. It is important to distinguish between the monitored infusion of nitroglycerin in a coronary care unit vs the sublingual bolus self-administered by the patient at home. Although patients with stable coronary artery disease are also subject to sublingual nitroglycerin-induced hypotension, patients with unstable angina and acute myocardial infarction seem especially prone to this danger. Possible factors involved in this increased sensitivity include concomitant right ventricular infarction during inferior infarction and paradoxical nitroglycerin-induced coronary narrowing.

Regarding the ability of acutely administered nitroglycerin early in the course of acute myocardial infarction to open an occluded coronary artery or favorably affect infarct size or mortality, Rentrop et al found that only 8 percent of 65 patients with early acute myocardial infarction had recanalization of a totally occluded artery following a 75-minute infusion of intracoronary nitroglycerin. (This figure is similar to what might be expected to occur spontaneously, and is much less than the 60 percent recanalization rate in the group of Rentrop et al receiving streptokinase.) Furthermore, there was no improvement in mortality or ejection fraction between the group treated with intracoronary nitroglycerin and a concomitantly randomized control group.

With regard to the potential importance of sublingual nitroglycerin in preventing sudden death during an ischemic episode, systematically acquired objective data are obviously difficult, if not impossible, to obtain. It should be noted, however, that frequent episodes of transient, even prolonged, ischemia are very common in patients with stable coronary artery disease, and in the overwhelmingly large majority of instances they terminate spontaneously with absolutely no sequelae.

Although 72 percent of the physicians and 49 percent of the patients felt that the response of a symptom to sublingual nitroglycerin could provide valuable diagnostic information regarding the cardiac origin of that symptom, our findings cast doubt on the validity of this assumption. The patients uniformly claimed that nitroglycerin relieved their symptoms, even symptoms for which nitroglycerin could not be expected to be of benefit, or for which it was even contraindicated. Even if the "relief" was partial and occurred well beyond 5 to 10 minutes, it was nevertheless considered related to the nitroglycerin. Although most patients claimed to know when to use nitroglycerin, closer examination revealed that most did or would use it incorrectly at least part of the time. Furthermore, one wonders how patients (55 percent of our group) who use nitroglycerin only once or twice a year, or maybe not at all, can have an accurate impression of what type of chest pain is truly due to myocardial ischemia, and for which nitroglycerin should be taken.

Conclusions

The six cases we describe point up some of the potentially adverse effects of sublingual nitroglycerin as it is commonly prescribed: hypotension and syncope during acute myocardial infarction as well as during noncardiac chest pain; delay in seeking appropriate medical care during the early hours of acute myocardial infarction and in the course of early postinfarction ischemic rest pain; worsening of nonischemic conditions such as paroxysmal supraventricular tachycardia; and undue anxiety over being without nitroglycerin tablets. Our data indicate that patient use of the drug is often incorrect, and that drawing diagnostic conclusions from the patient's response to nitroglycerin will often be misleading.

We believe that in patients with well-defined, chronic anginal syndromes, the self-administration of sublingual nitroglycerin prior to or during exertional chest pain or even during recurring ischemic rest pain is clearly beneficial. On the other hand, the routine prescribing of sublingual nitroglycerin after a myocardial infarction to patients without clearly defined ischemic pain syndromes involves potential risks that may outweigh potential benefits and should therefore be carefully considered in each individual patient.

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