A Longitudinal Evaluation of Dipyridamole Drug Use in an Ambulatory Elderly Population*

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**Study objective:** To determine the pattern of dipyridamole use over the past 14 years.  
**Design:** A longitudinal health screening program of ambulatory elderly participants was used to study changes in dipyridamole drug use. Participants included all subjects screened in the Florida Geriatric Research Program since 1978. The main outcome measure in this study was self-reported dipyridamole use at every visit to the program since August 1, 1978.  
**Results:** A total of 3.6% of men (mean age, 82.6 years) and 3.4% of women (mean age, 80.8 years) reported the use of dipyridamole in the 1991-1992 period. The prevalence of dipyridamole use ranged from a low of 1.6% in 1978-1979 to a high of 7.3% in 1986-1987. There was a significant increase in the use of this drug from 1978-1979 to 1991-1992 (p<0.038). Over the 14-year period of study, the percent of subjects using dipyridamole con-

Dipyridamole (DPR) is a vasodilator and antiplatelet drug that was marketed in 1963.¹ The drug has been used in the long-term treatment of angina pectoris based on the belief that the drug would reduce anginal episodes, improve exercise tolerance, and reduce medication requirements. Eventually the drug was found to be ineffective in the treatment of angina pectoris.¹,² Dipyridamole is indicated for use as an adjunct to coumarin anticoagulants in the prevention of postoperative thromboembolic complications of cardiac valve replacement.² A number of prosthetic valve studies have shown that the addition of DPR to warfarin further reduces embolic episodes without increasing the bleeding risk.³ Dipyridamole's use has limitations. Even with use in patients with prosthetic heart valves, it should not be used alone, without an oral anticoagulant, or for the prevention of postoperative thromboembolic complications.² Even though there is abundant evi-
tained health questionnaire and a form for listing both prescribed and nonprescribed medications used on a regular basis. Since August 1978, detailed information has been collected on both prescribed and nonprescribed medication use.

When participants arrive for their screening appointments, information on the health questionnaire and medication history form is reviewed by clinic personnel. During their annual screening visits, participants receive a physical and laboratory assessment, including blood pressure measurements, an electrocardiogram, hemogram, and SMAC-23 biochemical determination. Participants in the program are believed to represent a stable population. For instance, in an analysis of 1,306 subjects who entered the program in 1978-1979 but failed to return for all of their scheduled visits, it was found that 686 (52.5%) died, 233 (17.8%) moved from the area, and 387 (29.6%) were unavailable for follow-up.3

Dipyridamole use was determined from self-report at each annual visit. The DPR use data were summarized for the years 1978-1979 to 1991-1992. Since the only indication for DPR is in conjunction with coumarin anticoagulant drugs, the percent of subjects reporting DPR use and coumarin anticoagulant use was also determined.

To determine if there was a statistically significant difference in the prevalence of dipyridamole used by participants between the 1-year period from August 1, 1978 to July 31, 1979, and the period between August 1, 1991 and July 31, 1992, two separate analyses were performed. Three mutually exclusive groups of participants were studied to provide a comparison of independent samples over the 14-year period. The groups were as follows: group 1 (n=1,843)—all subjects with a clinic visit in 1978-1979 and no visit in 1991-1992; group 2 (n=1,148)—all subjects who entered the program after 1978-1979 and had a clinic visit in 1991-1992; and group 3 (n=461)—all subjects who had a visit to the program in both 1978-1979 and 1991-1992.

The first analysis to determine whether the prevalence of DPR drug use changed from 1978-1979 to 1991-1992 was a two-sample Z-test comparing the independent groups 1 and 2. A second analysis addressing the same question compared the change in prevalence in the group 3 subjects using a McNemar test.

**RESULTS**

The age and gender of subjects studied and those reporting the use of DPR at the first (1978-1979), seventh (1984-1985), and 14th (1991-1992) periods is shown in Table 1. In the 1978-1979 time period, there were a total of 2,303 participants, including 1,448 (62.9%) women and 855 (37.1%) men. In the 14th period, there was a total of 1,621 study subjects with 1,124 (69.3) women and 497 (30.7%) men. The mean (± SD) age of participants in the first period was 74.5±5.4 years and this had increased to 78.8±6.6 years by the 1991-1992 period. The prevalence of subjects reporting DPR use for each yearly interval is shown in Figure 1. Additionally, the percent of DPR users who also reported the concurrent use of a coumarin anticoagulant drug is shown in Figure 1. The percent of participants using DPR increased from 1.6% in 1978-1979 to 3.4% in 1991-1992. The highest prevalence of DPR use (7.3%) occurred in the 1986-1987 time period while the lowest prevalence was in 1978-1979.

To determine if there was a change in DPR prescribing over this 14-year period, two mutually exclusive groups were compared. There were 1,843 subjects screened in the program in 1978-1979, but who were not present in 1991-1992, and 32 (1.7%) of these subjects reported the use of DPR in 1978-1979. There were 1,148 subjects present in 1991-1992 who were not screened in 1978-1979 and 36 (3.1%) of these subjects reported the use of DPR in 1991-1992. After adjusting for age and gender, there was a significant increase in the reported use of DPR between 1978-1979 and 1991-1992 (p<0.038).

A total of 461 participants screened in the 1978-1979 time period completed all of their visits through 1991-1992. A total of 2 (0.4%) of these subjects reported DPR use in 1978-1979 compared with 18 (3.9%) in the 1991-1992 period. There was a significant change in the use of DPR in these subjects over the 14-year period (p<0.001). Of the two subjects who reported the use of DPR in 1978-1979, both were still using the drug in 1991-1992.

In 1978-1979, four subjects (11.1%) who reported the use of DPR also reported use of a coumarin anticoagulant drug concurrently. By the 1991-1992 time period, 17.9% of the subjects who reported DPR use were concurrently administering an anticoagulant. However, there was no statistically significant increase in the concurrent use between the 1978-1979 and the 1991-1992 period (p>0.188).

**DISCUSSION**

Dipyridamole use was found to have increased significantly over the past 14 years in this ambulatory

| Table 1—Age and Gender Distribution of Participants Reporting Dipyridamole Use |
|---|---|---|---|
| **Period** | **Men** | **Women** | **Total** |
| | **No.** | **%** | **Mean Age, yr** | **No.** | **%** | **Mean Age, yr** | **No.** | **%** | **Mean Age, yr** |
| 1978-1979 | 15 | 1.8 | 75.2 | 21 | 1.5 | 77.5 | 36 | 1.6 | 76.6 |
| 1984-1985 | 57 | 7.4 | 78.8 | 68 | 4.8 | 79.3 | 125 | 5.7 | 79.0 |
| 1991-1992 | 18 | 3.6 | 82.6 | 38 | 3.4 | 80.8 | 56 | 3.5 | 81.4 |

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elderly population, both in an independent sample of participants attending the screening program in 1978-1979 and 1991-1992 and in the same subjects who attended all clinic visits over the past 14 years. This was a surprising finding in view of the tremendous amount of literature over the years that has discouraged the use of this drug as a treatment for angina pectoris and as an antithrombotic agent.

FitzGerald\(^7\) reviewed the status of DPR as an antithrombotic drug in the secondary prevention of acute myocardial infarction, transient cerebral infarction, preservation of patency after coronary-artery bypass, prevention of occlusion in obliterative arterial diseases of the lower limbs, prevention of venous thrombosis and thrombolism, and thrombotic complications of cardiac valve disease and concluded that in view of the cost and dose-related adverse effects of DPR, the emerging consensus did not support its use as an antiplatelet drug. Major compendiums list treatment in combination with coumarin anticoagulants in the prevention of postoperative thromboembolic complications of cardiac valve replacement as the only indication for DPR.\(^8\)

Dipyridamole use increased steadily from the first study period in 1978-1979 to the 1986-1987 period. Thereafter, DPR use declined from 7.0% in 1987-1988 to 3.4% in 1991-1992. The explanation for this precipitous decline in DPR use is not clear since the Physicians' Desk Reference (PDR) in 1978 had indicated a lack of efficacy for this drug in angina pectoris. The rating of "possibly effective" in angina pectoris was listed in this text until 1988 when the indication was dropped completely. From 1988 to 1994, the only FDA indication listed in the PDR for DPR is as an adjunct to coumarin anticoagulants in cardiac valve replacement.\(^9\)

Dipyridamole is not an innocuous medication and the benefit to risk considerations should be made when prescribing this medication. A month supply of Persantine brand of dipyridamole (50 mg, three times a day) would cost the pharmacists approximately $45 while the cost for the generic version would be approximately $3 to $6. Therefore, prescribing results of this study suggest that there is a tremendous economic waste occurring since efficacy for the drug is lacking in most instances in which it is prescribed.

One limitation of this study is that the indication for DPR use in these subjects could not be ascertained. Since no information was available on participants who had heart valve replacement, appropriateness of DPR use even when the drug was used in combination with coumarin anticoagulants could not be determined.

In summary, most DPR use in these elderly subjects appears to be unwarranted and many elderly subjects are being subjected to the risk of drug exposure without potential benefit. Educational programs are needed to improve the use of DPR in elderly subjects.

![Figure 1. Percentages of men (squares), women (circles), and total (triangles) subjects who used dipyridamole from 1978 to 1992, and percent of DPR users (diamonds) concurrently reporting the use of coumarin anticoagulants.](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21712/)
REFERENCES

2 American Hospital Formulary Service drug information. Am Soc Hosp Pharm 1994; 1180-81
3 Rowe GG. Aspirin and dipyridamole and their limitations in the therapy of coronary artery disease. Clin Cardiol 1990; 13:165-70
4 Simonsen LLP. What are pharmacists dispensing most often?
8 Physicians’ desk reference. Montvale, NJ: Medical Economics Data Production, 1994; 619

Pharmacy Times 1993; 59:29-44