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The Effect of Dosage Regimen on Medication Compliance

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THE EFFECT OF DOSAGE REGIMEN

ON MEDICATION COMPLIANCE

by

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ABSTRACT

THE EFFECT OF DOSAGE REGIMEN
ON MEDICATION COMPLIANCE

BY: ERNEST W. KEICH

According to recent data, between 25% and 50% of patients are noncompliant in their therapy regimen in some manner. The fourth report of the Joint National Committee on the Detection, Evaluation, and Treatment of High Blood Pressure (Neal, 1989) states that noncompliance is the major problem in hypertension control.

It was hypothesized there would be a difference in the compliance of hypertensive patients whose medication regimen consisted of single daily dosing as opposed to those patients whose regimen consisted of two or more times a day dosing.

Potential subjects for the study were hypertensive patients selected from a rural, southeastern Georgia setting who patronized a local pharmacy. The pharmacy's records from January 1, 1989 through October 15, 1991 were accessed to identify patients prescribed only antihypertensive therapy and whose therapy had been consistent for at least fourteen months. Fifty-five subjects met this criteria.

A data collection form was developed so that information from pharmaceutical records (computerized and

printed patient profiles) could be obtained in a standardized manner. The form consisted of twelve questions which addressed demographics, types of medication, physician information, payor type, and medication therapy.

From the information obtained, the relationship between ten variables (age, gender, town of residence, race, marital status, payor type, whether subject had children, class of medication, physician setting, medication regimen) and compliance percentage was analyzed. Analysis of data was accomplished by univariate and multivariate analysis of variance (ANOVA) to test for significant differences between compliance percentage and the factors of interest for the study.

Dosage regimen (once a day versus two or more times a day) was the only statistically significant factor related to compliance percentage.

INTRODUCTION

The problem of patient compliance in drug therapy continues to be a major concern for healthcare providers, and the subject of much research. Much of this research centers around the effects of noncompliance in antihypertensive therapy. This noncompliance hinders effective treatment by physicians often needlessly prolonging the time necessary to stabilize the blood pressure of patients. The lack of compliance has also resulted in otherwise unnecessary hospital admissions due to complications of unmanaged hypertension (Chan, Larsen, Laventurier, Strandberg, & Sullivan, 1989).

Noncompliance in the treatment of hypertension is a multi-faceted problem. Up to 30% of prescriptions written for antihypertensives are never filled. Many patients fail to have their prescriptions refilled on time. Often follow-up appointments with physicians are never kept. Most hypertensive patients average 3.6 prescriptions which they must administer themselves. This multi-drug therapy may lead to confusion and memory lapse resulting in medications being taken improperly (Fedder, 1990).

All of the above offer an opportunity to hinder medication compliance. Perhaps the most effective aspect that would improve this compliance would be to simpli-

fy drug therapy. Simplification could be accomplished in two ways: First, through the use of combination products, if a patient is now taking two separate blood pressure medications, perhaps he could be prescribed a product which combines the two drugs, thereby reducing the total number of medications consumed; second, by reducing the number of daily doses of medication, if possible offering a regimen of once a day dosing rather than more frequent daily dosing.

PURPOSE

The purpose of this study was to investigate the effect of a once a day medication dosage regimen as opposed to more frequent daily dosing on the compliance of hypertensive patients. The compliance percentages for hypertensive patients were calculated and the relationship of dosage regimens examined.

SIGNIFICANCE

Uncontrolled hypertension can have severe health complications. These complications can manifest themselves in the form of coronary disease, cerebral vascular accidents (commonly called strokes), myocardial infarction, or other ischemic diseases. Among the black population, hypertension is primarily responsible for their high mortality rates from heart and kidney disease and stroke (Coleman, 1990).

Improper medication administration has been shown

to prolong illness and contribute to hospitalization. Concerning hospitalization, Chan et al (1989) reported that the ratio of days without antihypertensive drugs was significantly higher in a re-admit group of patients as compared with a no re-admit group of patients.

At a time when the nation is alarmed at the rocketing costs of health care, especially hospitalization; the exploration of every avenue to enhance favorable patient outcomes has gained importance. With the advent of potent antihypertensive drugs, noncompliance has become the most limiting factor in the management of hypertension (Luscher & Vetter, 1990).

HYPOTHESIS

There is a statistically significant difference in the mean compliance percentage of hypertensive patients whose medication regimens consist of once a day dosing as opposed to those patients whose regimens consist of more frequent daily dosing.

DEFINITIONS

(1) Compliance the extent to which a patient obtained from the pharmacy his medication as scheduled.

(2) Dosage regimen the prescribed medications, their routes of administration, and their dosage frequencies as indicated for an individual's course of therapy.

(3) Combination medication a compound containing two or more antihypertensive medications in a single dosage form.

(4) Compliance percentage refers to the percentage obtained by dividing the number of pills or dosage forms the customer purchased during the time period of study by the number of pills prescribed by the physician during the time period of study. For patients on more than one antihypertensive medication, the medication having the lowest compliance will be used in determining this percentage.

ASSUMPTIONS

The study assumed that the number of pills bought by patients was equal to the number of pills they consumed. The assumption was also made that the patients frequented only the pharmacy chosen for the study as their single source of prescription medications.

LIMITATIONS

The study had several limitations, primarily resulting from the information available on the pharmaceutical records. The importance placed on the physician's influence by each patient was not measured. The amount of health knowledge possessed by each patient was not determined.

The amount of family support and encouragement was not measured. The patient's understanding of his regimen was not accessed; nor was the impact of side effects on the patient's adherence to his medication regimen.

Additional limitations included: the lack of information on the patient's marital adjustment; the lack of a mechanism to determine if the physician may have given the patient oral instructions different from the written prescription; and the lack of sufficient age data so as to be able to determine the impact this variable had on the resulting compliance percentages.

The cost of the medication and whether or not the patient properly monitored his blood pressure also were not assessed.

CHAPTER 2 LITERATURE REVIEW

The lack of drug compliance is recognized by health-care practioners as a major health problem. The degree and extent to which this problem manifests itself has been the subject of many research efforts. This type of research has proven to be difficult due to the numerous definitions used for the term "compliance" by the various investigators (Luscher, Siegenthaler, H. Vetter, & W. Vetter, 1985).

In a recent work reviewing fourteen studies on medication compliance, Luscher, et. al. (1985) reported that twelve different definitions for compliance were utilized. Two studies used "mean compliance rate" as their definition of compliance and two studies defined compliance as greater than 80% of pills taken. Results of these studies yeilded compliance percentages ranging from 19% to 87%. The lack of standardization of definition for compliance might explain some of the differences found in these studies.

Although there is no firmly established definition for compliance, researchers have spent much effort in determining factors which contribute to non-compliance. These factors range from psychological and personal choice behaviors to drug therapy and treatment specific aspects.

Seventeen studies were reviewed to determine factors associated with compliance percentage. The relationship

of the following factors and their impact on medication compliance was explored.

Although the amount of "physician influence" was mentioned as a factor related to compliance (Neal, 1989; Cadoret, Troughton, & Widmer, 1983), no empirical data was presented to support this relationship. Anecdotally, however, many patients will comply with their regimen only if encouraged by their physician (Neal, 1989).

Overall health knowledge of the patient is another factor considered related to compliance. However, review of the literature revealed relatively little support for a strong correlation between the two (Klein, 1988) and no statistical data was presented for Klein's study.

How well the patient understands his medication regimen was discussed as a contributing factor in compliance. The Virginia affiliate of The American Heart Association surveyed 425 physicians as to why they felt some of their patients did not adequately control their hypertension. The lack of understanding of medication regimen by the patient was the major reason given in 82% of the cases of uncontrolled hypertension (Moore, 1988).

Studies also concentrated on patient education and compliance counseling. Black, Elden, Geary, Hovell, Kamachi, and Kirk (1985) found an increase from 60% to

100% in compliance percentage after patient counseling. Moore (1988) found that frequent blood pressure monitoring improved compliance in some patients. This study recommended company sponsored blood pressure monitoring in the work place.

Physician setting was mentioned as having an affect on compliance, but only in a single study which did not present statistical data (Neal, 1989). This study found that patients seeing physicians in private settings demonstrated better compliance than those seeing physicians in clinic settings.

In 1990, Groff, Jono, Trevino and Young reported a relationship between marital adjustment and remembering to take blood pressure medication. They used a 32-item Dyadic Adjustment Scale to measure the subject's perception of affection, consensus, cohesion and satisfaction in marriage. This study supported the concept that better marital adjustment does contribute to greater compliance with prescribed medical regimens.

The effect of the amount of family support has also been found to be a determinant of medication compliance. The extent to which the patient obtains support from family members was stated as being directly related to a patient's compliance (Cadoret, Troughton, & Widmer, 1983).

However, no statistical data relating to this factor was presented.

An obvious reason for a patient being unable to comply is the cost of medication. Although cost was discussed as a factor for compliance, no statistical data relating medication expense to compliance was presented in a study by Fletcher (1989).

Both age and side effects were also the focus of research related to medication compliance. Interestingly, in reviewing literature on compliance, age was a factor seldom considered in this research. Klein (1988) found that the elderly patients try very hard to be compliant. This study quoted two reports: the Maryland Statewide Hypertension Survey as reported by Entwisle, German, Klein, Levine and Southard (1984), found that the patients most likely to be actively taking their medication were the elderly; and a report from the National, Heart, Lung, and Blood Institute (Haines & Ward, 1981) which stated that, "Younger hypertensives were more likely to discontinue their medications than older ones".

Side effects were discussed in two studies as a factor possibly impacting compliance; however, the results were conflicting. The first study was directed at how physicians could improve their patients medication compliance. In this study Moore, (1988) found that side

effects, whether real or perceived, are often a cause for patients to discontinue their medication. However, Klein (1988) reported that the inverse relationship of compliance and side effects was very weak and possibly of limited clinical importance.

The effect of race and gender on medication compliance was considered. Moore (1988) found that inadequate hypertension control was most fequent in young blacks and that a major factor contributing to this lack of control was non-compliance with antihypertensive therapy. Chan et al (1989) found in a study of underutilization of antihypertensive drugs and associated hospital re-admissions, 61% were black and 64% were female. Luscher and Vetter (1990) found that dropouts during antihypertensive therapy tended to be male and of low socioeconomic status. However, this study also stated that patient characteristics such as sex and race were unreliable predictors of compliance with medication therapy.

Two additional factors affecting compliance appeared in more studies than any other. The first was the number of different medications taken by the patient. The second was the number of times a day the patient had to take each medication. Much of the literature describing these two factors stressed simplification of the patients drug therapy. It is strongly recommended that for increased

compliance, the medication therapy should be simple and, if possible, a once-a-day dosing regimen (Morgan, Murphy, Nowson, & Snowdon, 1986). Another recommendation is to prescribe combination medications. The combination medications would enhance compliance by reducing the total number of pills taken each day and because they are usually less costly (Moore, 1988).

As is evidenced, the impact of non-compliance is great both in terms of monetary and health costs. The contributory factors are many; some easier to manipulate than others. Prescribing a simpler dosage regimen certainly appears to offer a measurable positive affect on medication compliance.

CHAPTER 3 METHODOLOGY

This study was an indepth case study of selected hypertensive patients in an effort to determine the relationship of drug regimen and medication compliance. A twelve question data collection tool was developed and utilized to record accumulated information of medication purchases in a standardized manner.

The population consisted of hypertensive patients receiving medications from a pharmacy in a rural setting. The pharmacy was located in a town of approximately 2000 people. There was not another pharmacy within an eight mile radius of the one chosen for this investigation. The county and town were mid-to-lower economic areas with little industrial development and were largely agriculturally based.

Since registered pharmacists have legal access to patient records and are required by professional ethics to maintain patient confidentiality, there was no need to obtain permission to review records from the subjects. Printed and computerized profiles from January 1, 1989 to October 15, 1991 were reviewed retrospectively for all patients utilizing the pharmacy.

Hypertensive patients who met the following criteria were selected as the sample for the study. First, that they were taking only antihypertensive medications during

this study period. This criteria implied that the patient was taking a "pure" medication regimen (no other medications were prescribed). Second, that they were taking the same regimen of antihypertensives for at least fourteen months. This second criteria implied the following: that the patient's blood pressure was stablilized and there was no need to change medication regimen, that the patient was compliant, and the patient was experiencing no significant side effects.

Each eligible patient was assigned an unique indentification number which was used instead of a patient's name on all data abstraction forms. All information relating the patient's name to his identification number was destroyed; thus, ensuring confidentiality.

For each patient, the principle researcher completed a "Hypertensive Patient Data Collection Form" (See appendix A). Information was abstracted from the pharmacy's patient profiles. This information included the following: age, gender, zip code, race, marital status, payor type (private, medicaid, third party, or other), whether the patient had children, class of medication purchased, physician setting (private or clinic), medication regimen (once a day, twice daily, three times daily, four times daily, five times daily or more), medication name,

and compliance percentage.

The compliance percentage for each patient was determined by dividing the number of pills that the patient purchased over at least a fourteen month period (the numerator) by the number of pills that should have been taken for the same time period as determined by the recorded medication dosage regimen (the denominator). For patients on multiple hypertensive medications, the medication having the lowest compliance was used in determining this percentage. This method was selected since the most consistent a subject could be in terms of medication compliance would be indicated by their lowest compliance percentage.

The statistical technique used to test the study's hypothesis was analysis of variance. A one-way analysis of variance was used to assess the relationship of compliance percentage and each categorical variable included in the study. Comparisons were considered significantly different if a p-value of .05 or less was computed. For regimen, a dichotomous variable was created: 1) Those patients who took their medications once daily; 2) Those who took their medications two or more times per day.

A multivariable ANOVA model was constructed to test the relationship between regimen and compliance when ad-

justing for race and gender. These two variables were associated with compliance rate in other studies (Chan et al, 1989).

CHAPTER 4 ANALYSIS AND FINDINGS

Fifty-five pharmacy patrons met the study's inclusion criteria. Information abstracted for these subjects utilizing the "Hypertensive Patient Data Collection Form" (Appendix A) was used for the analysis. Statistical analysis of the data was performed using the Statistical Package for Social Science (Norusis, 1988).

There were two continuous variables considered in the study; age and compliance percentage (Table I). For the fifty five subjects, age information was available for eighteen patients only. The mean age for these eighteen patients was 60.78 years. The mean compliance percentage for the sample was 83.25%.

TABLE I.

DESCRIPTION OF CONTINUOUS VARIABLES OF SAMPLE

FACTOR	NUMBER	MEAN	STD. DEV.
Age(years)	18	60.78	13.49
Compliance Percentage	55	83.25	17.75

Frequencies and percentages of the categorical factors included in the study are reported in Table II.

TABLE II.

DESCRIPTION OF CATEGORICAL VARIABLES OF SAMPLE

FACTOR	NUMBER	PERCENTAGE
Gender		
a) Male	31	56.4
b) Female	24	43.6
Town of Residence		
a) Rincon	5	9.1
b) Springfield	26	47.3
c) Guyton	13	23.6
d) Eden	2	3.6
e) Clyo	7	12.7
Missing data	2	3.6
Race		
a) White	40	72.7
b) Black	14	25.5
Missing data	1	1.8
Marital Status		
a) Married	42	76.4
b) Divorced	1	1.8
c) Widowed	10	18.2
Missing data	2	3.6
Payor Type		
a) Private	46	83.6
b) Medicaid	1	1.8
c) Third party	3	5.5
d) Other	5	9.1
Has Children		
a) Yes	48	87.3
b) No	5	9.1
Missing data	2	3.6
Class of Medication		
a) Diuretic	3	5.5
b) Antiadrenergic	7	12.7
c) Calcium blocker	11	20.0
d) Ace-inhibitor	19	34.5
e) Combination	14	25.5
f) Other	1	1.8
Physician Setting		
a) Private	49	89.1
b) Clinic	6	10.9
Medication Regimen		
a) Once daily	33	60.0
b) Twice daily	18	32.7
c) Three times/day	3	5.5
d) Every other day	1	1.8

The sample was predominantly male (56.4%) and married (76.4%). The majority (70.9%) of the subjects resided in two towns, Springfield and Guyton. The majority (72.7%) of the sample was white and had children (87.3%). The sample was predominantly (83.6%) private pay and 80.0% of the subjects received one of three classes of medication: calcium channel blockers, ace-inhibitors or a combination product. The majority (89.1%) of the patients saw physicians in private settings and were on a once-a-day medication regimen (60.0%).

The results of one-way analysis of variance (ANOVA) are presented in Table III. From this analysis, the only study factor to show a significant relationship in effecting compliance percentage was medication regimen (89.14 versus 74.6 mean percentage, p= 0.0026).

In the multivariable ANOVA model which included compliance percentage (dependent variable), regimen, race, and gender; regimen was again found to be statistically significant (p= 0.006). The mean percentage for once a-day was 89.15, and the mean percentage for two or more times a day was 75.05. Race and gender were not significantly related to compliance percentage.

TABLE III.

UNIVARIATE ANALYSIS COMPARING MEAN COMPLIANCE PERCENTAGE FOR SELECT STUDY FACTORS

FACTOR	NUMBER	MEAN	STD DEV	PROB-ABILITY
Gender				0.2550
a) Males	31	80.83	20.15	
b) Females	24	86.37	13.86	
Town of Residence				0.9224
a) Rincon	5	79.64	32.27	
b) Spring-field	26	82.52	17.57	
c) Guyton	13	82.64	16.46	
d) Eden	2	93.90	4.67	
e) Clyo	7	84.11	14.68	
Race				0.8490
a) White	40	83.30	19.00	
b) Black	14	84.36	14.16	
Marital Status				0.8394
a) Married	42	83.07	17.82	
b) Divorced	1	74.80	00.00	
c) Widowed	10	85.33	19.44	
Payor Type				0.7338
a) Private	46	82.35	18.51	
b) Medicaid	1	99.20	00.00	
c) Third pty.	3	83.30	14.52	
d) Other	5	88.28	13.84	
Has Children				0.1107
a) Yes	48	82.08	18.25	
b) No	5	95.48	4.61	
Physician Setting				0.3118
a) Private	49	82.39	18.15	
b) Clinic	6	90.23	13.27	
Class of Medication				0.6438
a) Diuretic	3	94.90	4.33	
b) Anti-adrenergic	7	85.53	15.45	
c) Calcium Blocker	11	78.16	26.95	
d) Ace-inhibitor	19	85.85	13.93	
e) Combin-ation	14	79.56	16.86	
f) other	1	90.40	00.00	
Regimen				.0026*
a) Once/day	33	89.14	11.12	
b) 2 or more times/day	21	74.60	22.56	

* $p < .05$

DISCUSSION AND CONCLUSIONS

This study was unique in the selective nature of the sample. No other research that was reviewed included patients taking only antihypertensive medications or required the subjects to remain on the same antihypertensiv medication regimen for an extended period of time, such as fourteen months.

The implications resulting from this criteria were that the subjects' medication regimens were "pure" (they were not taking other medications); that the subjects' blood pressures were stabilized, thus there was no need to change medication regimens; that the subjects were experiencing no significant side effects; and that they were for the most part compliant.

These implications suggest a very specific population which may affect generalizability of the study results. However, this select study sample enhances the internal validity of the results in a way no other study has to date. Specifically, in showing that within this highly compliant group, once-a-day regimens showed significantly higher compliance than two or more times a day regimens.

Based on the information presented in this study, the impact of dosage regimen on compliance percentage is apparent. Those patients whose regimen consists of

once a day therapy had a significantly higher (p=0.0026) compliance percentage (89.14%) than those patients taking the medications two or more times a day (74.6%). This relationship also held after adjusting for age and gender. The mean compliance percentages found in this study compared closely to those found in similar studies. Cadoret, Troughton, and Widmer (1983) found a mean compliance percentage of 87.5% for patients taking medications once or twice a day and 78% for patients taking medications three or four times a day.

This study supports efforts to educate physicians to utilize newer antihypertensive medications which are taken once a day. It should be noted that 40% of the subjects in this study were on a more than once-a-day regimen. If patients can be switched to once-a-day medication and safely stabilized, then better compliance should be attained and ultimately lead to more effective blood pressure control.

Although this study did show a significant relationship between compliance percentage and regimen, the small size of the sample may have diminished statistical importance of other study factors. In addition, the source of information, pharmacy patient profiles, lacked data for certain variables. These missing data included health knowledge of subject, patient's understanding of his medication regimen, patient's marital adjustment,

whether the subject properly monitored his blood pressure, and if the physician may have given the patient oral instructions different from the written prescription. No statement of their impact on compliance percentage in this study can be offered.

The assessment of the effect of age on compliance was also limited in the study because of the sparsity of data. However, a univariate ANOVA model (n=18) examining compliance rate and age found no significant relationship between these two variables. Other authors stated that the elderly were more compliant (Klein, 1988).

Further research is indicated on the possible relationships of other factors (side effects, cost of medications, and patient's understanding of regimen) and their affect on compliance percentage, not only to produce new findings but also to add support to the findings of this study.

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Appendix A

HYPERTENSIVE PATIENT DATA COLLECTION FORM

1. I.D. # _____

2. Birthdate: Month ____ Day ____ Year _____

3. Gender (Circle): (1 = male, 2 = female)

4. Zip Code _____

5. Race (Circle): (1 = white, 2 = black, 3 = asian, 4 = hispanic, 5 = other)

6. Martial Status (Circle): (1 = married, 2 = single, 3 = divorced, 4 = widowed)

7. Payor Type (Circle): (1 = private, 2 = medicaid, 3 = third party, 4 = other)

8. Children (Circle): (1 = yes, 2 = no)

9. Medication Class (Circle): (1= diuretic, 2= antiadrenergic, 3= calcium channel blocker, 4= ACE-inhibitor, 5=vasodilator 6= combination, 7= other)

10. Physician's name: _____

11. Physician's practice setting (Circle): (1= private 2= clinic)

12. a) Regimen #1

	Drug #1	Drug #2	Drug #3
medication name	_____	_____	_____
date began	_____	_____	_____
#times/day	_____	_____	_____
#dosages/adminis.	_____	_____	_____
date discontinued	_____	_____	_____
# of dosages should have taken	_____	_____	_____
# of dosages actually taken	_____	_____	_____

b) Regimen #2	Drug #1	Drug #2	Drug #3
medication name	_____	_____	_____
date began	_____	_____	_____
#times/day	_____	_____	_____
#dosages/adminis.	_____	_____	_____
date discontinued	_____	_____	_____
# of dosages should have taken	_____	_____	_____
# of dosages actually taken	_____	_____	_____

c) Regimen #3	Drug #1	Drug #2	Drug #3
medication name	_____	_____	_____
date began	_____	_____	_____
#times/day	_____	_____	_____
#dosages/adminis.	_____	_____	_____
date discontinued	_____	_____	_____
# of dosages should have taken	_____	_____	_____
# of dosages actually taken	_____	_____	_____

Appendix B

THE EFFECT OF DOSAGE REGIMEN ON MEDICATION COMPLIANCE

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Abstract

According to recent data between 25% and 50% of patients are noncompliant in their therapy regimen in in some manner. The purpose of this study was to determine the relationship of the frequency of daily doses and medication compliance of hypertensive patients. The subjects of the study were fifty-five patients who were prescribed only antihypertensive therapy and whose therapy had been consistent for at least fourteen months. Pharmacy records were accessed to determine the compliance of these subjects. Patients on a once-a-day regimen demonstrated a statistically significant ($p= 0.0026$) different mean compliance percentage of 89.14% compared to a mean compliance percentage of 74.6% for those on a two or more times a day regimen.

INTRODUCTION

The problem of patient compliance in drug therapy continues to be a major concern for healthcare providers, and the subject of much research. Much of this research centers around the effects of noncompliance in antihypertensive therapy. Noncompliance hinders effective treatment by physicians, often needlessly prolonging the time necessary to stabilize the blood pressure of patients. Lack of compliance has also resulted in otherwise unnecessary hospital admissions due to complications of unmanaged hypertension (1).

Noncompliance in the treatment of hypertension is a multi-faceted problem. Up to 30% of prescriptions written for antihypertensives are never filled. Many patients fail to have their prescriptions refilled on time. Often follow-up appointments with physicians are never kept. Most hypertensive patients average 3.6 prescriptions for different medications which they must administer themselves. This multi-drug therapy may lead to confusion and memory lapse resulting in medications being taken improperly (2).

All of the above indicate that lack of medication

compliance is a major hindrance to the treatment of hypertension. Perhaps the most effective aspect that would improve this compliance would be to simplify drug therapy. Simplification could be accomplished in two ways. First, through the use of combination products. If a patient is now taking two separate blood pressure medications, perhaps he could be prescribed a product which combines the two drugs, thereby reducing the total number of medications consumed. The second method of simplication would be to reduce the number of daily doses of medication; if possible offer a regimen of once a day dosing rather than more frequent daily dosing.

The purpose of this study was to investigate the effect of a once a day medication dosage regimen on the compliance of hypertensive patients as opposed to more frequent daily dosing. The compliance percentages for hypertensive patients were calculated by dividing the number of pills purchased during the time period of study by the number the number of pills prescribed by the physician during the time period of study. For patients on more than one antihypertensive medication, the medication having the lowest compliance was used in determing this percentage.

Methods

The population consisted of hypertensive patients receiving medications from a pharmacy in a rural setting. The pharmacy was located in a town of approximately 2000 people. There was not another pharmacy within a nine mile radius of the one chosen for this investigation. The county and town were mid-to-lower economic areas with little industrial development and largely agriculturally based.

Hypertensive patients who met the following criteria were selected as the sample for the study. First, that they were taking only antihypertensive medications during this study period. This criteria implied that the patient was taking a "pure" medication regimen (no other medications were prescribed). Second, that they were taking the same regimen of antihypertensives for at least fourteen months. This second criteria implied the following: that the patient's blood pressure was stablilized and there was no need to change medication regimen, that the patient was compliant, and the patient was experiencing no significant side effects. Based on these requirements, fifty-five patients were included in the study. Each patient was assigned an unique indentification number which was used instead of a patient's name on all data abstraction forms. All information relating the patient's name to

his identification number was destroyed; thus, ensuring confidentiality.

Since registered pharmacists have legal access to patient records and are required by professional ethics to maintain patient confidentiality, there was no need to obtain permission to review records from the subjects. Printed and computerized profiles from January 1, 1989 to October 15, 1991 were reviewed retrospectively for all patients patronizing the pharmacy.

A twelve question data collection tool was developed and utilized to retrieve accumulated information of medication purchases in a standardized manner. For each patient, the principle researcher completed the "Hypertensive Patient Data Collection Form". Information abstracted from the pharmacy's patient profiles included the following: age, gender, zip code, race, marital status, payor type (private, medicaid, third party, or other), whether the patient had children, class of medication purchased, physician setting (private or clinic), medication regimen (once a day, twice daily, three times daily, four times daily, five times daily or more), medication name, and compliance percentage.

The compliance percentage for each patient was determined by dividing the number of pills that the

patient purchased over at least a fourteen month period by the number of pills that should have been taken for the same time period as determined by the recorded medication dosage regimen. For patients on multiple hypertensive medications, the medication having the lowest compliance was used in determining this percentage. This method was selected since the most consistent a subject could be in terms of medication compliance would be indicated by their lowest compliance percentage.

The statistical technique used to test the study's hypothesis was analysis of variance. A one-way analysis of variance was used to assess the relationship of compliance percentage and each categorical variable included in the study. Comparisons were considered significantly different if a p-value of .05 or less was computed. For regimen, a dichotomous variable was created: 1) Those patients who took their medications once daily; 2) Those who took their medications two or more times per day.

A multivariable ANOVA model was constructed to test the relationship between regimen and compliance when adjusting for race and gender. These two variables were commonly associated with compliance rate in other studies (1).

Results

Statistical analysis of the data was performed using the Statistical Package for Social Science (4). Information abstracted for the fifty-five subjects utilizing the "Hypertensive Patient Data Collection Form" was used for the analysis.

There were two continuous variables considered in the study; age and compliance percentage (Table I). For the fifty five subjects, age information was available for eighteen patients only. The mean age for these eighteen patients was 60.78 years. The mean compliance percentage for the sample was 83.25%.

TABLE I.

DESCRIPTION OF CONTINUOUS VARIABLES OF SAMPLE

FACTOR	NUMBER	MEAN	STD. DEV.
Age(years)	18	60.78	13.49
Compliance percentage	55	83.25	17.75

Frequencies and percentages of the categorical factors included in the study are reported in Table II.

TABLE II.

DESCRIPTION OF CATEGORICAL VARIABLES OF SAMPLE

FACTOR	NUMBER	PERCENTAGE
Gender		
a) Male	31	56.4
b) Female	24	43.6
Town of Residence		
a) Town I.	5	9.1
b) Town II.	26	47.3
c) Town III.	13	23.6
d) Town IV.	2	3.6
e) Town V.	7	12.7
Missing data	2	3.6
Race		
a) White	40	72.7
b) Black	14	25.5
Missing data	1	1.8
Marital Status		
a) Married	42	76.4
b) Divorced	1	1.8
c) Widowed	10	18.2
Missing data	2	3.6
Payor Type		
a) Private	46	83.6
b) Medicaid	1	1.8
c) Third party	3	5.5
d) Other	5	9.1
Has Children		
a) Yes	48	87.3
b) No	5	9.1
Missing data	2	3.6
Class of Medication		
a) Diuretic	3	5.5
b) Antiadrenergic	7	12.7
c) Calcium blocker	11	20.0
d) Ace-inhibitor	19	34.5
e) Combination	14	25.5
f) Other	1	1.8
Physician Setting		
a) Private	49	89.1
b) Clinic	6	10.9
Medication Regimen		
a) Once daily	33	60.0
b) Twice daily	18	32.7
c) Three times/day	3	5.5
d) Every other day	1	1.8

The sample was predominantly male (56.4%) and married (76.4%). The majority (70.9%) of the subjects resided in two towns. The majority (72.7%) of the sample was white and had children (87.3%). The sample was predominantly (83.6%) private pay and 80.0% of the subjects received one of three classes of medication: calcium channel blockers, ace-inhibitors or a combination product. The majority (89.1%) of the patients saw physicians in private settings and were on a once-a-day medication regimen (60.0%).

The results of one-way analysis of variance (ANOVA) are presented in Table III. From this analysis, the only study factor to show a significant relationship in effecting compliance percentage was medication regimen (89.1 versus 74.6 mean percentage at a $p = 0.0026$).

In the multivariable ANOVA model which adjusted for race and gender, regimen was again found to be significantly different at $p= 0.006$ (89.15 mean percentage for once-a-day versus 75.05 mean percentage for two or more times a day).

Discussion

This study was unique in the selective nature of the sample. No other research reviewed considered patients taking only antihypertensive medications or required the

TABLE III.

UNIVARIATE ANALYSIS COMPARING MEAN COMPLIANCE PERCENTAGE FOR SELECT STUDY FACTORS

FACTOR	NUMBER	MEAN	STD DEV	PROB-ABILITY
Gender				0.2550
a) Males	31	80.83	20.15	
b) Females	24	86.37	13.86	
Town of Residence				0.9224
a) Town I.	5	79.64	32.27	
b) Town II.	26	82.52	17.57	
c) Town III.	13	82.64	16.46	
d) Town IV.	2	93.90	4.67	
e) Town V.	7	84.11	14.68	
Race				0.8490
a) White	40	83.30	19.00	
b) Black	14	84.36	14.16	
Marital Status				0.8394
a) Married	42	83.07	17.82	
b) Divorced	1	74.80	00.00	
c) Widowed	10	85.33	19.44	
Payor Type				0.7338
a) Private	46	82.35	18.51	
b) Medicaid	1	99.20	00.00	
c) Third pty.	3	83.30	14.52	
d) Other	5	88.28	13.84	
Has Children				0.1107
a) Yes	48	82.08	18.25	
b) No	5	95.48	4.61	
Physician Setting				0.3118
a) Private	49	82.39	18.15	
b) Clinic	6	90.23	13.27	
Class of Medication				0.6438
a) Diuretic	3	94.90	4.33	
b) Anti-adrenergic	7	85.53	15.45	
c) Calcium Blocker	11	78.16	26.95	
d) Ace-inhibitor	19	85.85	13.93	
e) Combin-ation	14	79.56	16.86	
f) other	1	90.40	00.00	
Regimen				.0026*
a) Once/day	33	89.14	11.12	
b) 2 or more times/day	21	74.60	22.56	

* $p < .05$

subjects to remain on the same antihypertensive medication regimen for an extended period of time such as fourteen months.

The implications resulting from this criteria were that the subjects' medication regimens were "pure" (they were not taking other prescription medications); that the subjects' blood pressures were stabilized thus there was no need to change medication regimens; that the subjects were experiencing no significant side effects; and that they were compliant.

These implications suggest a very specific population which may affect generalizability of the study results. However, this select study sample enhances the internal validity of the results in a way no other study has to date. Specifically, in showing that within highly compliant groups, once-a-day regimens showed significantly higher compliance than two or more times a day regimens.

Based on the information presented in this study, the impact of dosage regimen on compliance percentage is apparent. Those patients whose regimen consists of once a day therapy had a significantly higher ($p=0.0026$) compliance percentage (89.14%) than those patients taking the medications two or more times a day (74.6%). This relationship also held after adjusting for age and gender. The mean compliance percentages found in this study com-

pared closely to those found in similar studies. Cadoret, Troughton, and Widmer(5) found a mean compliance percentage of 87.5% for patients taking medications once or twice a day and 78% for patients taking medications three or four times a day.

This study supports efforts to educate physicians to utilize newer antihypertensive medications which are taken once a day. It should be noted that 40% of the subjects in this study were on a more than once-a-day regimen. If patients can be switched to once-a-day medication and safely stabilized, then they should experience better compliance which would lead to more effective blood pressure control.

Although this study did show a significant relationship between compliance percentage and regimen, the small size of the sample may have diminished statistical differences between other study factors. In addition, the source of information, pharmacy patient profiles, lacked data for certain variables. These missing data included health knowledge of subject, patient's understanding of his medication regimen, patient's marital adjustment, whether the subject properly monitored his blood pressure, and if the physician may have given the patient oral instructions different from the written prescription.

No statement of their impact on compliance percentage in this study is founded.

The effect of age on compliance was also limited in the study because of the sparsity of data. However, a univariate ANOVA model (n=18) examing compliance rate and age found no significant relationship between these two variables. Other authors stated that the elderly were more compliant (5).

Further research is indicated on the possible relation ships of other factors (side effects, cost of medications, and patient's understanding of regimen) and their affect on compliance percentage, not only to produce new findings but also to add support to the findings of this study.

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