

FINAL REPORT

A MULTISITE EVALUATION OF THE ACUTE EFFECTS OF
PHENYLPROPANOLAMINE IN NORMAL VOLUNTEERS

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ABSTRACT

Two hundred sixteen (216) healthy normotensive volunteers (mean age = 29.6), presenting with various degrees of overweight participated in a double blind, placebo-controlled evaluation of the effects of phenylpropanolamine HCL (PPA) on blood pressure, pulse, and mood. Two dosage forms of PPA were studied (75 mg sustained release and 25 mg t.i.d.) in comparison with placebo. Subjects in each of four weight categories were randomly assigned to one of the three drug conditions. The weight categories were normal weight (n=36), mildly overweight (15-30%, n=72), moderately overweight (31-45%, n=72), and severely overweight (over 46%, n=36). Subjects received a test medication (either an active product or placebo) 3 times during a 12 hour testing session. Subjects in one group (Group A) received a 75 mg sustained release dose on their first medication occasion and placebo capsules on the other two dosing occasions. Subjects in another group (Group B) received 25 mg doses at each medication occasion. Subjects in the other group (Group C) received placebo at each medication occasion. Subjects were studied for a 12 hour testing session.

Measurements of blood pressure (both standing and supine), pulse, and subjective drug effect (using the Addiction Research Center Inventory- ARCI) were obtained 11 times during the session at baseline (prior to drug administration) and at 1/2 hour, 1 hour, 2 hours, 4 hours, 4-1/2 hours, 6 hours, 8 hours, 8-1/2

hours, 10 hours, and 12 hours post initial dosing.

Mixed design analysis of variance revealed no overall main effects for drug treatments on pulse or blood pressure for either body position. This finding is quite consistent with research conducted at a number of other well-established clinical sites. Subjects in the heavier weight categories consistently showed more rapid pulse rates than did those subjects of normal or near normal weight. However, no significant differences in drug effect as a function of weight classification were observed. As expected, most measures showed main effects for measurement time (circadian effects), indicating that subjects' physiological and subjective state changed over the course of the session. Significant interactions for drug treatment and measurement time were obtained for systolic blood pressure measures taken in both body positions and for pulse in the standing position only.

One way analysis of variance of peak diastolic blood pressure during the course of the session indicated a main effect for drug treatment in the supine position only. Peak diastolic change from baseline, however, was reliably related to drug treatment when measured in both body positions. The peak effects observed, although statistically reliable, were small and not considered to be clinically significant. Subjective effects, as measured by the Addiction Research Center Inventory, did not differentiate the drug treatment conditions but did show normal circadian variation. The present results are consistent with much previous research indicating that no clinically significant increases in

blood pressure or pulse are associated with PPA at the currently recommended dose.

Data Report: Site 1 Boston

Protocol:

A MULTISITE EVALUATION OF THE ACUTE EFFECTS OF
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INTRODUCTION

Phenylpropanolamine hydrochloride (PPA) is a synthetic compound with actions similar to ephedrine. However, PPA is generally believed to produce less CNS stimulation than ephedrine. PPA is currently marketed over-the-counter (OTC) in the United States both as a nasal decongestant and as a weight control aid. Recently FDA and others have raised questions about the safety and appropriateness of OTC availability of PPA (Federal Register, Vol. 47, No. 39, 1982). In their publication, the agency requested additional information on the effects of PPA on a variety of safety parameters including blood pressure, pulse, and self-reported side effects. Previous work sponsored by the Thompson Medical Company investigated the effects of two dosage forms of PPA (75 mg sustained release and 25 mg t.i.d) in comparison with placebo. Measures of blood pressure, pulse, mood, and subjective drug effects were taken over the course of a 12 hour session in a group of 150 normal volunteers. No adverse

effects on any of the measures were observed. This result was replicated in a crossover design using 59 normal volunteers exposed to both the 75 mg sustained release formulation and placebo. The present study is part of a multi-site extension of this work (Funderburk et al., 1982a, 1982b, 1982c) designed to provide an independent evaluation of the effects of PPA in normal volunteers. In addition, the present study was also designed to evaluate weight classification (in terms of degree of overweight) as a variable which could influence the physiological and subjective effects of PPA at recommended dose levels.

OBJECTIVE

The present study aims to provide an objective characterization of the effects of PPA on various behavioral and physiological parameters over a 12 hour testing session. Normal volunteers in four weight classes (normal weight, mildly overweight, moderately overweight and severely overweight) were studied to evaluate the effects of PPA over a wide range of weight classes.

RATIONALE

PPA has been used as an anorexiant for over 40 years and has long been an ingredient in many over-the-counter cough-cold products (see, e.g., Silverman, 1980). Recently, however, some reports have appeared suggesting that PPA--generally in doses higher than those approved for over-the-counter use in the United States--may be associated with adverse hypertensive effects or

other amphetamine-like side effects (e.g., Horowitz, 1980; Dietz, 1981). In contrast, a number of well controlled studies of PPA at recommended dose levels have been conducted which suggest that PPA (at recommended dose levels) is not associated with adverse effects. Silverman et al. (1980) reported no adverse hypertensive effects of a 25 mg dose of PPA either alone or in combination with 100 mg of caffeine. Hoebel (paper in preparation, 1982) noted no adverse hypertensive effects of 150 mg PPA (75 mg b.i.d.) in a group of six normotensive individuals. Funderburk et al. (1982a, 1982b, 1982c) in a series of double-blind placebo controlled studies noted no adverse effects on blood pressure, pulse, mood or subjective state in 150 normal volunteers studied for a 12 hour period following doses of 75 mg sustained release PPA or a 25 mg t.i.d. dosage formation. Similar results were found in a crossover comparison (n=59) of 75 mg sustained release PPA and placebo.

The present study was undertaken to extend the examination of PPA effects on blood pressure, pulse, and subjective state in another large, carefully controlled clinical investigation.

INVESTIGATIVE METHODS

Subjects

Subjects were 216 healthy normal volunteers (mean age= 29.6) (both male and female). The study population consisted of 189 Caucasians, 14 Blacks, 2 American Indians, 2 Orientals, and 7

"others". Seventy-two (33.3%) of the subjects were women. All had given informed consent and had been screened to meet the following criteria:

1. between 18 and 65 years of age
2. weight stratification (according to the Metropolitan Life Insurance Scales) 36 normal weight 72 mildly overweight (15-30%) 72 moderately overweight (31-45%) 36 severely overweight (46+%)
3. no current use of medications which would compromise the validity of the evaluation of the test products.
4. no physical or allergic contraindications to consumption of PPA at the dose levels used in this study.
5. no hypertensive history defined as a diastolic blood pressure greater than 94mmHg.
6. no diabetics.
7. no history of severe emotional disturbance (severe depression, etc.), chronic alcoholism, or drug abuse.
8. evidence that the subject would participate in the research and be cooperative
9. good general health based on a medical history interview conducted within one month of the study start and a recent

physical examination.

10. female subjects certified that they were not pregnant or nursing a baby for the duration of the protocol.

Design and Procedure

This investigation is a large-sample parallel group design in which approximately 864 subjects (approximately 216/site) are tested at four sites under treatment conditions as detailed below. This portion of the report describes the results obtained at the Boston site under the medical direction of Dr. xxx Blackburn.

1. General Procedures

- a. Subject control. Subjects were instructed to be free of all medications for the week prior to the administration of a test product. Subjects who ingested substances which compromised the validity of the study were excluded. Study medications were administered under clinical supervision. Subjects remained at the test facility for the entire testing period during test days.

- b. Meals and food restrictions. On test days subjects were provided with a choice of standard noontime meals. Foods containing xanthines (e.g., coffee, tea, cola) were not permitted on study day, and subjects were instructed not to use these foods in their breakfast before coming to the test facility.

c. Drug administration. In this investigation two currently marketed dose forms of a test product containing PPA (PPA, 75 mg sustained - release and 25 mg t.i.d. were compared with placebo. Medications were administered following double-blind procedures. On each test day subjects received the test product at approximately 8:00 am, 12 Noon, and 4 pm, or equivalent spacing if test day started early (e.g., 7 am, 11 am, 3 pm).

Subjects were randomly assigned to one of three drug treatment conditions stratified by weight. One group of subjects (Condition A) received the 75 mg sustained release product at their first dosing and placebo capsules on subsequent dosings. Another group of subjects (Condition B) received 25 mg t.i.d. and a third group of subjects (Condition C) received placebo, as illustrated below. All medications were taken with a full glass of water.

Dosing Schedule on a Test Day

	Dose 1 (approx. 8:00 am)	Dose 2 (approx. 12 noon)	Dose 3 (approx. 4:00 pm)
Condition A	75 mg sustained	placebo	placebo
Condition B	25 mg PPA	25 mg PPA	25 mg PPA
Condition C	placebo	placebo	placebo

d. Clinical measures. Clinical measures of subjective state of blood pressure and pulse were obtained 11 times during each experimental session: once prior to initial drug administration (0 hr) and at 1/2 hr, 1 hr, 2 hr, 4 hr, 4-1/2 hr, 6 hr, 8 hr, 8-1/2 hr, 10 hr, and 12 hr following initial drug administration.

Blood pressure (after standing for 2 minutes and after being supine for 5 minutes) was measured using procedures recommended by the American Heart Association (Kirkendall et al., 1980). Clinical measures of subjective states were obtained using a self-administered standardized drug effect scale at each measurement interval (Addiction Research Center Inventory; ARCI). These measures were supplemented by subjective reports of subjects and the observations of research staff.

e. Subjective drug effects were measured using the short version of the Addiction Research Center Inventory (ARCI). This is a standardized, self-administered inventory which compares the

subjective effects of a test compound with those of a variety of CNS-active drugs (see Haertzen, 1974, for a detailed description). The inventory requires approximately 5 minutes to complete. The scales used in this study, and the characteristics they reflect, are:

1. AMP: empirical scale which measures similarity to amphetamine effects.
2. BG: group variability scale which measures similarity to benzedrine effects. Interpreted as a measure of intellectual efficiency and energy.
3. MBG: group variability scale which measures a morphine-benzedrine effect. Interpreted as a measure of euphoria.
4. PCAG: group variability scale which measures pentobarbital-chlorpromazine-alcohol effects. Interpreted as a measure of sedation, fatigue, and low motivation.
5. LSD: empirical scale which measures similarity to LSD effects. Interpreted as a measure of anxiety, tension, difficulty in concentration, depersonalization, and psychomimetic changes. Also interpreted as a measure of dysphoria.

This inventory was administered in association with each of the 11 clinical measurement occasions. This version of the ARCI

contains empirically derived scales which have been validated in thousands of subjects since its initial use in the 1950s. The scales are known to be sensitive to the subjective changes produced by a wide variety of drug and non-drug stimuli. It is particularly useful for characterizing the psychoactive effects of drugs (Haertzen & Hickey, 1984; Jasinski et al., 1984).

f. Physical procedures. All subjects were kept in the test facility throughout the test day. All activity was sedentary, e.g., watching tv, reading, etc., or generally non-stressful.

2. Design

The overall study design may be viewed as a parallel groups study in which 864 subjects (216/site) were randomly assigned to one of the three treatment conditions (stratified according to weight). This report focuses on one of the four study sites.

This portion of the overall multisite study may be viewed as a 3 (drug treatment conditions) x 4 (weight classes) x 11 (measurement occasions) mixed design. Mixed design analysis of variance procedures were used to evaluate data from this component of the study. Separate analyses were conducted for each of the dependent variables. Factors in the analysis were drug treatment assignment (Condition A vs B vs C), weight classification (normal, mildly overweight, moderately overweight, and severely overweight), and measurement occasion (0 hr, 1/2 hr, etc.). Treatment assignment and weight class were between-groups

factors while measurement occasion was a within-subjects factor. For all tests involving repeated measures factors, a conservative F test was used in evaluating statistical significance (see, e.g., Geisser & Greenhouse, 1958).

In addition to these traditional types of statistical analyses, special attention was given to individual changes in diastolic blood pressure observed during the course of the session. Four distinct analytical approaches were used to examine these individual effects: (text)

1. Evaluation of the number of cases in each drug treatment group showing diastolic blood pressure > 94 mm Hg during the session, independent of baseline level of blood pressure.
2. Evaluation of the number of cases in each drug treatment group showing certain levels of change in diastolic blood pressure (<10 mm Hg, 11-25 mm Hg, > 25 mm Hg) during the course of the session.
3. Analysis of variance applied to the peak diastolic blood pressure observed in any individual, independent of baseline level.
4. Analysis of variance applied to peak change readings observed in any individual, relative to baseline level of blood pressure.

Each of these analyses was applied to observations of both standing and supine diastolic blood pressure.

RESULTS

Specific results of the analysis of variance for each of the variables studied are summarized below.

Pulse tended to be slightly more rapid in subjects in the two higher weight categories as compared with subjects in the two lower weight categories. This effect was evident in both the standing and supine body positions (mean difference = 6.52 bpm, 7.6 bpm; $F = 7.95, 18.29$, respectively, $p < .01$ for both). Reliable changes in pulse were obtained over the course of the session for all treatment conditions in both body positions which reflected a decrease in pulse rate early in the session (of approximately 7 bpm) followed by a tendency to return towards the basal pulse rate at midday (standing $F=22.05$, $p < .01$; supine $F=31.21$, $p < .01$). Subjects who received 75 mg SR tended to show an earlier and more prolonged return towards baseline pulse rate at midday relative to the other treatment groups for the standing position only ($F=3.75$, $p < .05$).

Standing systolic blood pressure was slightly (approximately 3 mm Hg) but reliably lower during the late afternoon and midmorning portions of the session for all treatment groups

($F=6.11$, $p < .01$). Subjects in the 75 mg SR drug condition, however, showed a prolongation of the late afternoon decrease in systolic blood pressure relative to the other treatment groups ($F=6.48$, $p < .01$). No main effects for or interactions with weight category were identified. No main effects were identified for drug treatment group. The mean difference between placebo and either of the active drug treatments was less than 2 mm Hg.

Standing diastolic blood pressure showed significant changes over the course of the session which reflected a small (albeit statistically reliable) increase in diastolic blood pressure during the midmorning portion of the session of approximately 2 mm Hg ($F=8.22$, $p < .01$). No main effects for or interactions with weight class or treatment group were obtained. The mean difference between placebo and either of the active drug treatments was less than 2 mm Hg. The range of change from baseline was also small ranging from 6.33 mm Hg for the placebo group to 9.02 mm Hg for the 75 mg sustained release group. There was a small, but statistically reliable main effect for weight category ($F = 2.90$, $p < .05$). In general, subjects in the heaviest category tended to have higher mean standing diastolic blood pressure as compared with subjects of more normal weight. The largest difference between weight categories was 4.28 mm Hg. No other main effects were observed.

Analysis of the individual peak response obtained during the course of the session did not identify main effects for or

interactions with drug treatment group. Only nine individuals (2 treated with placebo, 3 treated with 75 mg SR, 4 treated with 25 mg t.i.d.) showed standing diastolic blood pressure readings > 94 mm Hg at any point in the session. Peak change from baseline was slightly higher for the group which received 25 mg t.i.d. (9.02 mm Hg) relative to the 75 mg SR (7.88 mm Hg) or placebo (6.33 mm Hg) treatment groups ($F=3.45$, $p < .05$). Mean peak differences between drug treatment groups, in both absolute and change score measures, were less than 2 mm Hg. No main effects for or interactions with weight category were identified for the individual response variables. These results are detailed in Appendix III (Tables 1,2,3,4,7, and 8).

Supine systolic blood pressure was reliably (approximately 4 mm Hg) higher during the midday portion of the session for all treatment groups ($F=11.11$, $p < .01$). Subjects in the 75 mg SR treatment group, however, showed an enhancement of the midday elevation relative to the other treatment groups ($F=8.00$, $p < .01$). No statistically significant effects were attributable to weight category. No main effects for drug treatment group were identified. The mean differences between placebo and either of the active drug treatments was less than 3 mm Hg.

Supine diastolic blood pressure was slightly (approximately 4 mm Hg) but reliably higher during the midmorning and afternoon portions of the session for all treatment conditions ($F=14.53$, $p < .01$). No main effect for or interactions with drug treatment

group or weight category were identified. The mean difference between placebo and either of the active drug treatments was less than 2.5 mm Hg.

Analysis of the various individual response variables identified small but statistically reliable effects attributable to drug condition. Although frequency of peak responses during the course of the session were higher for both the 75 mg SR and the 25 mg t.i.d. groups than for the placebo group (83.03 mm Hg, 81.13 mm Hg, and 78.68 mm Hg, respectively; $F=4.21$, $p < .01$). Peak change from baseline was also slightly higher for the two active drug conditions relative to placebo (12.0 mm Hg, 11.38 mm Hg, and 9.0 mm Hg for 75 mg SR, 25 mg t.i.d. and placebo, respectively; $F=4.89$, $p < .01$). Mean peak differences between drug conditions, in both absolute and change score measures, were less than 5 mm Hg. No main effects for or interactions with weight class were identified for the individual response variables. These results are detailed in Appendix III (Tables 1,2,5,6,9, and 10).

Subjective effects were measured using the Addiction Research Center Inventory (ARCI). As described previously, scales studied were AMP, BG, MBG, PCAG, and LSD. Data from 2 subjects were excluded from the analysis of subjective effects due to incomplete data on these self-report forms. This data loss is minimal and is considered a random event and therefore does not affect the interpretation of the results.

All of the ARCI variables except LSD showed significant and consistent changes over the course of the session for subjects in all treatment groups. Scores on the AMP, BG and MBG scales were generally higher early in the session and decreased later in the session (F=3.03, 5.74, and 16.56 respectively, $p < .05$, $< .01$, $< .01$). Scores on the PCAG scale were generally lower early in the session and increased later in the session (F=11.79, $p < .01$). Such changes are consistent with the general "mood" effects which might be expected over the course of a 12 hour experimental session. No main effects for drug treatment or weight category was found. No statistically reliable interactions were identified.

Summary tables of means, standard deviations, and analysis of variance results for each variable studied are presented in the Appendix to this report.

DISCUSSION

The present study evaluated the acute effects of two dosage forms of phenylpropanolamine (75 mg sustained release, 25 mg t.i.d.) in comparison with placebo. Measures of drug effect on pulse, blood pressure (both standing and supine) and subjective state (ARCI) were obtained over a 12 hour testing session.

No significant main effects for drug treatment were observed in

the overall mixed-design analyses. Differences in blood pressure between drug treatment groups were small, averaging less than 3 mm Hg. This result is very consistent with previous studies conducted at other well established clinical sites. Overall differences in pulse rate between treatment groups averaged less than 4 bpm. In contrast, weight class was significantly related to pulse. Subjects in the heavier weight categories consistently showed more rapid pulse rates (an average difference of 6.2 - 7.6 bpm) than did subjects of normal or near normal weight. In addition, standing diastolic blood pressure was reliably elevated in the heaviest subjects than compared with those of normal or near normal weight (average difference of 3.8 mm Hg.). No interaction between drug effect and weight category was found.

Results from the analysis of various individual response parameters were more marked than those from the overall analysis. A statistically reliable difference in peak diastolic response attributable to drug condition were obtained for the supine position. Both active treatment groups showed higher peak values than did the placebo group, but this effect, however, was small and is not regarded as clinically significant. The mean difference obtained between the active and placebo groups was less than 4 mm Hg. Peak change from baseline was also higher for the two active drug groups relative to the placebo group for the supine position (mean difference < 4 mm Hg). Maximum change from baseline was higher for the 25 mg t.i.d. treatment condition as

compared to the sustained release or placebo drug treatment groups in the standing position. These effects, however, reflect very small between group differences (less than 3 mm Hg for the supine position and less than 4 mm Hg for the standing condition) and, again, are not likely to be clinically relevant. Weight category was not associated with the individual response measures.

Statistically significant differences in all physiological measures were found over the course of the session in both standing and supine positions. These changes are extremely small and were not related to weight category. Differences in circadian variation were obtained for systolic blood pressure in both positions and for pulse rate in the standing position which were related to treatment condition. The tendency for pulse rates to return towards baseline levels following a midmorning decrease occurred earlier for the group receiving 75 mg SR than for the other treatment groups. Maximum positive changes were obtained between 4 and 4-1/2 hours for SR and between 4-1/2 and 6 hours for all other groups. The magnitude of the midday return towards basal pulse rates, however, did not differ among treatment groups. The treatment group which received 75 mg SR showed enhancement of the midday increase in supine systolic blood pressure compared to the other treatment groups. The pattern of variation over the course of the session, however, was similar for all groups. The late afternoon decrease in standing

systolic blood pressure which characterized all treatment groups was prolonged for the subjects who received 75 mg SR. However, the absolute magnitude and onset of the standing systolic minimum was unrelated to treatment condition. Although time course effects were obtained which were significantly related to drug treatment, the observed differences fall within the range of normal circadian variation in blood pressure and pulse (see, e.g., Funderburk, et al., 1982a, b; Miller-Craig et al., 1978; Noble, 1983; Robertson, 1983.).

The present results also suggest that PPA, in the dosage forms studied, had no systematic effect on subjective ratings of drug effect as measured by a standardized drug inventory, the ARCI. No statistically reliable differences between drug treatments were observed on any of the measures of drug effect. The effects of the two PPA treatments were not differentiated from that of the placebo treatment. This finding is consistent with that of Seppala, Nuotto, and Korttila (1981) in that no significant euphoric effects were noted for subjects treated with PPA, and with the previous work sponsored by Thompson Medical Company (Funderburk et al., 1982c; Noble, 1983, Robertson, 1983). As was the case with the physiological measures, subjective state showed circadian changes over the course of the session. In general, subjects in all treatment groups reported feeling more energetic early in the session as compared with later in the session.

Overall, the present findings suggest that phenylpropanolamine,

in the dosage forms studied, is not associated with adverse effects on blood pressure, pulse, or subjective drug experiences. The small but statistically reliable treatment effects which were obtained for the individual response variables are not considered to be of clinical significance. The results are generally consistent with those conducted at the Behavioral Pharmacology Research Unit (Johns Hopkins School of Medicine; Funderburk et al., 1982a, 1982b, 1982c; The University of California (Noble, 1983), and the University of Washington (Robertson, 1983).

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TABLE 1

FREQUENCY OF DIASTOLIC BLOOD PRESSURE > 94 MG HG

DRUG CONDITION	STANDING		SUPINE	
	YES	NO	YES	NO
PPA 75mg SR	3	69	5	67
PPA 25mg t.i.d.	4	68	2	70
Placebo	2	70	3	69

TABLE 2

PEAK CHANGE FROM BASELINE IN DIASTOLIC BLOOD PRESSURE

DRUG CONDITION	STANDING			SUPINE		
	<10	10-25	>25	<10	10-25	>25
PPA 75 mg SR	46	26	0	30	36	6
PPA 25 T.I.D.	42	29	1	28	39	5
PLACEBO	52	19	1	37	34	1

 $\chi^2 = 4.22, df = 4, NS$ $\chi^2 = 5.26, df = 4, NS$

No significant effects due to drug treatment group were identified.

TABLE 3

MEAN PEAK STANDING DIASTOLIC BLOOD PRESSURE

WEIGHT CLASSIFICATION

DRUG CONDITION	NORMAL WEIGHT	MILDLY OVERWEIGHT	MODERATELY OVERWEIGHT	SEVERELY OVERWEIGHT	MARGINAL OVERWEIGHT
PPA 75MG SR	79.50 (9.19)	81.58 (5.37)	81.58 (8.06)	86.00 (7.91)	82.17
PPA 25MG TID	82.33 (5.77)	81.42 (8.47)	83.83 (7.62)	85.00 (8.74)	83.15
PLACEBO	84.17 (8.80)	81.58 (7.55)	83.17 (7.91)	82.50 (6.04)	82.86
MARGINAL MEAN	82.0	81.53	82.86	84.50	

TABLE 4

ANALYSIS OF VARIANCE

PEAK STANDING DIASTOLIC BLOOD PRESSURE

	SUM OF SQUARES	DEGREES OF FREEDOM	MEAN SQUARE	F	PROBABILITY
DRUG CONDITION (C)	39.80	2	19.90	<1	NS
WEIGHT CLASS (W)	254.26	3	84.75	1.44	NS
INTERACTION (C X W)	239.41	6	39.90	<1	NS
ERROR	11975.33	204	58.70		

TABLE 5

MEAN PEAK SUPINE DIASTOLIC BLOOD PRESSURE

WEIGHT CLASSIFICATION

DRUG CONDITION	NORMAL WEIGHT	MILDLY OVERWEIGHT	MODERATELY OVERWEIGHT	SEVERELY OVERWEIGHT	MARGINAL MEAN
PPA 75MG SR	83.00 (10.60)	83.50 (6.65)	82.50 (7.51)	83.17 (9.51)	83.04
PPA 25MG TID	81.67 (7.85)	78.92 (7.37)	81.42 (9.32)	84.50 (10.27)	81.63
PLACEBO	77.50 (8.66)	78.33 (9.34)	79.17 (9.38)	79.67 (9.38)	78.67
MARGINAL MEAN	80.72	80.25	81.03	82.45	

TABLE 6

ANALYSIS OF VARIANCE

PEAK SUPINE DIASTOLIC BLOOD PRESSURE

	SUM OF SQUARES	DEGREES OF FREEDOM	MEAN SQUARE	F	PROBABILITY
DRUG CONDITION (C)	637.85	2	318.93	4.21	<.05
WEIGHT CLASS (W)	117.98	3	39.33	<1	NS
INTERACTION (C X W)	190.52	6	31.75	<1	NS
ERROR	15451.33	204	75.74		

TABLE 7

PEAK CHANGE FROM BASELINE-STANDING DIASTOLIC BLOOD PRESSURE
WEIGHT CLASSIFICATION

DRUG CONDITION	NORMAL WEIGHT	MILDLY OVERWEIGHT	MODERATELY OVERWEIGHT	SEVERELY OVERWEIGHT	MARGINAL MEAN
PPA 75MG SR	9.00 (5.36)	7.00 (5.60)	6.00 (4.90)	7.50 (5.54)	7.38
PPA 25MG TID	11.00 (9.70)	7.67 (6.06)	7.42 (5.91)	10.00 (4.43)	9.02
PLACEBO	7.17 (7.36)	8.92 (6.04)	5.38 (4.75)	3.83 (4.47)	6.33
MARGINAL MEAN	9.06	7.86	6.27	7.11	

TABLE 8

ANALYSIS OF VARIANCE

PEAK CHANGE FROM BASELINE-STANDING DIASTOLIC BLOOD PRESSURE

	SUM OF SQUARES	DEGREES OF FREEDOM	MEAN SQUARE	F	PROBABILITY
DRUG CONDITION (C)	236.68	2	118.34	3.45	<.05
WEIGHT CLASS (W)	209.92	3	69.97	2.04	NS
INTERACTION (C X W)	271.89	6	45.31	1.32	NS
ERROR	7000.96	204	34.32		

TABLE 9

PEAK CHANGE FROM BASELINE-SUPINE DIASTOLIC BLOOD PRESSURE

WEIGHT CLASSIFICATION

DRUG CONDITION	NORMAL WEIGHT	MILDLY OVERWEIGHT	MODERATELY OVERWEIGHT	SEVERELY OVERWEIGHT	MARGINAL MEAN
PPA 75MG SR	15.17 (7.21)	10.50 (10.25)	10.67 (8.38)	14.50 (9.88)	12.71
PPA 25MG TID	14.33 (6.92)	11.50 (6.83)	8.00 (11.24)	15.00 (6.35)	12.21
PLACEBO	8.83 (5.75)	11.42 (7.23)	8.25 (7.01)	5.83 (4.30)	8.58
MARGINAL MEAN	12.78	11.42	8.97	11.78	

TABLE 10

ANALYSIS OF VARIANCE

PEAK CHANGE FROM BASELINE-SUPINE DIASTOLIC BLOOD PRESSURE

	SUM OF SQUARES	DEGREES OF FREEDOM	MEAN SQUARE	F	PROBABILITY
DRUG CONDITION (C)	648.67	2	324.33	4.89	<.05
WEIGHT CLASS (W)	424.04	3	141.35	2.13	NS
INTERACTION (C X W)	678.74	6	113.12	1.71	NS
ERROR	13526.33	204	66.31		