# Duration of effect of single daily doses of reserpine and hydroflumethiazide evaluated by noninvasive technology in hypertensive patients

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Reserpine's long-lasting antihypertensive action is advantageous in the treatment of the chronically ill who can take medication only once a day. To evaluate the 24-hour effect on blood pressure of single doses of reserpine (0.125 mg) and hydroflumethiazide (50 mg) combined in one tablet (Salutensin), an ambulatory blood pressure monitor was used that automatically measures and records blood pressure every 7.5 minutes for 26 hours.

## Methods and materials

Data are derived from 21 patients with primary (essential) hypertension who completed the protocol. There were 15 men and 6 women; 12 were black and 9 white. Ages ranged from 32 to 74 years (mean, 54 years). Hypertensive complications were not a reason for exclusion from the study, but only 3 patients had evidence of target organ disease. One had a history of myocardial infarction, one had azotemia (serum creatinine, $\geq$1.5 mg/dl), and one had both azotemia and angina pectoris. None had accelerated hypertension (Keith-Wagener-Barker groups III and IV).

The plan and purpose of the investigation were explained to the patients, and each signed an informed consent form before being included in the study.

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All subjects had a history of hypertension; 16 were taking antihypertensive medication when selected, but discontinued therapy at least one month before entering the study.

Patients were seen in the office at two-week intervals throughout the study. Blood pressure was measured in the right arm with a standard mercury manometer; the 5th Korotkoff phase was used as the diastolic blood pressure. At each visit, after an initial 10-minute rest, three blood pressure recordings were taken at 5-minute intervals with the patient seated. The average of the three readings was taken as the blood pressure for each visit.

To qualify, each subject had to have an average diastolic blood pressure of >95 mm Hg on each of three consecutive office visits. Average diastolic blood pressure of ≥120 mm Hg on any visit disqualified the patient.

Before treatment with the reserpine/hydroflumethiazide combination was started, the ambulatory blood pressure monitor was applied and worn for 24 hours. A complete history and physical examination were obtained before starting therapy as were fasting blood glucose, serum uric acid, creatinine, and potassium as well as an electrocardiogram (ECG) and chest roentgenogram.

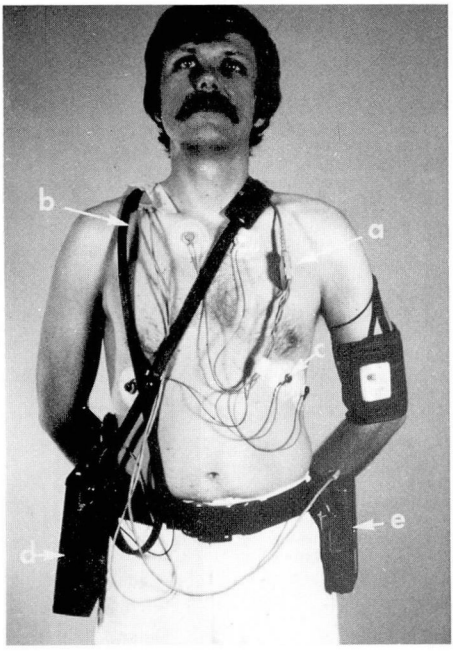
Therapy was started with one combination tablet of reserpine, 0.125 mg and hydroflumethiazide, 50 mg (Salutensin) once daily in the morning. Study endpoint was reached when average diastolic blood pressure was ≤90 mm Hg on each of two consecutive office visits. When this occurred, automated 24-hour blood pressure monitoring was repeated as were the determinations of serum uric acid, creatinine, potassium, and fasting blood glucose and ECG. The study drug was then discontinued.

If goal diastolic blood pressure had not been reached at the third office visit (six weeks), a second tablet of Salutensin was added to the regimen (two tablets were taken each morning). Whether or not goal blood pressure was reached by the end of the 12th week (six office visits), ambulatory blood pressure monitoring, blood tests, and ECG were repeated and the study drug was withdrawn. However, if the average diastolic blood pressure was ≤90 mm Hg for the first time on visit six, the study was extended for two more weeks before final monitoring of blood pressure, blood chemistry, and ECG was repeated.

A satisfactory office blood pressure response was defined as an average of ≤90 mm Hg diastolic on the last two consecutive office visits.

The automated ambulatory blood pressure monitor (Del Mar Avionics)[1–3] is based on Korotkoff sounds picked up by a microphone in a sphygmomanometer cuff, which is applied to the patient's nondominant arm and is automatically inflated by a compressor at predetermined intervals of 7.5, 15, or 30 minutes (*Figs. 1 and 2*). The Pressurometer II model also included simultaneous two-channel Holter recording of the ECG on magnetic tape along with the blood pressure readings. The magnetic tape is scanned by an electrocardioscanner. The resulting print-out includes premature beat counts, heart rate, ST-segment deviations and digital blood pressure recordings, as well as a graphic display of blood pressure.

The Pressurometer III model does not include simultaneous recording of the ECG although, as with the model II, ECG leads are attached so that the R wave can trigger deflation of the sphygmomanometer cuff. In model III the blood pressure data are stored in a solid state memory and transferred to an electrostatic printing system.



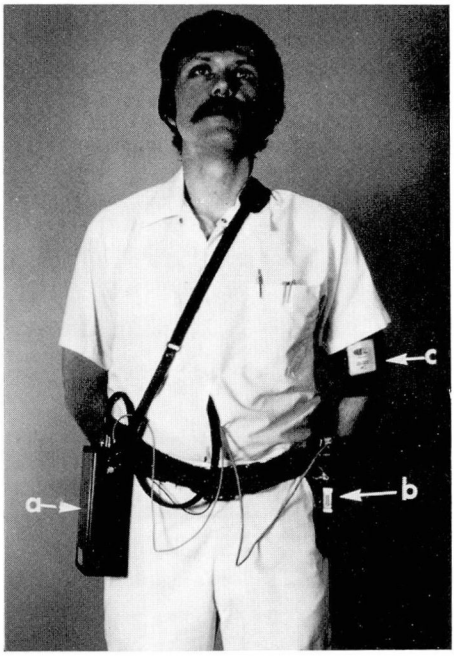




**Fig. 1.** The Del Mar Avionics Pressurometer II ambulatory blood pressure and ECG recording system on a subject. Components of the system are (a) ECG cable, (b) cuff inflation tubing, (c) ECG electrode, (d) pressurometer II, and (e) electrocardiocorder.

**Fig. 2.** The Del Mar Avionics Pressurometer II ambulatory blood pressure and ECG recording system on a fully dressed subject. Components of the system are (a) pressurometer II, (b) electrocardiocorder, (c) pressure cuff with transducer assembly under the cuff.

Intrapatient comparisons have shown a good correlation between determinations of blood pressure obtained by the Pressurometer and those obtained by the conventional auscultatory method[1, 2] as well as by direct arterial measurements.[1]

Auscultatory blood pressure measurements were made at the time of application and again at the time of removal of the automated blood pressure equipment to assure similar readings.

Technical problems with the automated equipment frequently necessitated repeating 24-hour recordings until at least 60% of the readings appeared valid.

Thirteen patients were monitored with the Pressurometer II and 4 were monitored with the Pressurometer III; 4 had pretherapy monitoring on Pressurometer II and post-therapy monitoring on Pressurometer III.

Thirty-five patients signed informed consent to participate in the study. Five were disqualified because the diastolic pressure did not average >95 mm Hg on three consecutive visits and one was disqualified because the diastolic pressure was ≥120 mm Hg. One woman could not tolerate wearing the automated blood pressure equipment and was excluded. Seven were disqualified for other reasons.

## Results

### *Effect on office blood pressure*

Sixteen patients had diastolic blood pressure of ≤90 mm Hg on each of their

**Table 1.** Salutensin study

| | Pretreatment | | | | | Post-treatment | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | 24-hour BP (mm Hg) | | | | | 24-hour BP (mm Hg) | | |
| Case | Variable | Last pretreatment office BP (mm Hg) | Mean ± SD | 90% Range | % of time DBP ≥95 | Variable | Last post-treatment office BP (mm Hg) | Mean ± SD | 90% Range | % of time DBP ≥95 |
| * 1 | Systolic | 157 | 139 ± 28 | 108–216 | ... | Systolic | 131 | 136 ± 28 | 105–224 | ... |
| | Diastolic | 105 | 97 ± 16 | 77–114 | 54 | Diastolic | 95 | 103 ± 52 | 77–117 | 70 |
| 2 | Systolic | 138 | 131 ± 23 | 101–162 | ... | Systolic | 126 | 119 ± 29 | 95–218 | ... |
| | Diastolic | 103 | 100 ± 15 | 79–121 | 72 | Diastolic | 87 | 90 ± 58 | 74–97 | 9 |
| 3 | Systolic | 143 | 142 ± 32 | 110–210 | ... | Systolic | 139 | 138 ± 22 | 108–174 | ... |
| | Diastolic | 103 | 85 ± 16 | 61–107 | 20 | Diastolic | 86 | 85 ± 15 | 63–106 | 28 |
| 4 | Systolic | 157 | 140 ± 17 | 116–165 | ... | Systolic | 117 | 114 ± 17 | 91–130 | ... |
| | Diastolic | 106 | 105 ± 12 | 88–124 | 82 | Diastolic | 80 | 89 ± 63 | 71–100 | 9 |
| 5 | Systolic | 139 | 123 ± 31 | 96–216 | ... | Systolic | 143 | 113 ± 22 | 96–140 | ... |
| | Diastolic | 110 | 93 ± 12 | 76–118 | 40 | Diastolic | 97 | 85 ± 12 | 75–102 | 13 |
| 6 | Systolic | 165 | 168 ± 58 | 134–227 | ... | Systolic | 123 | 138 ± 36 | 91–226 | ... |
| | Diastolic | 111 | 115 ± 25 | 93–159 | 93 | Diastolic | 77 | 96 ± 28 | 66–142 | 41 |
| 7 | Systolic | 160 | 151 ± 21 | 123–182 | ... | Systolic | 137 | 137 ± 31 | 107–218 | ... |
| | Diastolic | 100 | 110 ± 21 | 81–133 | 84 | Diastolic | 80 | 97 ± 24 | 69–122 | 53 |
| 8 | Systolic | 152 | 145 ± 21 | 111–176 | ... | Systolic | 99 | 112 ± 33 | 87–220 | ... |
| | Diastolic | 99 | 99 ± 22 | 75–118 | 59 | Diastolic | 67 | 87 ± 63 | 66–103 | 6 |
| 9 | Systolic | 178 | 183 ± 24 | 156–230 | ... | Systolic | 160 | 151 ± 25 | 123–193 | ... |
| | Diastolic | 111 | 127 ± 54 | 90–177 | 94 | Diastolic | 78 | 99 ± 61 | 74–120 | 41 |
| * 10 | Systolic | 165 | 157 ± 32 | 109–204 | ... | Systolic | 143 | 130 ± 23 | 104–172 | ... |
| | Diastolic | 109 | 102 ± 25 | 75–170 | 57 | Diastolic | 89 | 74 ± 13 | 55–95 | 5 |
| 11 | Systolic | 150 | 147 ± 16 | 128–167 | ... | Systolic | 143 | 125 ± 13 | 106–143 | ... |
| | Diastolic | 102 | 96 ± 12 | 79–110 | 60 | Diastolic | 90 | 86 ± 14 | 66–103 | 20 |
| 12 | Systolic | 164 | 140 ± 33 | 91–195 | ... | Systolic | 121 | 117 ± 24 | 81–149 | ... |
| | Diastolic | 98 | 94 ± 62 | 59–122 | 39 | Diastolic | 81 | 82 ± 14 | 55–100 | 15 |
| 13 | Systolic | 140 | 155 ± 21 | 126–186 | ... | Systolic | 126 | 132 ± 18 | 112–152 | ... |
| | Diastolic | 96 | 85 ± 15 | 71–98 | 10 | Diastolic | 80 | 80 ± 20 | 65–89 | 4 |
| * 14 | Systolic | 147 | 163 ± 22 | 128–193 | ... | Systolic | 130 | 145 ± 25 | 115–201 | ... |
| | Diastolic | 98 | 112 ± 21 | 86–138 | 86 | Diastolic | 80 | 92 ± 19 | 75–134 | 22 |
| 15 | Systolic | 173 | 138 ± 29 | 99–197 | ... | Systolic | 128 | 120 ± 25 | 86–155 | ... |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Diastolic | 100 | 97 ± 26 | 68–138 | 45 | Diastolic | 80 | 84 ± 23 | 58–116 | 20 |
| 16 | Systolic | 173 | 194 ± 26 | 165–237 | ... | Systolic | 144 | 174 ± 17 | 145–200 | ... |
| | Diastolic | 113 | 125 ± 19 | 102–150 | 99 | Diastolic | 87 | 105 ± 14 | 87–128 | 80 |
| 17 | Systolic | 152 | 136 ± 24 | 109–169 | ... | Systolic | 116 | 116 ± 22 | 86–143 | ... |
| | Diastolic | 103 | 91 ± 21 | 68–110 | 31 | Diastolic | 79 | 81 ± 17 | 58–102 | 14 |
| * 18 | Systolic | 171 | 171 ± 15 | 151–196 | ... | Systolic | 150 | 131 ± 13 | 110–153 | |
| | Diastolic | 110 | 116 ± 15 | 98–131 | 99 | Diastolic | 100 | 92 ± 11 | 77–102 | 43 |
| * 19 | Systolic | 141 | 138 ± 21 | 116–177 | ... | Systolic | 153 | 140 ± 18 | 114–162 | ... |
| | Diastolic | 107 | 106 ± 15 | 91–122 | 90 | Diastolic | 110 | 99 ± 13 | 82–112 | 70 |
| 20 | Systolic | 160 | 129 ± 23 | 88–169 | ... | Systolic | 108 | 123 ± 23 | 96–144 | ... |
| | Diastolic | 96 | 80 ± 17 | 54–108 | 19 | Diastolic | 70 | 66 ± 24 | 47–91 | 4 |
| 21 | Systolic | 170 | 142 ± 19 | 109–167 | ... | Systolic | 103 | 118 ± 27 | 85–148 | ... |
| | Diastolic | 100 | 94 ± 18 | 65–118 | 52 | Diastolic | 70 | 77 ± 23 | 50–96 | 8 |

* 2 Salutensin tablets daily.
DBP = diastolic blood pressure.

last two office visits and were considered to demonstrate a satisfactory response to therapy. Fourteen of these were taking only one tablet daily and two required two tablets daily.

Five patients (cases 1, 3, 5, 18, and 19) (*Table 1*) did not achieve average office blood pressures ≤90 mm Hg for the last two visits. Three were taking two tablets daily. One could not tolerate two tablets daily because of side effects. Another stopped treatment after four weeks because of intolerable nasal stuffiness from reserpine (patient 3) (*Table 1*). At his last office visit before discontinuing treatment, his average diastolic blood pressure was 86 mm Hg, but because he did not have two consecutive office visits with diastolic blood pressure ≤90 mm Hg he was classified as an unsatisfactory responder.

*Effect on ambulatory blood pressure*

*Figure 3* is a graphic display of three-reading rolling averages of blood pressure measured by the ambulatory blood pressure monitor on one of the patients in the study.

Office blood pressures and summaries of the 24-hour monitoring are presented for each patient both at pretreatment and post-treatment in *Table 1*. The central 90% range, and the mean and standard deviation of all systolic and diastolic blood pressures are presented. Percentage of time during the 24 hours that the diastolic blood pressure was ≥95 mm Hg, the arbitrary cutoff point, is indicated.

During the 24-hour blood pressure measurement, systolic pressure varied by as much as 135 mm Hg (all varied by at least 37 mm Hg) in the truncated range previously defined. Measurements of diastolic blood pressure varied by as much as 95 mm Hg, and all varied by at least 23 mm Hg.

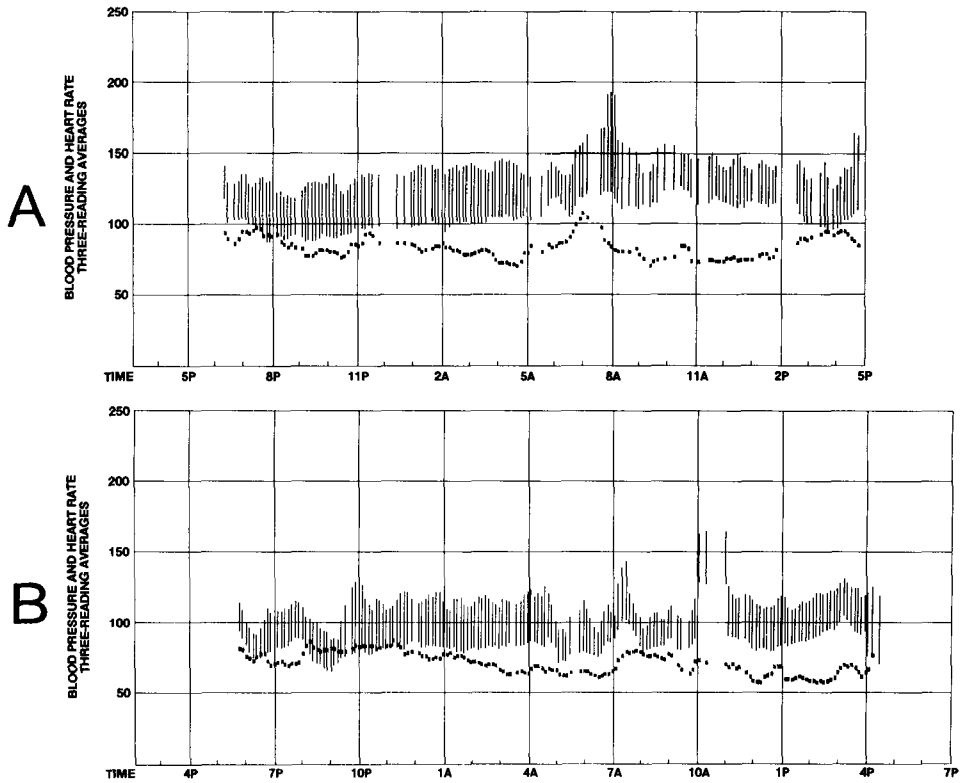



**Fig. 3.** Graphic display of 3-reading rolling averages of blood pressure and pulse rate as recorded by the Avionics Pressurometer in a 58-year-old male with primary hypertension, before (**A**) and at the end (**B**) of the period of treatment with reserpine, 0.125 mg and hydroflumethiazide, 50 mg (Salutensin) once daily.

Before treatment, correlation between the value of the office diastolic blood pressure and the diastolic blood pressure percentage ≥95 mm Hg was significant ($p < 0.01$). However, after treatment (Spearman) this correlation was only marginally significant ($p < 0.10$).

To consider the effect of treatment on diastolic blood pressure, attention is focused on the percentage of time during the 24-hour monitoring period that the diastolic blood pressure was ≥95 mm Hg. *Table 2* shows the mean and range of this percentage before and after treatment. Clearly, there is a significant effect from treatment ($p < 0.001$ by Wilcoxon signed rank test). In two patients (cases 1 and 3) the percentage actually increased with treatment. In one other patient (case 13) there was very little change in percentage. However, in the remaining 18 patients there were marked improvements (*Table 3*). For two patients (13 and 20) the percentage of time diastolic blood pressure exceeded 95 mm Hg before treatment was

**Table 2.** Percent of time diastolic blood pressure ≥95 mm Hg

| | |
|---|---|
| Pretreatment | |
| Mean | 61.2%* |
| Range | 10%–99% |
| Post-treatment | |
| Mean | 27.4%* |
| Range | 4%–80% |

* $p = <0.001$ by Wilcoxon signed rank test.

less than 20%. Finally, even though there were marked improvements with therapy for some patients, the percentage of time with high diastolic blood pressure post-treatment equaled or exceeded 40% for 7 patients (cases 1, 6, 7, 9, 16, 18, and 19). Five of these (cases 6, 7, 9, 16, and 18) responded satisfactorily with respect to office blood pressure readings (*Table 3*).

Mean values for systolic and diastolic blood pressures and pulse rate for each individual, pretherapy and post-therapy are shown in *Table 4*. For all 21 patients the average 24-hour blood pressure was reduced from 149 to 130 mm Hg systolic and from 105 to 88 mm Hg diastolic. The average pulse rate was reduced from 82 to 73 beats/min. All reductions were highly significant.

**Table 3.** Percent of time diastolic blood pressure ≥95 mm Hg

| Post-treatment compared to pretreatment | | | Number of patients |
|---|---|---|---|
| Increased | | | 2 |
| Minimal decrease | <10% | | 1 |
| Decreased | >10% | | 18 |
| | ≥25% | 12 | |
| | 10%–25% | 6 | |
| Total | | | 21 |

Average blood pressures were higher from 8 A.M. to 8 P.M. than from 8 P.M. to 8 A.M., both before and during therapy, but for both periods they were significantly lower during therapy than before. Treatment did not obliterate this diurnal difference. The standard deviations for systolic and diastolic blood pressure did not change significantly as a result of treatment (*Table 5*).

*Side effects*

At each visit, before and during the treatment period, symptoms volunteered by the patient were recorded on a special form and were classified as mild, moderate, or severe. At the end of the study an attempt was made to determine whether the symptoms were related to the drugs.

Five patients had side effects definitely attributed to one or both of the drugs contained in Salutensin (*Table 6*). Eight patients had no side effects attributable to the drugs and 11 patients had symptoms possibly drug related including 3 who also had side effects that could definitely be attributed to drugs (*Table 7*).

Two patients could not complete the protocol because of side effects. Both

**Table 4.** Individual mean values before and at the end of the treatment period

| | Pretreatment | | | Post-treatment | | | |
|---|---|---|---|---|---|---|---|
| Period | Mean | SD | Range | Mean | SD | Range | p |
| 24 Hour | | | | | | | |
| Systolic (mm Hg) | 149 | 18 | 123–194 | 130 | 15 | 112–174 | <.0001 |
| Diastolic (mm Hg) | 105 | 22 | 80–186 | 88 | 10 | 66–105 | <.0001 |
| Pulse rate (b/m) | 82 | 16 | 58–119 | 73 | 14 | 57–116 | <.0002 |
| 8 A.M.–8 P.M. | | | | | | | |
| Systolic (mm Hg) | 154 | 20 | 127–203 | 134 | 16 | 114–177 | <.0002 |
| Diastolic (mm Hg) | 105 | 12 | 80–129 | 91 | 10 | 68–104 | <.0001 |
| Pulse rate (b/m) | 86 | 14 | 67–122 | 76 | 14 | 60–115 | <.0001 |
| 8 P.M.–8 A.M. | | | | | | | |
| Systolic (mm Hg) | 144 | 18 | 120–187 | 126 | 15 | 109–170 | <.0001 |
| Diastolic (mm Hg) | 99 | 14 | 78–130 | 85 | 11 | 65–106 | <.0002 |
| Pulse rate (b/m) | 79 | 16 | 56–118 | 69 | 14 | 52–107 | <.0002 |

**Table 5.** Individual standard deviations before and at the end of treatment period

| Period | Pretreatment Mean | Pretreatment Range | Post-treatment Mean | Post-treatment Range | p |
|---|---|---|---|---|---|
| 24 hour | | | | | |
| Systolic (mm Hg) | 26 | 15–58 | 23 | 13–36 | 0.14 |
| Diastolic (mm Hg) | 24 | 12–62 | 28 | 11–63 | 0.55 |
| Pulse Rate (b/m) | 15 | 8–30 | 13 | 7–27 | 0.03 |
| 8 A.M.–8 P.M. | | | | | |
| Systolic (mm Hg) | 27 | 14–80 | 23 | 12–37 | 0.38 |
| Diastolic (mm Hg) | 23 | 7–86 | 25 | 8–92 | 0.79 |
| Pulse rate (b/m) | 13 | 7–40 | 13 | 7–38 | 0.69 |
| 8 P.M.–8 A.M. | | | | | |
| Systolic (mm Hg) | 22 | 12–29 | 22 | 1–37 | 0.79 |
| Diastolic (mm Hg) | 21 | 8–93 | 22 | 7–80 | 0.44 |
| Pulse rate (b/m) | 14 | 6–30 | 11 | 4–29 | 0.02 |

**Table 6.** Side effects from reserpine and/or hydroflumethiazide (5 patients)

| Side effects | No. of patients: Severity Mild | Moderate | Severe |
|---|---|---|---|
| Nasal congestion | 0 | 1 | 2* |
| Dryness of mouth | 1 | 2 | 0 |
| Epigastric burning | 0 | 1 | 0 |
| Decreased energy level | 0 | 1 | 0 |
| Impotence | 0 | 0 | 1 |

* Forced premature discontinuation of treatment in both.

**Table 7.** Side effects possibly related to reserpine and/or hydroflumethiazide (11 patients)*

| Side effects | No. of patients: Severity Mild | Moderate | Severe |
|---|---|---|---|
| Nausea | 0 | 1 | 0 |
| Anorexia | 1 | 0 | 0 |
| Dryness of mouth | 1 | 0 | 0 |
| Paresthesia | 3 | 0 | 0 |
| Increased appetite | 1 | 0 | 0 |
| Mental depression | 1 | 1 | 0 |
| Headache | 1 | 2 | 0 |
| Impotence | 1 | 0 | 0 |
| Loss of libido | 0 | 1 | 0 |
| Pruritis | 0 | 1 | 0 |
| Aching and malaise | 0 | 2 | 1 |
| Edema | 1 | 1 | 0 |
| Diarrhea | 1 | 0 | 1 |
| Abdominal cramps | 0 | 1 | 0 |
| Dizziness | 2 | 2 | 0 |
| Constipation | 1 | 0 | 0 |
| Nightmares | 1 | 0 | 0 |

* Includes 3 patients who also had side effects that could definitely be attributed to the drugs.

complained of severe nasal congestion and in addition one complained of generalized aching, malaise, and depression. The latter refused to take two tablets daily and his diastolic pressure did not fall to ≤90 mm Hg. The other patient refused to continue taking medication after four weeks even though his diastolic blood pressure was 86 mm Hg on the second office visit. These patients accounted for 2 of the 5 treatment failures based on office blood pressure.

No patient had a change in the ECG at the end of treatment.

The results of blood chemistry determinations before and at the end of the treatment period are summarized in *Table 8.* An unanticipated finding was a significantly lower average blood glucose at the end of the study than before treatment was started.

Although the average serum potassium was significantly lower at the end of treatment than it was before treatment, no patient had serum potassium <3.2 mEq/L at the end of the treatment

**Table 8.** Effect of treatment with reserpine/hydroflumethiazide on blood constituents

| | Potassium (mEq/L) | | Glucose (mg/dl) | | Uric acid (mg/dl) | | Creatinine (mg/dl) | |
|---|---|---|---|---|---|---|---|---|
| | Control | Rx | Control | Rx | Control | Rx | Control | Rx |
| Mean | 4.2 | 3.8 | 105.8 | 91.2 | 6.6 | 7.1 | 1.1 | 1.1 |
| SD | 0.4 | 0.3 | 24.1 | 19.8 | 1.2 | 1.5 | 0.2 | 0.2 |
| p* | <0.009 | | <0.006 | | <0.15 | | <0.35 | |

* Sign test.

period and none required potassium supplementation.

There were no significant changes in the concentrations of serum uric acid or serum creatinine as the result of treatment with the reserpinehydroflumethiazide combination.

## Comment

Taking medication only once daily for a chronic disease such as hypertension is generally considered to be advantageous in enhancing compliance. Combinations of a long-acting adrenergic inhibiting drug such as reserpine with a diuretic in a single tablet offer this advantage.

In a study of 21 patients with mild to moderate hypertension, 16 had diastolic blood pressures in the office controlled (≤90 mm Hg) with one or two tablets of reserpine (0.125 mg) hydroflumethiazide (50 mg) combination taken once daily in the morning.

To estimate the control of blood pressure for these patients throughout a 24-hour period, an automated device was used to record blood pressure every 7.5 minutes. The percentage of time that the diastolic blood pressure was ≥95 mm Hg during the 24-hour period of monitoring was reduced from 61.2% before treatment to 27.4% at the end of treatment ($p < 0.001$). For 18 of 21 patients treatment produced >10% decrease in the percentage of time that diastolic readings were ≥95 mm Hg.

Although the averages of the 24-hour systolic and diastolic blood pressures were reduced significantly by the reserpine-hydroflumethiazide combination, the blood pressure variability was not greatly affected by antihypertensive therapy as indicated by the absence of significant change in standard deviations (*Table 5*). This was true during the 8 A.M. to 8 P.M. interval as well as during the 8 P.M. to 8 A.M. interval. Standard deviations were calculated by using *all* readings obtained in the 24-hour period, not just the central 90% range shown in *Table 1*.

Only 2 of 21 patients experienced side effects severe enough to require deviation from protocol. In both cases the side effect was nasal congestion. Eight patients had no side effects at all. Eight patients had symptoms that could not definitely be attributed to the drugs, 2 patients had side effects definitely drug related and 3 had both.

There were no clinically significant changes in serum potassium, serum creatinine or serum uric acid. Surprisingly, the average blood glucose concentration was lower at the end of the study than it was before treatment was started.

Use of the automated ambulatory blood pressure monitor to evaluate duration of effect of antihypertensive agents is relatively new. Priest et al[4] have reported results of this monitoring technique in one patient receiving captopril for management of resistant hy-

pertension. Garrett[5] has studied pindolol and hydrochlorothiazide using this method. Other studies of the duration of effect of antihypertensive agents are ongoing in other laboratories using this modality.

Continuous intra-arterial blood pressure recordings have been used to evaluate the duration of antihypertensive effect of some drugs,[6] but this is a complicated, invasive procedure with limited applicability.

## Summary

A combination tablet containing reserpine, 0.125 mg, and hydroflumethiazide, 50 mg (Salutensin) taken once daily in the morning controlled office diastolic blood pressure in 16 of 21 patients with mild to moderate hypertension. Twenty-four hour blood pressure monitoring before and at the end of the treatment period revealed that the average percentage of diastolic blood pressure determinations ≥95 mm Hg decreased from 61.2 to 27.4 (*Table 1*) and by at least 10% for 18 of 21 patients.

Only 5 of 21 patients had side effects that could definitely be attributed to the drugs and in only 2 were these annoying enough to force a deviation from protocol.

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