

Polydipsia in Chronic Psychiatric Patients: Therapeutic Trials of Clonidine and Enalapril

Robert M. Greendyke, M.D., Alan J. Bernhardt, Ph.D., Hedy E. Tasbas, M.D.,
and Kathleen S. Lewandowski, Ph.D.

A six month long double-blind, placebo-controlled, crossover design pharmacological study was conducted on 14 chronically psychotic, institutionalized patients who suffered from chronic water abuse ("psychogenic polydipsia"). Effects of clonidine and enalapril administered separately and individually were assessed for possible beneficial effects on both physiological parameters such as diurnal weight gain, urine output, and serum sodium levels and on signs of delirium as measured by neurobehavioral testing. Improvement, particularly in tests reflecting fluid

consumption, was found with either or both drugs in approximately 60% of test subjects, although no behavioral improvement was demonstrated. As a result of evidence for delayed and carry-over effects the authors recommend that future studies employ phases longer than one month and/or include washout periods. [Neuropsychopharmacology 18:272-281, 1998] © 1998 American College of Neuropsychopharmacology. Published by Elsevier Science Inc.

KEY WORDS: Enalapril; Clonidine; Chronic water abuse; Psychogenic polydipsia; Drug trial; Crossover design

The present article describes a pharmacological study on patients with chronic psychoses (primarily schizophrenia) who experience chronic water abuse (psychogenic polydipsia). A recent survey in this hospital identified 61 psychiatric inpatients who suffer from this condition, approximately 40 of whom evidenced recurrent intermittent water intoxication.

The magnitude of the problem is considerable. Investigators have reported evidence of inappropriate excessive fluid consumption in 6-17% of psychiatric inpatients (DeLeon et al. 1994). Although asymptomatic in its milder and early forms, the problem may increase in severity with time, progressing to a syndrome variably including neurological abnormalities (headache, mus-

cle cramps, blurred vision, weakness, tremors, restlessness, confusion, lethargy, delirium, seizures, coma, and death), behavioral and cognitive problems, gastrointestinal symptoms, urinary tract disease (incontinence, hydronephrosis, renal failure), congestive heart failure, and metabolic abnormalities (hypocalcemia, osteopenia).

The fact that the pathophysiology of water intoxication is complex and probably multifactorial (Vieweg et al. 1986a; Vieweg et al. 1988a; Goldman et al. 1988) makes the treatment difficult, inasmuch as particular therapeutic approaches may be beneficial in only certain patients and escape statistical recognition in small studies. Incomplete understanding of why certain patients drink fluids to excess hampers selection of potentially beneficial drugs, a problem compounded by the observation that patients with water intoxication exhibit both polydipsia and impaired water excretion as their disease progresses. Various possible etiologies have been proposed for polydipsia, including hyperactivity of hypothalamic thirst centers, secondary effects of neuroleptic medications, an increase in endogenous opiate receptor effects, and delusions having to do with fluid intake and for hyponatremia and water intoxication, including inappropriate release of the antidiuretic

From the Departments of Pathology and Laboratory Medicine, Psychiatry, Psychology and Nursing, Department of Veterans Affairs Medical Center, Canadaigua, New York.

Address correspondence to: Dr. A. Bernhardt, Primary Care Substance Abuse Clinic, Tuscaloosa Veterans Affairs Medical Center, 3701 Loop Road, Tuscaloosa, AL 35405.

Received December 16, 1996; accepted August 29, 1997.

hormone, vasopressin (SIADH), and a lowering of the threshold for antidiuretic hormone (ADH) release (or resetting of the hypothalamic osmostat) (Boyd 1990; Crammer 1991; Goldman 1991; Illowsky and Kirch 1988; Patel 1994; Riggs et al. 1991).

Various therapeutic approaches based on these postulated mechanisms have been used with beneficial though limited effects claimed (Vieweg et al. 1985a; Vieweg 1994). Drugs used have included naloxone (Nishikawa et al. 1992), lithium (Khamnei 1984; Raskind and Christopher 1974), lithium plus phenytoin (Vieweg et al. 1988b), demeclocycline (Nixon et al. 1982; Goldman and Luchins 1985; Nixon et al. 1982; Khamnei 1984; Vieweg et al. 1988c), propranolol (Shevitz et al. 1980, Goldstein and Folsom 1991; Kathol et al. 1986), sodium chloride (Vieweg et al. 1985b; Goldman et al. 1994), captopril

(Goldstein 1986; Sebastian and Bernardin 1990; Kathol et al. 1986; Lawson et al. 1988), and enalapril (Sebastian and Bernardin 1990). Clozapine treatment appears particularly promising (Spears et al. 1993; Munn 1993; Lee et al. 1991; Henderson and Goff 1994; Leadbetter et al. 1994; Leadbetter and Shutty 1994; Lyster et al. 1994; DeLeon et al. 1995) (see review by Vieweg et al. 1994). Some successes with behavioral approaches have been reviewed by Vieweg (1993).

METHODS

Two drugs were chosen for preliminary investigation of possible beneficial effects in chronic water abuse, both selected because they have been implicated in reducing

Table 1. Demographic Data on Study Patients

Pt. No.	Group Number	Diagnosis (DSM IV)	Age (yrs)	Duration of Psychiatric Hospitalization (years)	Estimated Duration of Water Abuse (years)	Current Medications
1	3	chronic schizophrenia	44	12	?	haloperidol lithium
2	3	chronic schizophrenia	67	39	32	lorazepam carbamazepine fluphenazine nortriptyline
3	3	chronic schizophrenia	65	15	8	carbamazepine risperidol
4	3	chronic schizophrenia	50	11	?	lorazepam haloperidol
5	1	chronic schizophrenia	61	21	15	lithium risperidol valproate
6	1	chronic schizophrenia	56	8	5	lorazepam carbamazepine risperidol trazadone
7	1	chronic schizophrenia	43	18	2	lorazepam risperidol
8	1	chronic schizophrenia	38	12	5	benztropine risperidol lorazepam
9	2	chronic schizophrenia	46	14	8	risperidol trazadone
10	2	chronic schizophrenia affective psychosis	49	20	?	carbamazepine chlorpromazine lithium
11	2	chronic schizophrenia	31	8	?	fluphenazine lithium trazadone valproate
12	2	post-traumatic psychosis	44	14	1	carbamazepine fluphenazine
13	2	undifferentiated psychosis	50	29	2	chlorpromazine valproate lorazepam
14	2	schizophrenia	46	10	4	risperidol

Table 2. Scheme of Drug Administration

Patient Group	Phases					
	1	2	3	4	5	6
1	Placebo ^a	Placebo	Clonidine	Placebo	Enalapril	Placebo
2	Placebo ^a	Placebo	Enalapril	Placebo	Clonidine	Placebo
3	Placebo ^a	Placebo	Placebo	Clonidine	Placebo	Enalapril

^aWater restriction was used during phase 1 but not thereafter. Experimental design used. All phases were 4 weeks in duration with the exception of phase 2, which was 5 weeks in duration.

water intake: clonidine, an α -adrenergic blocking agent, and enalapril, an angiotensin-converting enzyme inhibitor (Sebastian and Bernardin 1990; Crammer 1991; Verghese et al. 1993). Both agents have been widely used for treatment of hypertension. The inpatient psychiatric population of the hospital was surveyed, using a questionnaire administered to head nurses to detect patients in whom water abuse had been observed. A total of 61 patients was identified in a population of 244. These patients were then visited by two of the authors, their nursing attendants interviewed and their clinical records reviewed to assess the nature and severity of the problem. Patients with specific etiologies for polydipsia were excluded as were those considered too frail to tolerate the drug regimen proposed. Although we appreciated the role that carbamazepine can play in impairing water excretion, it was noted that in three of the five patients receiving the drug, their problem with water abuse antedated its use. Similarly, the five patients being treated with lithium, which may cause a secondary polydipsia, had exhibited water abuse during prolonged periods over the years in which lithium was not given.

Written authorization and consent from 17 male patients and their next of kin were obtained. One patient dropped out of the investigation because of the multiple venipunctures involved. The remaining 16 patients were randomly assigned to three groups (group 1, $n = 5$; group 2, $n = 5$, and group 3, $n = 6$). Two patients (one from group 1 and one from group 3) were dropped from the study because they failed to exhibit sufficient evidence of a current problem with excessive water intake during the two initial baseline phases. All 14 of these patients had histories of at least occasional water intoxication in addition to polydipsia. Severity ratings of these patients' water intoxication based upon interviews with staff who were familiar with them placed two in the mild range, seven in the moderate range, and five in the moderate to severe range. Table 1 presents pertinent demographic data on the 14 patients who completed the study. A double-blind, placebo-controlled, crossover design was used as shown in Table 2. Clonidine was administered in a dose of 0.2 mg PO BID and enalapril 10 mg PO BID in single capsules prepared to appear identical to the placebo, which was also administered PO BID. The study

Table 3. Range of Abnormality in Study Patients without Water Restriction but before Experimental Drug Treatment

Pt. No.	Selected Baseline (Phase 2) Assessment Data								
	CUO			PDWG			SNa		
	Min	Max	Mean	Min	Max	Mean	Min	Max	Mean
1	3.3	16.4	12.5	-1.3	6.1	1.4	125	141	136
2	3.9	12.2	6.1	-3.0	5.1	2.0	126	138	133
3	4.3	10.4	6.5	-2.9	10.4	4.5	128	139	132
4	1.0	6.8	2.0	-0.7	3.8	1.3	137	140	138
5	1.8	12.5	6.5	-0.3	9.3	2.9	129	141	138
6	1.3	5.8	3.7	-2.5	5.1	0.6	122	132	127
7	2.9	18.7	13.7	-0.9	2.1	0.4	139	141	141
8	0.7	5.2	2.3	-1.9	7.0	3.4	128	138	134
9	2.0	11.1	5.8	-1.1	2.9	1.0	133	138	135
10	1.2	4.74	2.5	0.3	3.7	1.8	138	142	140
11	1.4	7.6	4.4	-1.1	2.8	1.0	139	142	141
12	0.8	1.7	1.1	0	3.9	2.0	127	137	132
13	1.4	6.14	2.9	-1.8	2.9	1.8	136	139	138
14	1.9	10.8	5.4	-2.3	7.2	3.1	124	138	131

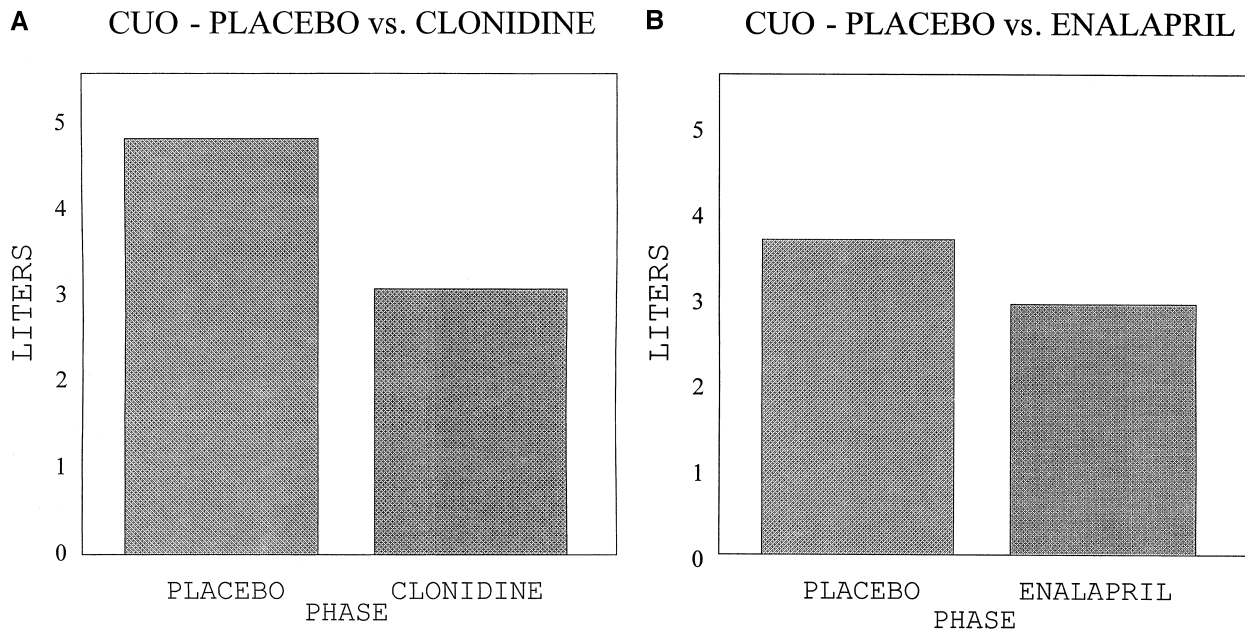


Figure 1. Calculated 24-h urine output in 14 patients treated with placebo, clonidine, and enalapril.

patients were all cohorted in one area of a single hospital floor.

Initial patient assessment included a detailed medical and psychiatric history, repeat physical examination, cognitive testing, electrocardiogram (EKG) and laboratory evaluation, including complete blood count (CBC), serum electrolytes, glucose, liver function tests, T4, and urinalysis. Current medications (see Table 1) were maintained unchanged throughout the 6 months of the study. Any fluid restriction being imposed on the study patients

was terminated after 1 month except for emergency situations. Assessment measures included: twice daily determinations of body weight (6:00 A.M. and 7:00 P.M.), vital signs TID for week 1 of each experimental phase and QD thereafter, determination of serum sodium, creatinine and osmolality plus urine osmolality and creatinine twice a week (3:00 P.M. Tuesday and Friday) and weekly CBC. Behavioral and cognitive functioning were assessed using the Nursing Observation Scale for Inpatient Evaluation (NOSIE) (administered by the same nurses on

Table 4. Changes in Dependent Variables in Individual Subjects with Drug Treatment

Positive Response to:	Pt. No.	Clonidine								Enalapril							
		CUO	UOSM	SNa	DWGP	NOSIE	BPRS	BCOG	CUO	UOSM	SNa	DWGP	NOSIE	BPRS	BCOG		
Clonidine and enalapril	2	42%	29%	0.8	-14%	-6%	-16%	-5%	41%	47%	-1.1	40%	3%	19%	-30%		
	3	55%	125%	1.9	122%	24%	4%	-20%	45%	51%	-3.3	50%	-13%	5%	75%		
	7	75%	261%	-0.4	-80%	-9%	3%	-19%	63%	24%	-0.9	15%	-4%	14%	-8%		
Clonidine only	1	45%	52%	0.2	-54%	24%	14%	1%	1%	-40%	-3.5	-1%	28%	-2%	4%		
	8	49%	15%	2.5	36%	-14%	-8%	-22%	-56%	4%	-1.2	-45%	-4%	-6%	-31%		
	10	39%	76%	-0.4	30%	-3%	-7%	-4%	-17%	-34%	-2.3	-18%	-4%	5%	-4%		
	13	46%	31%	0.3	-54%	1%	-22%	-17%	14%	-21%	-1.0	19%	-12%	25%	-17%		
Enalapril only	6	2%	-31%	-0.6	73%	-26%	3%	11%	22%	51%	-0.7	-51%	-3%	12%	-11%		
	9	9%	32%	0.8	-34%	17%	-2%	50%	57%	57%	0.5	-16%	14%	-25%	50%		
Neither drug	4	-24%	-11%	0.0	-36%	-6%	-20%	-17%	0%	13%	-1.1	5%	3%	7%	-2%		
	5	16%	-4%	0.4	59%	8%	13%	125%	18%	9%	0.4	28%	-4%	1%	-42%		
	11	-13%	11%	-0.9	-11%	0%	-6%	8%	20%	-25%	-0.1	-12%	-8%	11%	8%		
	12	-96%	26%	-3.1	-38%	6%	4%	-6%	-76%	-42%	-2.5	50%	-2%	3%	-6%		
	14	-10%	26%	4.7	12%	19%	6%	-38%	34%	-3%	-1.4	69%	-25%	15%	-38%		

All cells show percent improvement during drug phase compared with previous placebo phase except serum sodium, where improvement is expressed as positive change in absolute value.

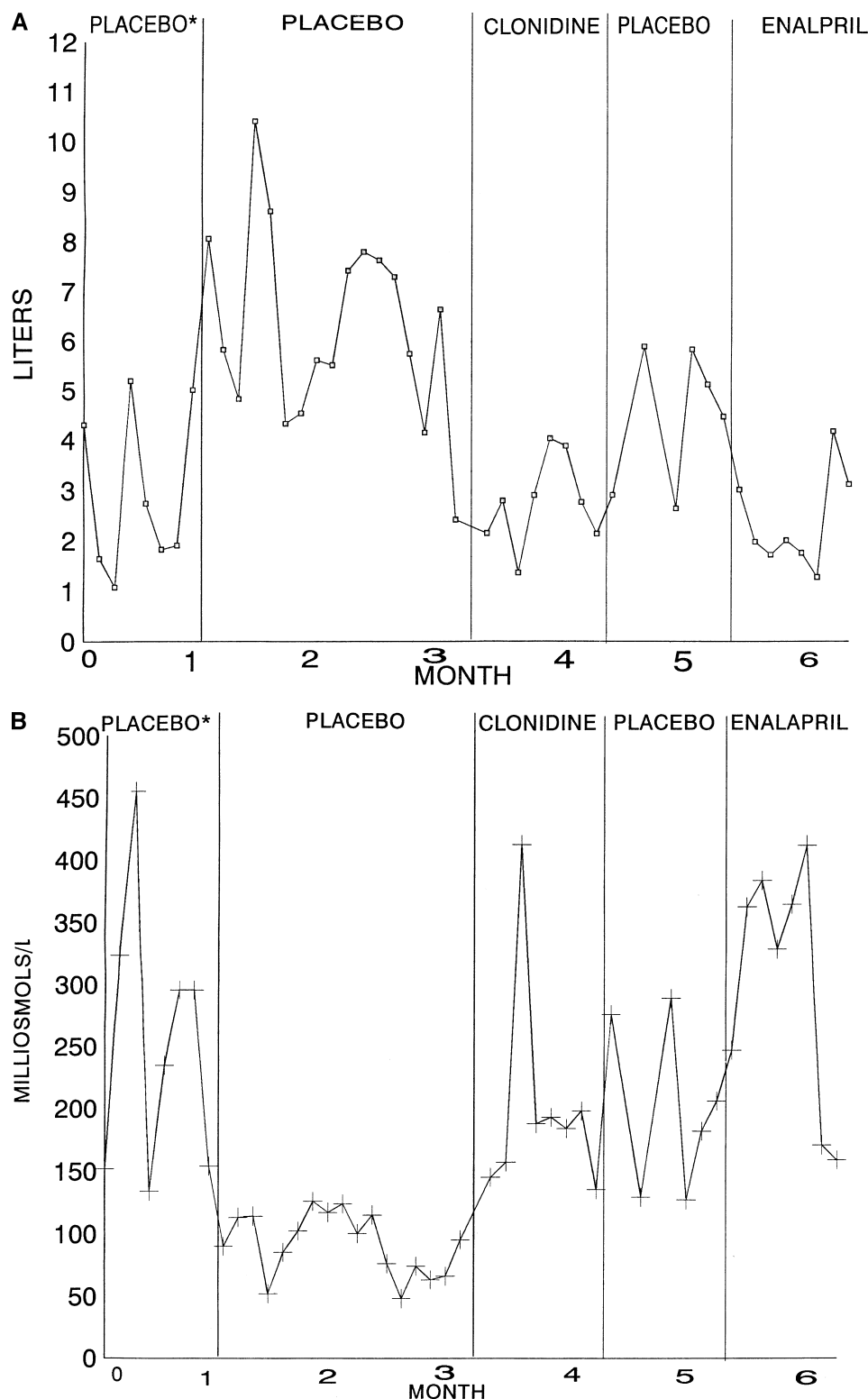


Figure 2. Selected results on one of the study patients (patient #3): (A) Calculated urine output (L/24 h); (B) 3:00 P.M. urine osmolality (mOsm/L); (C) Serum sodium (mEq/L); (D) 8:00 A.M. to 3:00 P.M. weight gain (lb). *Placebo plus water restriction. Free access to fluids was permitted throughout subsequent phases.

the same patients once per week), the Brief Psychiatric Rating Scale (BPRS) (administered once weekly by one of the psychiatrist authors, and a clinical nurse specialist) and brief psychological testing, comprising elements of the Mini-Mental state examination, Benton Temporal

Orientation, and the Digit Span subscale (multiple forms) of the WAIS-R, administered weekly by one of the psychologist authors, and a psychology assistant.

Because of the patients' inability to cooperate, traditional intake and output records could not be main-

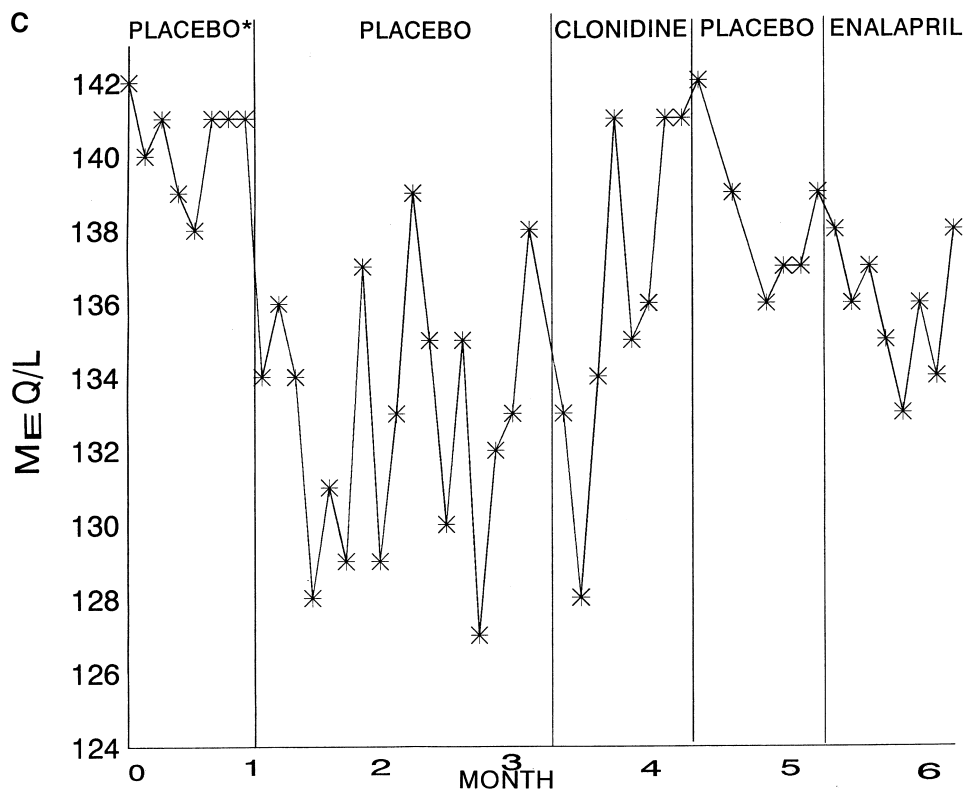
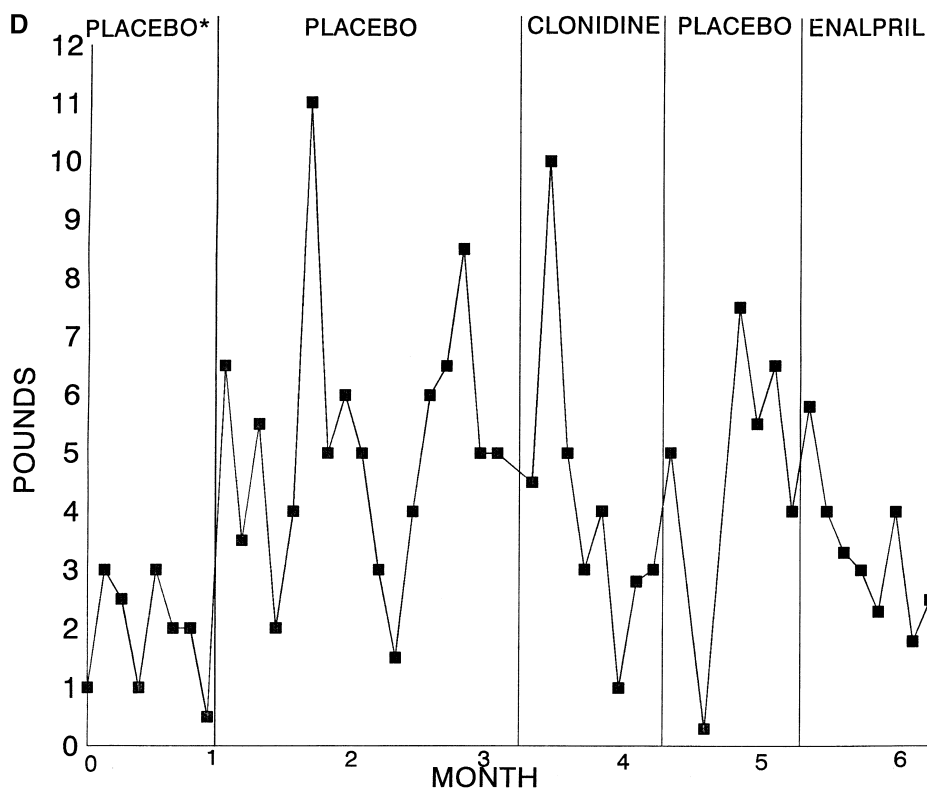


Figure 2. Continued.



tained, and surrogate measures were used as described by previous authors (Vieweg et al. 1992). Thus, diurnal weight gain provided a crude minimum estimate of fluid consumption or more specifically fluid retention in excess of excretion (Vieweg et al. 1988a, b, c, 1989a,

b, c, 1990). Calculated urine output (CUO) was based upon the work of Vieweg et al. (1986b, 1988a, 1992), using expected 24-h creatinine production and urine creatinine levels to calculate predicted excretion. Table 3 shows selected baseline (phase 2) assessment data.

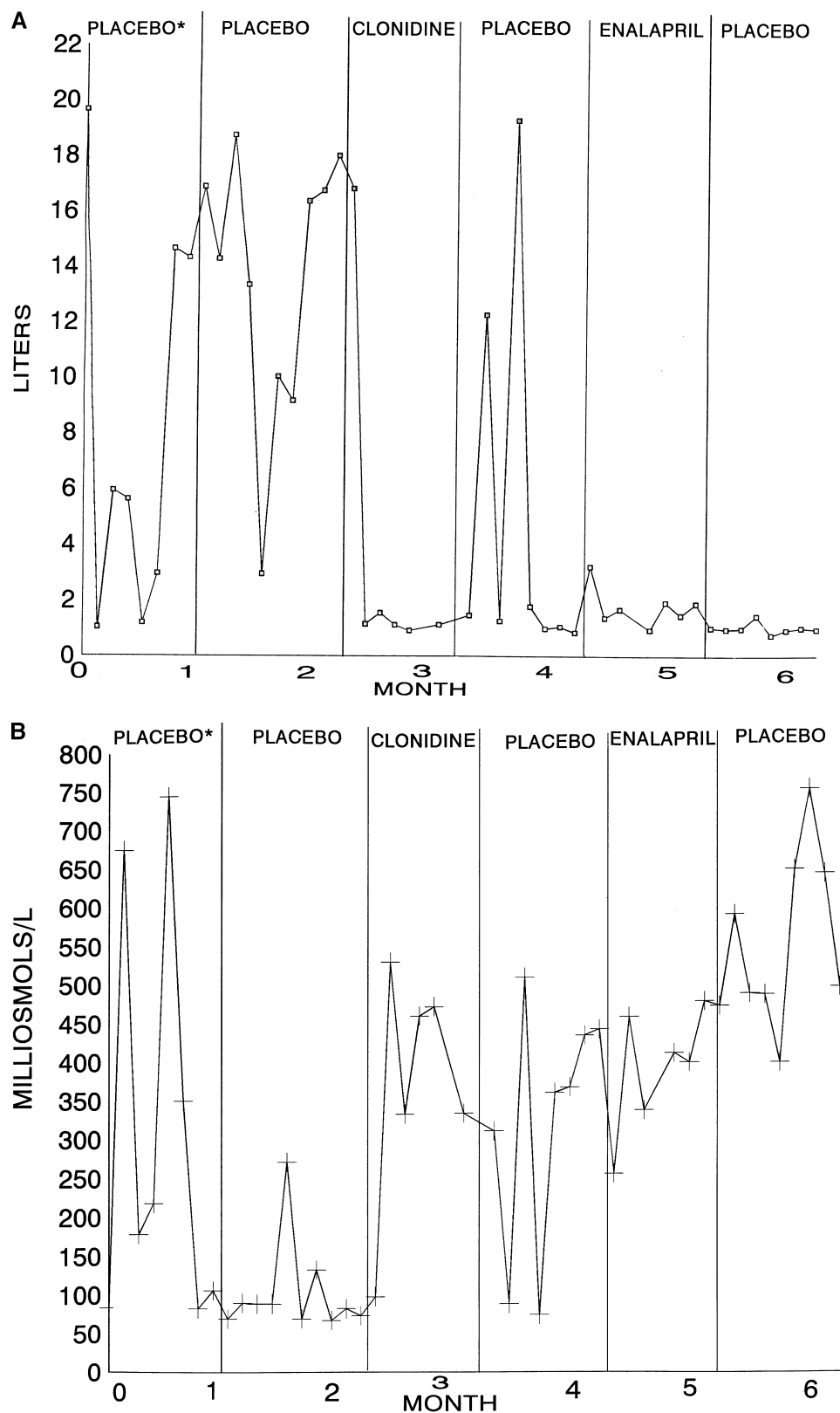


Figure 3. Selected results on one of the study patients (#7): (A) Calculated urine output (L/24 h); (B) 3:00 P.M. urine osmolality (mOsm/L). *Placebo plus water restriction. Free access to fluids was permitted throughout subsequent phases.

RESULTS

The outcome measures used to assess possible drug effects can be conveniently grouped as biological changes,

including calculated urine output (CUO), urine osmolality (UOSM), serum sodium (SNa), and percentage diurnal weight gain (PDWG), plus secondary psychiatric or neurobehavioral changes as measured by the NOSIE,

BPRS, and brief cognitive testing (BCOG). The results of group-statistical analyses conducted are reported first, followed by a detailed examination of individual subject's responses to the two experimental medications.

One tailed *t*-tests for correlated measures, comparing subjects' mean scores during phase 1, the first baseline phase, to phase 2, the second baseline phase, resulted in significant *p* values showing adverse effects of subjects' free access to water after a month of water restriction on all four biological variables, including CUO ($p < .001$), UOSM ($p < .001$), SNa ($p < .05$), and PDWG ($p < .05$). Similar comparisons on the three behavioral measures failed to yield significant results.

One tailed *t*-tests for correlated measures found CUO to be significantly lower ($p < .05$) and UOSM to be significantly higher ($p < .01$) during the clonidine phase than the preceding placebo phase. *T*-tests comparing the enalapril treatment phase with the preceding baseline phase yielded a significant difference in the same (predicted) direction for CUO ($p < .01$) only. Comparisons on all other dependent variables failed to yield significant results. These tests used an *n* of 14 (collapsing across groups), because the counterbalanced design of the study controlled for order effects. Mean CUOs for drug versus placebo phases are depicted graphically in Figure 1.

Based upon the magnitude of the percentage of change in the predicted direction on the two measures most directly affected by excessive drinking, CUO and UOSM, the authors classified subjects as being "responders" or "nonresponders" to the two experimental drugs. The criteria for judging a subject to be a "responder" was that he showed a mean decrease on CUO and increase on UOSM of 30% or more. These data are summarized in Table 4, where it will be seen that, of the 14 patients who participated in the study, three responded well biologically to both drug treatments (improvement in CUO and UOSM), four responded favorably to clonidine only, two responded favorably to enalapril only, and five showed no clear evidence of benefit from either drug.

Figure 2 depicts data from a patient (#3 in Tables 1 and 3) who responded favorably to both drug treatments across all four biochemical measures (CUO, UOSM, SNa, and PDWG). With the exception of SNa values during the enalapril phase, all the other data show evidence of favorable changes during experimental drug phases and reversals during the placebo phase after the initial drug phase (ABAC). The U-shape of the curve connecting SNa values during the enalapril phase would be consistent with a delayed effect of enalapril. Behavioral measures showed no consistent pattern of change following introduction of drugs for this subject.

Figure 3 depicts data from another patient (#7 in Tables 1 and 3), who showed a reversal of his CUO and UOSM values in the predicted direction after the introduction of both clonidine and enalapril, providing

strong evidence of an effect of the experimental medications on his fluid intake. Unlike the previous subject, however, patient #7 did not show any favorable change in SNa or PDWG nor on any of the behavioral measures. A possible explanation for the difference between this subject's data and the previously discussed subject is discussed below.

Both subjects #3 and #7 above showed some evidence of delayed and prolonged effects of the experimental treatments. Similar evidence of delayed effects (ranging from 3 to 14 days) and prolonged effects (ranging from 1 to 4 weeks) was seen in over half of the patients who responded to drug treatment.

DISCUSSION

The results of this study suggest that drugs known to affect body water balance may diminish excess water intake in some patients with histories of water abuse. Indirect measures of fluid intake (CUO and UOSM) were beneficially affected by both clonidine and enalapril in some subjects. In fact, 60% of our study group clearly improved (using the criteria of a mean change of 30% or greater in the predicted directions for both CUO and UOSM), and a few subjects showed associated changes in serum sodium and percentage diurnal weight gain, while on even a brief trial of clonidine or enalapril. These numbers might be greater if trials were prolonged. Individual data presented on two subjects, demonstrated a direct effect of clonidine and enalapril on both CUO and UOSM in the predicted direction during both treatment and placebo phases. Individual data also illustrated a time lag after initial response to drug treatment as well as effects enduring as long as a month after drug treatment. As a result of evidence for carry-over effects of both fluid restriction and the study drugs on fluid intake, it is recommended that future studies use longer washout periods after drug and water restriction phases. Similarly, due to delayed effects, it may be useful to use longer drug phases also.

Finally, the data showed inconsistent changes in SNa and PDWG. Subject #3, for example, showed changes in these measures during the experimental phases, whereas subject #7 did not. Likewise, there was no consistent improvement in behavior or cognition in study patients during treatment phases. These findings may be explained by the fact that many subjects, in spite of their history of polydipsia, still had adequate renal function and therefore might not be expected to show changes in SNa or PDWG with excess fluid intake. Changes in those measures would occur only in patients who retain the excess water. It is postulated that many of the subjects still had good kidney function and did not retain fluid volume abnormally. The failure to achieve greater therapeutic effects could also be a consequence of the

relatively brief duration of the treatment phases. In most of our patients, water abuse was of prolonged duration (see Table 1) with changes unlikely to be reversed within the space of a single month of treatment. Although further studies will be required to replicate our findings, the initial data suggest that results comparable to water restriction may be obtainable through medication. We urge that future studies in this area use appropriate placebo controls and crossover designs with statistical analysis to allow more sophisticated evaluation of potentially beneficial drugs than has been possible with previously published work.

ACKNOWLEDGMENTS

The following persons are gratefully acknowledged for their many hours of dedicated work on this study: Betty Adams, R.N., Susan Green, R.N., Joanne Healy, R.N., M.A., C.S., Janet Kulnot, R.N., Mariane Lennon, R.N., Valorie Lombardo, R.N.C., and Bonnie White, B.A.

REFERENCES

- Boyd, MA (1990): Polydipsia in the chronically mentally ill: A review. *Arch Psychiatric Nurs* 4:166–175
- Crammer JL (1991): Drinking, thirst and water intoxication. *Br J Psychiatry* 159:83–89
- DeLeon J, Verghese C, Tracy JL, Josiassen RC, Simpson GM (1994): Polydipsia and water intoxication in psychiatric patients: A review of the epidemiological literature. *Biol Psychiatry* 35:408–419
- DeLeon J, Verghese C, Stanilla JK, Lawrence T, Simpson GM (1995): Treatment of polydipsia and hyponatremia in psychiatric patients: Can clozapine be a new option? *Neuropsychopharmacology* 12:133–138
- Goldman MB, Luchins DJ (1985): Demeclocycline improves hyponatremia in chronic schizophrenics. *Biol Psychiatry* 20:1149–1155
- Goldman MB, Luchins DJ, Robertson GL (1988): Mechanisms of altered water metabolism in psychotic patients with polydipsia and hyponatremia. *N Engl J Med* 318:397–403
- Goldman MB (1991): A rational approach to disorders of water balance in psychiatric patients. *Hosp Community Psychiatry* 42:488–494
- Goldman MB, Nash M, Blake L, Petkovic MS (1994): Do electrolyte-containing beverages improve water imbalance in hyponatremic schizophrenics? *J Clin Psychiatry* 55:151–153
- Goldstein JA (1986): Captopril in the treatment of psychogenic polydipsia (letter). *J Clin Psychiatry* 47:99
- Goldstein JA, Folsom T (1991): The successful treatment of psychogenic polydipsia and water intoxication with propranolol. *Minn Med* 74:29–32
- Henderson DC, Goff DC (1994): Clozapine for polydipsia and hyponatremia in chronic schizophrenics. *Biol Psychiatry* 36:768–770
- Illowsky BP, Kirch DG (1988): Polydipsia and hyponatremia in psychiatric patients. *Am J Psychiatry* 145:675–683
- Kathol EG, Wilcox JA, Turner RD, Kranfol Z, Olson SC (1986): Pharmacologic approaches to psychogenic polydipsia: Case reports. *Prog Neuro-Psychopharmacol & Biol Psychiatry* 10:95–100
- Khamnei AK (1984): Psychosis, inappropriate anti-diuretic hormone secretion and water intoxication. *Lancet* 1:963
- Lawson WB, Williams B, Pasion E (1988): Effects of captopril on psychosis and disturbed water regulation. *Psychopharmacol Bull* 24:176–178
- Leadbetter RA, Shutty MS, Higgins PB, Pavalonis D (1994): Multidisciplinary approach to psychosis, intermittent hyponatremia and polydipsia. *Schizophr Bull* 20:375–385
- Leadbetter RA, Shutty MS (1994): Differential effects of neuroleptics and clozapine on polydipsia and intermittent hyponatremia. *J Clin Psychiatry* 55:110–113
- Lee HS, Kwon KY, Alphas LD, Meltzer NY (1991): Effect of clozapine on psychogenic polydipsia in chronic schizophrenia. *J Clin Psychopharmacol* 11:222–223
- Lyster C, Miller AL, Seidel D, Kavanagh J (1994): Polydipsia and clozapine (letter). *Hosp Community Psychiatry* 45:610–611
- Munn NA (1993): Resolution of polydipsia and hyponatremia in schizophrenic patients after clozapine treatment. *J Clin Psychiatry* 54:439–440
- Nishikawa T, Tsuda A, Tanaka M, Nishidawa M, Koga I, Uchida Y (1992): Naloxone attenuates drinking behavior in a schizophrenic patient displaying self-induced water intoxication. *Clin Neuropharmacol* 4:310–314
- Nixon RA, Rothman JS, Chin W (1982): Demeclocycline in the prophylaxis of self-induced water intoxication. *Am J Psychiatry* 139:828–830
- Patel JK (1994): Polydipsia, hyponatremia, and water intoxication among psychiatric patients. *Hosp Community Psychiatry* 45:1073–1074
- Raskind MA, Christopher TG (1974): Water intoxication and psychosis (letter). *Am Inst Med* 80:280
- Riggs AT, Dysken MW, Kim SW, Opsahl JA (1991): A review of disorders of water homeostasis in psychiatric patients. *Psychosomatics* 32:133–148
- Sebastian CS, Bernardin AS (1990): Comparison of enalapril and captopril in the management of self-induced water intoxication. *Biol Psychiatry* 27:787–790
- Shevitz SA, Jameison RC, Petrie WM, Crook JE (1980): Compulsive water drinking treated with high dose propranolol. *J Nerv Ment Dis* 168:246–248
- Spears NM, Leadbetter RA, Shutty M (1993): Influences of clozapine on water dysregulation (letter). *Am J Psychiatry* 150:9
- Verghese C, DeLeon J, Simpson GM (1993): Neuroendocrine factors influencing polydipsia in psychiatric patients: An hypothesis. *Neuropsychopharmacology* 9:157–166
- Vieweg WVR (1993): Behavioral approaches in polydipsia. *Biol Psychiatry* 34:135–137
- Vieweg WVR (1994): Treatment strategies in the polydipsia-hyponatremia syndrome. *J Clin Psychiatry* 55:154–160
- Vieweg WVR, Rowe WT, David JJ, Spradlin W. (1985a): Oral

- sodium chloride in the management of schizophrenic patients with self-induced water intoxication. *J Clin Psychiatry* 141:46:16–19
- Vieweg WVR, David JJ, Rowe WT, Peach MJ, Veldhuis JD, Kaiser DL, Spradlin WW (1985b): Psychogenic polydipsia and water intoxication—concepts that have failed. *Biol Psychiatry* 20:1308–1320
- Vieweg WVR, Rowe WT, David JJ, Curnow, RT, Spradlin WW (1986a): Self-induced water intoxication and psychosis (SIWIP): Subcategory of the syndrome of inappropriate antidiuresis (SIAD). *Psychiatr Med* 4:277–290
- Vieweg WVR, David JJ, Rowe WT, Yank GR, Spradlin WW (1986b): Diurnal variation of urinary excretion for patients with psychosis, intermittent hyponatremia, and polydipsia (PIP syndrome). *Biol Psychiatry* 21:1031–1042
- Vieweg WVR, Robertson GL, Godleski LS, Yank GR (1988a): Diurnal variation in water homeostasis among schizophrenic patients subject to water intoxication. *Schizophr Res* 1:351–357
- Vieweg WVR, Weiss NM, David JJ, Rowe WT, Veldhuis JD, Kaiser DL, Spradlin WW (1988b): Treatment of psychosis, intermittent hyponatremia, and polydipsia (PIP syndrome) with lithium and phenytoin. *Biol Psychiatry* 23:25–30
- Vieweg WVR, Wilkinson EC, David JJ, Rowe WT, Hobbs WR, Spradlin WW (1988c): The use of demeclocycline in the treatment of patients with psychosis, intermittent hyponatremia, and polydipsia (PIP syndrome). *Psychiatr Q* 59:62–68
- Vieweg WVR, David JJ, Rowe WT, Peach MJ, Veldhuis JD, Kaiser DL, Spradlin WW (1988d): Correlation of parameters of urinary excretion with serum osmolality among patients with psychosis, intermittent hyponatremia, and polydipsia. *Psychiatr Med* 6:81–97
- Vieweg WVR, Godleski LS, Graham P, Kellogg E, Goldman F, Barber J, Bayliss EV, Glick J, Hundley PL, Yank GR (1989a): Diurnal weight gain in chronic psychosis. *Schizophr Bull* 15:501–506
- Vieweg WVR, Godleski LS, Hundley PL, Yank GR (1989b): Survey of diurnal weight gain and urine volume in chronic schizophrenia. *Can J Psychiatry* 34:779–784
- Vieweg WVR, Godleski LS, Mitchell M, Hundley PL, Yank GR (1989c): Abnormal diurnal weight gain among chronically psychotic patients contrasted with acutely psychotic patients and normals. *Psychol Med* 19:105–109
- Vieweg WVR, Godleski LS, Graham P, Barber J, Goldman F, Kellogg E, Bayliss EV, Glick J, Hundley PL, Yank GR (1990): Abnormal diurnal weight gain among institutionalized patients with manic-depressive spectrum disorders. *Psychiatr Med* 8:129–134
- Vieweg WVR, Pandurangi AK, Pelonero AL (1992): Estimating daily urine volume in chronic psychosis. *Biol Psychiatry* 36:768–770
- Vieweg WVR, Pandurangi A, Levenson J, Silverman J (1994): The consulting psychiatrist and the polydipsia-hyponatremia syndrome in schizophrenia. *Int J Psychiatry Med* 24:275–303