Effects of Antihypertensive Drugs on Recovery from Aphasia

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INTRODUCTION

A report by Feeney (1982) indicated that haloperidol slows recovery from hemiplegia in the rat. Since catecholamine antagonists are frequently given to stroke patients to lower blood pressure or to reduce agitation, one must wonder if these drugs may also slow recovery in man. None of the pharmacologic guides offers information on the drugs in relation to aphasia, or even to brain damage in general, since the available information on the side effects and adverse reactions of antihypertensive drugs is collected on normotensive subjects and only reports acute effects (Light, 1980).

Recently Faulkner et al. (1984) found that clonidine and hydrochlorothiazide (HCTZ) did not affect cognitive function in adolescents except for a slight reduction in arithmetic performance, but they concluded that "considerable gaps of information remain pertaining to chronic effects of antihypertensive agents on cognitive function in hypertensive patients." In clinical aphasiology, we have mostly gaps and little information. In one uncontrolled study, amphetamine given to stroke patients enhanced recovery and recovery endured after discontinuation of the drug (Clark and Mankikar, 1979). Two case reports describe the use of amphetamine to improve behavior after head trauma (Bugiani and Gatti, 1980; Lipper and Tuchman, 1976) and recently Porch, Wyckes, and Feeney (1985) described a case study in which a patient who was having a very good recovery was given haloperidol with disastrous effects on recovery. Much remains to be learned.

METHOD

This was a retrospective study of the recovery of 40 male aphasic patients. The test data of the subjects were accepted for analysis if 1) the patient had a history of only a left hemisphere CVA, 2) if he had PICA test results at one and six and/or twelve months post onset, and 3) if there were medical records available indicating whether or not the patient received antihypertensive medication. On the basis of these variables, the patients were sorted into either the non-drug group or the mixed drug group. The members of the mixed drug group were further divided into two subgroups; those who received propranolol, a beta-blocker which is an antihypertensive and anti-anxiety medication, and those on hydrochlorothorizide, a diuretic. There were no significant differences among the groups for age, education, or months of treatment for aphasia (Table 1).

The recovery of the four groups was examined using two types of data. First, HOAP predictions (Porch and Callahan, 1981) were computed for each patient in order to estimate the six and twelve month recovery targets. No correction factors were used. Actual PICA outcomes were then subtracted from the target to determine the amount by which the subjects exceeded or missed their targets. Positive target errors indicate that the patient exceeded the target and negative scores indicate by what amount the patient fell below the target. Mean target error for each group was derived for six months post-onset (TE6) and for twelve months postonset (TE12).

Table 1. Subject information.

Group	Age		Education		Treatment
	Mean	S.D.	Mean	S.D.	Mean
Non Drug	56.0	8.3	11.8	3.5	8.14
Mixed Drug	57.4	7.5	12.5	3.2	6.56
Propranolol	59.2	6.2	13.5	2.8	8.17
HCTZ	59.5	7.3	12.8	3.2	8.10

The second intergroup comparison used change scores over time as an indication of recovery. The 1 MPO PICA Overall percentile was subtracted from the six MPO PICA OA (6-1) and the 12 MPO PICA OA (12-1), and means for these differences scores were computed for each group. These change scores were then used as a measure of overall communicative change during recovery.

RESULTS

A comparison of the recovery data among groups is shown in Table 2. The initial severity levels at 1 MPO (OA1) were quite similar, although the difference between the lowest group, Non Drug, and the highest group, Mixed Drug, reached a .05 level of significance. Since all four groups started their recovery in the 30 to 40 percentile range, there was little danger of a ceiling effect reducing the potential for improvement, which in these groups would be expected to be 25 or 30 percentile points if the patients stayed on target.

The Second column (TE6) shows how much each group deviated from the 6 MPO target levels. Two groups, Non Drug and Propranolol, exceeded the six month target by about 5 percentile points and did not differ significantly from each other in target error. The Mixed Drug group and the HCTZ group both missed the target levels by about 5 percentile points. The Non Drug group and the Propranolol group each differed significantly from the Mixed Drug group and the HCTZ group. In the third column (TE12) the same effect is even more apparent at 12 MPO. The Non Drug group exceeds the predicted targets by an average of 8.47 percentile points and also of great interest is the Propranolol group which has the best outcome of all, exceeding the target levels by 12.33 percentile points. In contrast, neither the Mixed Drug or the HCTZ groups reached target levels, falling 5.87 and 7.00 percentile points respectively below predictions. Figure 1 shows the target errors in graphic form. The differences between either group above the target compared with either of the groups below the target were highly significant. The difference between the Non Drug group and the Propranolol group was not significant, nor was the difference between the two drug groups with negative target error.

Table 2. A comparison of PICA test results among drug groups and non drug groups.

GROUPS	OA1	TE6	TE12	6-1	12-1	N
Non Drug	29.52	4.52	8.47	25.57	28.95	23
Propranolol	33.50	6.00	12.33	28.67	29.80	6
Signif. Levels	ns	ns	ns	ns	ns	
Non Drug	29.52	4.52	8.47	25.57	28.95	23
Mixed Drug	43.94	-5.76	-5.87	19.22	20.00	18
Signif. Levels	.05	.005	.001	ns	.01	
Non Drug	29.52	4.52	8.47	25.57	28.95	23
HCTZ	40.20	-4.33	-7.00	18.90	19.56	10
Signif. Levels	ns	.05	.005	ns	.05	
Mixed Drug	43.94	-5.76	-5.87	19.22	20.00	18
Propranolol	33.50	6.00	12.33	28.67	29.80	6
Signif. Levels	ns	.005	.01	ns	.05	

Table 2 also shows the amount of change in the OA percentile that each group had between 1 and 6 MPO. The Non Drug group and the Propranolol group changed more than 25 percentile points during that period, while the other two drug groups changed only 19.22 and 18.90 percentile points respectively. Although these differences between the high change groups and the low change groups did not reach statistical significance, these differences would be considered to be clinically significant.

The one to 12 MPO differences are all in the same direction but of slightly larger magnitudes, and do reach statistical significance, especially between the two largest groups, the Non Drug and the Mixed Drug groups, where there is about a 9 percentile point difference. The group differences are shown in graphic form in Figure 1.

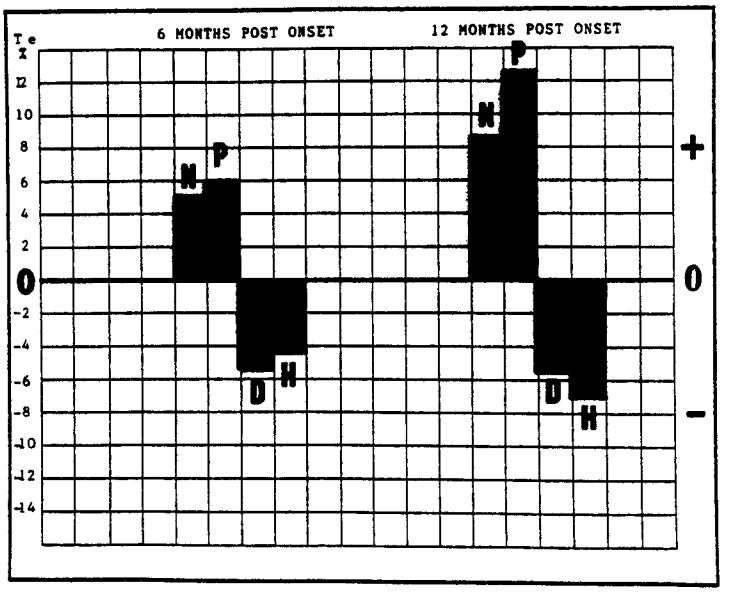

Figure 1. Mean target errors at six and twelve months post onset for each group: Non Drug (N), Propranolol (P), Mixed Drug (D) and Hydrochlorothiazide (H) groups. All + scores are significantly different from all - scores at the .01 level.

DISCUSSION

In 1981, Porch and Callaghan suggested that we continue in the search for possible correction factors to make HOAP predictions more accurate. Perhaps it's time that the clinical aphasiologist begin to take a closer look at the medications their patients are taking. This was a retrospective study of a fairly small number of patients, and subsequent, better controlled studies with more subjects may temper our present interpretations, but it seems that either thiazides negatively affect the aphasic patient's potential for recovery or else the type of patient that receives thiazides do less well during recovery because of the medical problems that require these drugs.

What should we advise the physicians to prescribe for our patients? At present, there doesn't seem to be a standard protocol for treating hypertension. Each physician has his own biases as to which drugs to use with each patient. With mild cases, low salt diets and mild sedatives are often used, but diuretics are very commonly used with all levels of hypertension. Propranolol is used much less frequently, perhaps because of possible side effects. The data we have presented here suggests that HCTZ is associated with poorer recovery and propranolol patients do well. While it may be premature to rush back to our centers and try to change current medical practice, it is clearly indicated that we can no longer ignore the medications our patients are taking. We should routinely duplicate the entire drug list from our patient's charts for our records, so that hypertension medications, as well as other drugs that may affect recovery may be better studied. Before we can convince physicians to attempt prospective, controlled studies, we will have to provide impressive retrospective data, and apparently we have already waited too long.

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DISCUSSION

C: One of the variables in this kind of study that will be difficult to control is the amount of drugs, that the patient's using. With some drugs a little bit may have a particularly good effect in a given patient, and with the concept that if a little bit is good giving more will be even better, you may lose the desired effect and pick up some negative effects. With the work that I've been doing in the last few years, we've found that physicians are very receptive to behavioral descriptions from us on our observations of the patients as the changes due to medications occur, with sensitivity to when the blood levels reach plateaus, so that is a way that in our work settings we could be very helpful. We find that some physicians are quite naive when it comes to what kinds of dosages they should give to, for instance, facilitate learning effects in our clients.

A: That's true. And the inter-drug effects are difficult to study because there is no way to control the kind of drugs the patient will be on. And then you have the problem of medical staffs changing, especially in a teaching hospital. Each physician seems to have biases as to what drugs may be best for a given situation and new drugs are continually coming on the scene. In addition, it's sometimes difficult to get blood levels with any regularity. Also, patients' sensitivity to drugs varies. I just had a patient with right hemisphere dominance for communication that I was trying to study who gradually became less and less responsive.

When we finally got a blood level we found that he was at toxic levels of dilantin.

C: I certainly agree that drug interaction could be a problem and, also, the age of the patient. People who are at advanced ages, fifty and above, may be affected differently by drugs as they get older, and I think that some physicians don't recognize that a patient who is eighty-five may not respond to a dosage in the same way as a patient who is fifty-five.

A: Yes, I know of a woman whose family complained that she was falling down more frequently and had slurred speech and memory problems. I found that the only medication that she was taking was Dalmane, a sleeping medication. When I checked the PDR I found a notation that said that in older patients Dalmane should be monitored because some patients develop ataxia, dysarthria, and memory problems. I suggested to the family that they stop the Dalmane and within a few weeks she returned to normal levels. I guess this represents a case of geriatric drug effect, but my plea here is that on all patients we should begin gathering clinical data and record the dosages on all of the drugs that our patients are taking, and, perhaps, we'll have enough data to make a stronger plea to our colleagues in medicine with regard to administering medications that might influence cognitive functioning.

Q: I noticed that the amount that your patients missed the target by wasn't very great, although it was significant. You used the means for the groups, but as far as individual patients are concerned, did they really miss the window around the target by very much?

A: Yes, the range was tremendous. In the slides that I showed, you might recall that in the non-drug group, there were only four patients who did not exceed their target while in the drug group, only three patients in the entire group exceeded the projected target. What you see in most studies is a bell-shaped curve around zero target error with the number of patients tapering off on either side of that point. In this study, the bell-shaped curve centered at a point eight percentile points above the target in the non-drug group and centered at five percentile points below that point for the drug group. Having two groups that differ by ten or fifteen percentile points in target error is not only statistically significant but it would be clinically significant.