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The Dexamethasone Suppression Test for Diagnosing Depression in Stroke Patients

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Depression following a cerebrovascular accident is common, disabling, and treatable. However, the consequences of a stroke often render the clinical evaluation for depression misleading or difficult to interpret. These factors make a laboratory test for depression especially desirable in this population. We reviewed and evaluated the literature on the dexamethasone suppression test (DST) as a diagnostic tool for depression in stroke patients. Nine studies were identified. Our findings included (1) substantial variation in both methods and results, (2) a median specificity of 87%, and (3) a median sensitivity of 47%. We show that if these estimates of sensitivity and specificity are supported by future studies with improved methodology, then the DST may be clinically useful for the minority of stroke patients in whom a careful evaluation for depression remains inconclusive.

KEY WORDS: dexamethasone suppression test; poststroke depression; diagnostic utility.

INTRODUCTION

Depression is an unfortunate but common complication of stroke (1–10). However, depression following a stroke is both underdiagnosed and undertreated (11–14). This is partly because the evaluation of a stroke patient for depression is commonly complicated by neurological syndromes such as aphasia, aprosodia, anosognosia for depressive signs, abulia, the syndrome of pathological crying, amnesia, dementia, and delirium (15,16).

One proposed laboratory test for depression, the dexamethasone suppression test (DST), is now seldom used and is not currently recommended for routine use by the APA Task Force on Laboratory Tests (17–19). One reason is that the DST is normally far less informative in the diagnosis of depression than the usual psychiatric history and exam. However, because the usual clinical exam is sometimes less reliable in the stroke patient, this conclusion might be premature in the poststroke population. We hypothesized that the DST might be more useful in this special population.

METHOD

We searched the literature for studies of the DST in poststroke depression using Medline, Current Contents, and PsycINFO using the key words "explode cerebrovascular disorders" and "dexamethasone." We also reviewed sources cited in a recent literature review (15). Each identified study was examined for essential features of its methods and results. Data compiled from these studies were then used to calculate estimated positive and negative predictive values for the DST in the diagnosis of depression.

RESULTS

Our literature search revealed nine clinical studies with sample sizes of twenty or more (20–29). The variation in results among these studies is quite large (Table 1). Sensitivity of the DST as a labora-

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Table 1. Summary of the Methods and Results of Nine Studies of the DST in Poststroke Depression[a]

Ref. No. (*n*)	Setting/time poststroke	Exclusion criteria	Assessment/definition of depression	Cortisol sampling	Percentage				
					Sens	Spec	Pos. PV	Neg. PV	Study prev.
24 (*n* = 25)	Rehab/11–111 days; mean, 37 days	History of psychiatric or endocrine disease	3 separate interviewers of patient and nurses	4 p m, 11 p m	75	89	92	67	64
23 (*n* = 20)	Rehab/16–71 days	Aphasia, certain medications, disorientation	Score on HDRS	8 am, 4 pm	0	83	0	82	15
4 (*n* = 48)	Rehab & outpt/ unspecified	"[Any] severe deficit in comprehension that would preclude reliable assessment of their emotional state"	HDRS, PSE-Mod, ZSRDS (combined score)	4 pm, 11 pm	33	70	50	82	31
25 (*n* = 61)	Rehab/unspecified	Neurosurgery or nonstroke brain lesions, certain medications, recent steroids, intercurrent medical illness	ZSRDS, HDRS, interview	8 am, 4 pm	47	87	86	50	62
26 (*n* = 31)	Inpt/mean, 81 days	"[Any] factor known to produce a false-positive or false-negative DST"	Interview. If asphasic, then relatives report	4 pm, 11 pm	80	100	100	91	32
27 (*n* = 20)	Rehab/<6 wk	Age <55, severe receptive aphasia, decreased consciousness, left-handedness, psychiatric history, drug abuse	HSRS, M-MMSE, DAC/VAC, RDC criteria	5 pm, 11 pm	100	14	33	100	30
22 (*n* = 29)	Outpt/mean, 106 wk; median, 36 wk	Traumatic brain injury, other neurological disease, prior depression or other psychiatric illness, alcohol or drug abuse	Structured interview, HSRD, DSM-III	4 pm	15	67	50	26	69
20 (*n* = 76)	Inpt & outpt/8–1280 days; median, 35 days	Aphasia, "other serious somatic or psychiatric illness," certain medications	Interview, "ratings scales," RDC criteria	8 am, 4 pm	6	95	25	78	22
29 (*n* = 42)	Inpt & follow-up/ followed 3 yr	Long list of medical conditions or drugs than can cause false-negative or false-positive DST, disorientation, or comprehension deficits	Serial interviews, DSM-III	7 am, 4 pm, 11 pm	70	97	88	91	24

[a]HDRS, Hamilton Depression Rating Scale; M-PSE, Modified Present State Exam; ZSRDS, Zung Scale for Rating Depressive Symptoms; DAC/VAC, mood symptom adjective checklists. PV, predictive value; Prev, prevalence of "depression", Sens, sensitivity; Spec, specificity. The informant is the patient only, unless indicated otherwise. In many studies the duration criterion for depression was modified or disregarded.

tory test for depression in stroke patients varies from 0 to 100%, while specificity varies from 14 to 100%. Prevalence of depression in the poststroke samples ranges from 22 to 64%.

The enormity of these variations is best explained by the marked differences in method from one study to another (Table 1). Important differences include the population under study, the instrument and methods used to evaluate a patient for depression, the inclusion and exclusion criteria, the timing of the evaluation after the stroke, and the method used to perform the DST. These differences were too numeróus to reveal any consistent relationships between results and particular differences in methods.

In spite of this large variability among studies, some broad conclusions can be drawn. (i) The median prevalence of mood disorder among poststroke patients in these studies is 32%. This is similar to the approximately 40% prevalence found in larger studies of poststroke depression (1, 2, 5, 6, 30). (ii) Specificity is high in nearly all of these studies (greater than or equal to 67% in eight of nine), and the median specificity of the nine studies is 87%. (iii) The sensitivity of the DST is more modest overall, with a median sensitivity of 47%. (iv) Assuming a prevalence of depression of 40%, and the sensitivity and specificity as above, the DST has a positive predictive value of 71% for the diagnosis of depression in stroke patients. Coincidentally, these assumptions yield a negative predictive value that is also 71%.

DISCUSSION

An ideal study might follow DST results in stroke patients over time with outcome measures such as rehabilitation success, mortality, or depressive symptoms. No such study has been performed. Nevertheless, the best available data suggest that, in a patient for whom no other information is available, a positive DST changes the likelihood of depression in a stroke patient from the population prevalence of 40% to approximately 71%. This may represent a clinically meaningful gain in information. For example, one case report describes a woman with suspected depression after suffering a stroke with a profound aphasia (31). An antidepressant was started after she was found to have a positive DST. As the woman's aphasia improved, it became clear that she had been depressed and that her depression was improving dramatically with antidepressant treatment. In addition, her DST result normalized with further resolution of her depression.

In a patient such as this, in whom neurological deficits make a clinical evaluation for depression incomplete, the pretest likelihood of depression can be estimated as the population prevalence of depression after stroke, as shown by point A in Fig. 1. In such patients, information gain from the DST is near its peak. On the other hand, in patients for whom clinical examination allows a confident determination that the patient is depressed or not depressed, the potential information gain from the DST is small (Fig. 1, points B and C).

Any clinical study of the DST for depression must compare the result of the DST against the result of the clinical examination. Since the clinical examination is the "gold standard," a thorough clinical examination is crucial for studies of the DST to be meaningful. The optimal clinical evaluation would include information from many sources, such as collateral information from the patient's family (15). This was demonstrated in one study in which some patients who were identified as not depressed by interview with the patient were then found to be depressed by a more comprehensive exam, in this case increasing the apparent specificity of the DST from 69 to 89% (15, 24). Since most studies reviewed did not obtain information from sources other than the patient, the predictive power of the DST might actually be better than that reported here.

One important caveat is that the studies reviewed generally excluded (with good reason) those subjects who were more difficult to evaluate clinically, such as those with aphasia. Although this is the best data currently available, there may be pitfalls in generalizing data obtained from subjects who are less difficult to evaluate to those who are more difficult to evaluate clinically. For example, a patient with a large volume stroke might be both more difficult to evaluate and more likely to have a false-positive DST (18, 21). Unfortunately, it is exactly these difficult-to-evaluate patients who would be most likely to benefit from a laboratory test for depression.

Future Directions

We recommend the following for future studies of the DST in depression following stroke. (i) Collection of additional information about depressive symptoms from sources such as the patient's family

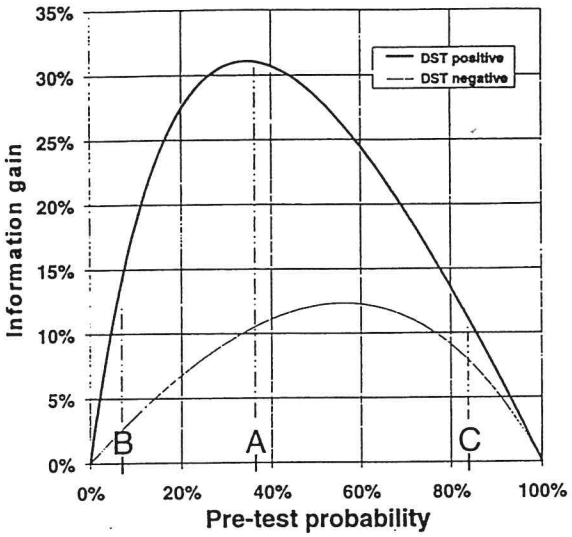

Fig. 1. Based on the studies reviewed, the DST is most useful at pretest probabilities near the prevalence of depression in stroke patients. Here we define "information gain" as the change in probability (of depression) that results from a positive or negative test result.

or nursing staff. (ii) Use of a criterion-based diagnostic system to evaluate for depression, such as major depressive episode by DSM-IV. This approach would require some guidelines for taking into account that some depressive symptoms might be caused directly by the stroke or its consequences, such as poor sleep because the patient is on a noisy inpatient unit. (iii) Adherence to the duration criteria for depression, e.g., at least 2 weeks of the syndrome. (iv) Examination of each patient for the specific neuropsychiatric impairments that might confound diagnosis (15). (v) Uniformity in the administration of the DST, such as using a single cortisol level at 0800 (32). (vi) A longitudinal design, with serial examinations for depression and clinical follow-up measures. (vii) Modifications of the DST, which might have greater sensitivity and specificity, should also be considered (33–35).

Conclusions

Studies performed to date of the DST as a test for depression in stroke patients are limited by a lack of uniformity of method and important methodological problems. The available data, although limited, suggest that, in some cases, the DST might add substantial diagnostic information and may be useful for the minority of stroke patients for whom a careful clinical evaluation for depression remains inconclusive. As in other applications of this test, sensitivity is low, so treatment should never be withheld on the basis of a negative DST. Further studies of the DST in this population, using more rigorous methods, are needed.

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