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Results of Dexamethasone Suppression Test in Early Alzheimer Dementia

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Summary. The frequency of an abnormal response to the Dexamethasone Suppression Test (DST) was examined in 24 non-depressed patients in the early stages of Alzheimer dementia. Results were compared with those obtained in 51 geriatric medical inpatients: 15 with major depression, 18 with dysthymic disorder and 18 normal controls. As an abnormal lack of suppression was found in 9 demented patients, in 9 with major depression, 1 with dysthymic disorder and in 2 the normal controls, it appears that DST alone is not useful in distinguishing dementia, even in its early stages, from major depression. In our experience abnormal DST results in demented patients were unrelated to mood.

Key words: Dexamethasone Suppression Test – Alzheimer dementia – Early stages

Introduction:

Numerous studies have emphasized the use of the Dexamethasone Suppression Test (DST) in identifying severe depression (Asnis et al. 1981), and further investigations have confirmed that this test may also be profitably used in geriatrics, since advanced age does not weaken the validity of the results (Tourigny-Rivard et al. 1981).

The diagnosis of depression in the elderly is complicated by its frequent coexistence with dementia, while occasionally depression may be entirely responsible for a patient's cognitive impairment and apathy.

A number of cases have been reported (Rudorfer and Clayton 1981) where the DST has appeared useful in distinguishing depressive states from progressive degenerative dementia. However, others (Spar and Gerner 1982) have suggested that the DST may be less specific in patients with dementia; it has been reported (Balldin et al. 1983) that both patients suffering from primary degenerative disorders and those with multi-infarct dementia, although not depressed, frequently show abnormal results of the DST.

Differential diagnosis from major depression is paritcularly important in the case of Alzheimer dementia in the early stages. Some data (Jenike and Albert 1984) suggest that DST may be a useful clinical tool in mildly impaired patients with Alzheimer disease, but is likely to be affected by the disease in moderately to severely impaired patients.

The aim of our study was to evaluate the DST in a selected group of geriatric patients in the early stages of Alzheimer type dementia and to compare the results with those obtained in a group of geriatric patients with major depression, in other patients with dysthymic disorder and in a group of controls.

Materials and Methods

From among 160 patients with dementia we selected 24 non-depressed subjects (9 men and 15 women) with no previous diagnosis of dementia. The most common reason for referral was memory impairment.

The mean age of our population was 68.6 (range 45–83; standard deviation 11.5). Most were married. The predominant social status was that of pensioner with a former working class occupation. Diagnosis of mild Alzheimer dementia (DAT) was made by a staff neurologist blind to the aim of the study and according to the criteria of the DSM III (APA 1980); diagnosis was confirmed, using the same criteria, by one of the authors (DDL). The presence of depressive disorder was excluded on the basis of the same criteria. None of the patients had been diagnosed as affected by dementia before the six months preceding the present evaluation.

The subjects were also tested with the Hachinsky scale (all patients scoring 4 or less), the Hasewaga scale (all patients scoring 21.5 or less, mean score 14, standard deviation 2.1) the

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Mini Mental State (in which the mean score was 14.0 and standard deviation 2.7), and the Hamilton Rating Scale for Depression (all patients scoring less than 18).

Diagnoses were also made on the basis of carefully compiled case histories, results of routine laboratory tests, VDRL, thyroid function study, EEG and cranial CT (in all cases). Findings on EEG or CT that suggested focal neurological diseases served as additional exclusion criteria.

We also studied 51 other subjects (18 men and 33 women) admitted to the 2nd medical division of the Geriatric Hospital, Padua (Northern Italy), for a variety of medical reasons. The social and marital status of these subjects did not differ significantly from those of the demented patients. 15 of them (5 men and 10 women; mean age 69.1, range 60–80 and standard deviation 8.4) had a major depressive disorder (MDD). 18 (2 men and 16 women, mean age 74.4, range 60–90, standard deviation 8.4) suffered from a dysthymic disorder (DD). The remaining 18 patients (mean age 72.8, range 60–88, standard deviation 7.6) were controls. All the 51 patients serving as controls were tested with the Mini Mental State and scored more than 18.

The psychiatric diagnosis were formulated according to the criteria of the DSM III, on the basis of clinical interview and psychiatric case history, in conditions blind to the results of the DST. No other psychiatric diagnosis except depression was found in these patients. None of the 75 subjects, patients or controls, had any particular clinical condition or took any drugs that might have affected the reliability of the DST according to the criteria cited by Carroll et al. (1981). Patients were studied no sooner than the 10th day following admission to avoid an acute hospitalization effect on the DST.

Baseline cortisol concentrations were assayed in a blood sample taken at 8.00 am on the day before the DST.

Two 0.5 mg capsules of dexamethasone were administered at 11.00 pm, and a blood sample was taken at 4.00 pm on the following day. The 4.00 p.m. sample was chosen as it is the time most frequently reported in the literature for once only sampling, given that it seems to couple good sensitivity and specificity (Brown 1981). Informed consent was obtained after the nature of the procedure had been fully explained.

If cortisol levels were 5 μg/dl or more in the sample, the test was considered positive and the corresponding subject a "non suppressor".

The blood samples for the calculation of cortisol values were taken in 10 ml vacutainer tubes, which were then centrifuged and stored at +4°C. The separated sera were kept in polystyrole test tubes at −20°C until the hormone assay could be performed. Cortisol concentrations were determined in duplicate with a specific radioimmunoassay, COAT-A-COUNT/cortisol kit (Diagnostic Products Corporation) which has a sensitivity limit of 0.2 μg/dl and a cross-reactivity for dexamethasone of 0.53. Coefficients of variation within and between the series were determined by assaying a serum pool from one patient and three commercial control sera (Lyphoceck, Immunoassay Control Serum-Human-Levels I, II and III; Lot 71110, Biorad, ECS Division); they were 7.4% and 4.3% respectively.

Statistical analysis was performed with the Mann-Whitney *U* test, the chi-square test (Yates' correction) and the Pearson's product-moment correlation.

Results

Of the 24 patients with DAT, 9 (38%) were non suppressors; non suppression also occurred in 9 of the 15 patients with MDD (60%), in 1 of the 18 subjects with DD (6%) and in 2 out of the 18 normal controls (11%) (Table 1). The difference in the frequency of non suppression between the DAT patients and the other groups examined was not significant according to the Chi-square test, with the single exception of the DD group ($P < 0.05$).

Table 1. Cortisol levels (in μg/dl) and non-suppression frequencies (Mean cortisol values per person ± SD)

	8.00 am	4.00 pm	DST + (%)
DAT ($N = 24$)	10.31 ± 5.28	5.16 ± 3.32	9 (37.5)
MDD ($N = 15$)	17.62 ± 6.46	7.49 ± 5.13	9 (60)
DD ($N = 18$)	12.8 ± 3.0	1.69 ± 2.1	1 (6)
Controls ($N = 18$)	12.18 ± 7.62	2.16 ± 1.98	2 (11)
	- DAT vs MDD: $P < 0.005$	- DAT vs DD: $P < 0.0001$ - DAT vs controls: $P < 0.0001$	- DAT vs DD: $P < 0.05$
		administration of 1 mg. of dexamethasone at 11.00 pm.	

Baseline cortisol differed significantly between the DAT and MDD groups, but not between the DAT and DD and control groups (Mann-Whitney U test).

Plasma cortisol levels were higher in DAT patients than in DD ($P < 0.0001$) and normal controls ($P < 0.0001$) (Mann-Whitney *U* test).

No differences between DAT and MDD patients emerged at this phase of the evaluation. We noted no correlations between blood cortisol values and scores on the Hasegawa ($r = +0.14$), the Hachinsky ($r = +0.11$) and the Mini Mental State ($r = -0.21$), nor were there differences in non suppression frequencies between the two sexes within the DAT group.

With a cutoff point of 5 μg/dl., sensitivity and specificity for DAT were 38 and 76% respectively (for MDD the figures were 60% and 80% respectively).

Discussion

The rate of non suppression after dexamethasone administration is 38%, a figure quite similar to that found by the present authors in a more heterogenous demented population (Magni et al. 1987); it also confirms the reports of other authors (abnormal responses

ranged from 35 to 50% of cases, according to the characteristics of the population and the methodology employed in the test (Spar and Gerner 1982; Raskind et al. 1982).

Comparison between the results of DAT patients and controls confirms the tendency for DAT patients to present higher postdexamethasone cortisol values; this tendency is best seen in the comparison of the DAT and the DD groups. In a previous study (Magni et al. 1986) we stressed the interestingly low percentage of nonsuppression in DD, which appears to suggest that the clinical criteria for the diagnosis of DD provided by the DSM III are better associated with DST results than those of other evaluations (excluding subgroups of depression affected by biological alterations similar to those found in major depression).

In the comparison with the MDD group, on the contrary, no difference emerged either in the examination of the frequency of non suppression rates or in the comparison of postdexamethasone cortisol values.

Baseline blood cortisol levels is the only element differentiating the two pathologies. A baseline hypersecretion of cortisol is in fact one of the best documented neuroendocrine alterations in depressive disturbances (Dam et al. 1985).

The finding of DST non suppression both in patients with depression and in those with dementia is now well established, and suggests that certain anomalies (alteration of noradrenergic and/or cholinergic and/or serotoninergic neurotransmission) (Pomara et al. 1984) are common at least to subpopulations of patients with these disturbances. According to Galletly et al. (1985), it is also possible that these demented patients may suffer from an atypical form of depression which cannot be identified by standard procedures.

It is noteworthy that in our study DST results were very similar to those obtained by other authors in more advanced stages of dementia (Raskind et al. 1982).

Obviously, in the absence of a post-mortem evaluation the diagnostic value of our clinical DAT diagnosis is limited.

Finally, with reference to the insufficient difference between the sensitivity and specificity of the DST administered to the two groups of patients (MDD and DAT at early stages) it may be argued that DST alone has limited value in this difficult differential diagnostic problem, and adds nothing to the diagnostic reliability of the clinician. The resolution of this problem will await further studies employing new and more reliable diagnostic tools and, eventually, adequate trial with antidepressants.

References

American Psychiatric Association (1980) Diagnostic and statistical manual of mental disorders, 3rd edn. APA, Washington, DC

Asnis GM, Sachar EJ, Halbreich U, Nathan RS, Ostrow L, Halpern FS (1981) Cortisol secretion and dexamethasone response in depression. Am J Psychiatry 138:1218–1221

Balldin J, Gottfries CG, Karlsson I, Lindstedt G, Langström G, Walinder J (1983) Dexamethasone suppression test and serum prolactin in dementia disorders. Br J Psychiatry 143:277–281

Brown WA (1981) The dexamethasone suppression test: clinical applications. Psychosomatics 22:951–954

Carroll BJ, Feinberg M, Greden JF, Tarika J, Albala AA, Haskett RF, James NM, Kronfol Z, Lohr N, Steiner M, Vigne JP de, Young E (1981) A specific laboratory test for the diagnosis of melancholia. Standardization, validation and clinical utility. Arch Gen Psychiatry 38:15–22

Dam H, Mellerup ET, Rafaelsen OJ (1985) The dexamethasone suppression test in depression. J Affective Disord 8: 95–103

Galletly CA, Morris H, Newcombe A (1985) The dexamethasone suppression test in elderly, non-depressed patients with dementia. Aust NZ J Psychiatry 19:95–96

Jenike MA, Albert MS (1984) The dexamethasone suppression test in patients with presenile and senile dementia of the Alzheimer's type. J Am Geriatr Soc 32:441–444

Magni G, Schifano F, De Leo D, De Dominicis MG, Garbin A, Zangaglia O (1986) The dexamethasone suppression test in depressed and non depressed geriatric medical inpatients. Acta Psychiatr Scand 73:511–514

Magni G, Schifano F, De Leo D, Zangaglia O (1987) The dexamethasone suppression test in dementia. Ital J Neurol Sci 8:125–128

Pomara N, Oxenkrug GF, McIntyre IM, Block R, Stanley M, Gershon S (1984) Does severity of dementia modulate response to dexamethasone in individuals with primary degenerative dementia. Biol Psychiatry 19:1481–1485

Raskind M, Peskind F, Rivard MF, Veith R, Barnes R (1982) Dexamethasone suppression test and cortisol circadian rhythm in primary degenerative dementia. Am J Psychiatry 139:1468–1471

Rudorfer MY, Clayton PJ (1981) Depression, dementia and dexamethasone suppression. Am J Psychiatry 138:701

Spar JE, Gerner R (1982) Does the dexamethasone suppression test distinguish dementia from depression? Am J Psychiatry 139:238–240

Tourigny-Rivard MF, Raskind M, Rivard D (1981) The dexamethasone suppression test in an elderly population. Biol Psychiatry 16:1177–1184

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