Comparison of 1 mg and 2 mg Overnight Dexamethasone Suppression Tests for the Screening of Cushing’s Syndrome in Obese Patients

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Abstract

Objective  Obesity is currently a major public health problem and one of the potential underlying causes of obesity in a minority of patients is Cushing’s syndrome (CS). Traditionally, the gold standard screening test for CS is 1 mg dexamethasone overnight suppression test. However, it is known that obese subjects have high false positive results with this test.

Design  We have therefore compared the 1 mg and 2 mg overnight dexamethasone suppression tests in obese subjects. Patients whose serum cortisol after ODST was >50 nM underwent and a low-dose dexamethasone suppression test (LDDST); 24-hour urine cortisol was collected for basal urinary free cortisol (UFC). For positive results after overnight 1-mg dexamethasone suppression test we also performed the overnight 2-mg dexamethasone suppression test.

Patients  We prospectively evaluated 100 patients (22 men and 78 women, ranging in age from 17 to 73 years with a body mass index (BMI) >30 kg/m² who had been referred to our hospital-affiliated endocrine clinic because of simple obesity. Suppression of serum cortisol to <50 nM (1.8 μg/dL) after dexamethasone administration was chosen as the cut-off point for normal suppression.

Measurements  Thyroid function tests, lipid profiles, homocysteine, antithyroglobulin, anti-thyroid peroxidase antibody levels, vitamin B12, folate levels, insulin resistance [by homeostasis model assessment (HOMA)] and 1.0 mg postdexamethasone (postdex) suppression cortisol levels were measured.

Results  We found an 8% false-positive rate in 1 mg overnight test and 2% in 2 mg overnight test (p=0.001). There was no correlation between the cortisol levels after ODST and other parameters.

Conclusions  Our results indicate that the 2 mg overnight dexamethasone suppression test (ODST) is more convenient and accurate than 1-mg ODST as a screening test for excluding CS in subjects with simple obesity.

Key words: Cushing’s syndrome (CS), obesity, insulin resistance, 1 mg / 2 mg overnight dexamethasone suppression test

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Introduction

Obesity is the most common manifestation, and weight gain is usually the initial symptom in Cushing’s syndrome (CS). Commonly-quoted clinical features such as obesity, while frequently present, are of low specificity for diagnosis. Physicians may be called upon to exclude CS in obese pa-
tients, who are increasingly present in the general population. The diagnosis of CS remains a challenge in clinical practice (1). CS is often diagnosed at an early stage in the natural history of the disease when there may be much more subtle clinical features. Basal morning cortisol and ACTH levels are usually normal in obesity (2). Urinary free cortisol is also reported to be normal in obese individuals (3). Biochemical confirmation of CS has relied upon low-dose dexamethasone suppression testing (4). Low-dose dexamethasone suppression testing, especially the 1-mg overnight test, has been the mainstay of biochemical screening and is recommended in most standard texts (1). Obese individuals seem to show adequate suppression after the overnight dexamethasone (1 mg) suppression test; although studies have shown that there is a small percent of no suppressors (5). The methodology of cortisol assays has changed over time, with newer assays having higher specificity (1, 6). To exclude CS, the concentration of cortisol in serum should be less than 50 nM after either test (7, 8). While obesity is a common finding, CS resulting from either a pituitary or adrenal lesion is a relatively rare entity (9).

In a study by Ness-Abramof et al (5), an overnight dexamethasone suppression test was performed in 86 obese individuals. Seventy-nine of them had adequate suppression, five had subclinical Cushing’s syndrome, and two had false positive responses. Although there have been previous reports focusing on the performance of overnight dexamethasone suppression test in obesity, some of them are quite old and in other reports all of the subjects or a proportion of them also have diabetes mellitus. Diabetes has been reported to be a confounding factor regarding the performance of the overnight test and is also associated with a higher prevalence of undiagnosed CS. Leibowitz et al found a high prevalence of hypercortisolism in poorly controlled obese patients with diabetes mellitus (10).

In fact there is some concern that by using higher doses of dexamethasone occasional patients with CS could be missed. The best means to uncover autonomous cortisol secretion is the 1 mg overnight DXM suppression test, which rarely fails to detect CS. To reduce false positive results, a higher dose (>1 mg) may be preferred (11). In general, most endocrinologists have used an overnight 1 mg test. The classical 2-day test may be more accurate than the overnight test but it is also more difficult to perform in everyday practice (12).

It was also reported that triglyceride and cholesterol levels are higher in patients with higher post-dexamethasone cortisol levels than in patients with fully suppressed cortisol levels (13). It is also reported that subjects with non-alcoholic hepatic steatosis had a significantly higher post-dexamethasone cortisol concentrations than those without HS (14).

We therefore decided to re-examine the validity of the overnight 1-mg ODST and compare the results of this test with overnight 2-mg ODST in obese subjects without concomitant diseases. We also decided to evaluate the correlation between the cortisol levels after ODST and other parameters.

**Research Methods and Procedures**

**Patients**

Data was collected from 100 consecutive patients with a body mass index (BMI) >30 kg/m² who were referred to our hospital-affiliated endocrine clinic (Gulhane University Endocrinology Department, Turkey) because of simple obesity between January 2007 and January 2008. Patients were excluded from the study if they smoked or had a family history of Cushingoid Syndrome or clear Cushingoid features.

The study sample consisted of 22 men and 78 women, ranging in age from 17 to 73 years (mean 39.2±12.2 years). The BMI, and index of adiposity, was calculated by dividing the body weight in kilograms by the square of the height in meters. Their BMIs ranged from 30 to 52 kg/m² with a mean±SD of 36.3±6 kg/m². The mean BMI of the 22 men was 35.0±6.0 and for the 78 women was 35.3±6.1. All patients were seen by the same physicians (MS, LK and AT) and underwent careful clinical examination to exclude the presence of specific signs of hypercortisolism, such as weakness associated with proximal muscle wasting, skin atrophy, ecchymoses, moon face, buffalo hump, or purple striae. Three physicians examined the patients separately who were blinded to the clinical findings of the previous examiner. None of the remaining patients was receiving any drug known to affect the HPA axis. Furthermore, there were no patients with either alcohol abuse or current or previous history of major mood disorders that required psychiatric intervention. The patients suffered from obesity alone; none had type 2 diabetes; hypertension; or polycystic ovary disease. Body height was measured without shoes to the nearest 0.5 cm and body weight without clothes. The waist and hip circumferences were also measured, with the subjects standing, using a 1-cm-wide metal measuring tape, and their waist to hip ratio (WHR) was calculated accordingly. In agreement with the World Health Organization’s recommendation (15), waist circumference was measured as the minimum value between the iliac crest and the lateral costal margin, whereas hip circumference was determined as the maximum value over the buttocks.

For exclusion of diabetes diagnosis all patients underwent 75 gr oral glucose tolerance tests. All patients were informed about the aim and procedure of the study and gave their written consent. The study was approved by the ethics committee of the Gulhane School of Medicine.

**Biochemical analysis**

Blood samples were obtained from all subjects to test the levels of fasting glucose, fasting plasma total homocysteine, vitamin B12, folic acid levels, insulin, DHEAS, hsCRP, thyrotropin, free T3, free T4 anti-thyroglobulin, anti-thyroid
peroxidase antibody, uric acid, urea, creatinin, white blood cell count, hemoglobin, hematocrite, thrombocyte, transaminases, total cholesterol, triglyceride, and high-density lipoprotein cholesterol. These levels were determined using commercially available methods. LDL cholesterol was calculated using Friedewald’s formula (16). Total homocysteine levels were determined using high pressure liquid chromatography; normal range was 5-12 mmol/L with a 0.4-5% intraassay coefficient of variation (CV). Antithyroglobulin, anti-thyroid peroxidase antibody levels, vitamin B12 and folate levels were assayed in serum by using a commercially available kit and Immulite 2000 auto analyzer (BIO-DPC, CA, USA); average ranges were 193-982 pmol/L and 3-17 pmol/L, with a 3.2-5.5% and 4.4-7% intraassay CV, respectively. DHEAS was measured by RIA using DHEAS Immulite 2000 auto analyzer kit and Immulite 2000 auto analyzer (BIO-DPC, CA, USA); average ranges were 193-982 pmol/L and 3-17 pmol/L, with a 3.2-5.5% and 4.4-7% intraassay CV, respectively. DHEAS was measured by RIA using DHEAS Immulite 2000 auto analyzer kit and Immulite 2000 auto analyzer (BIO-DPC, CA, USA); average ranges were 193-982 pmol/L and 3-17 pmol/L, with a 3.2-5.5% and 4.4-7% intraassay CV, respectively. DHEAS was measured by RIA using DHEAS Immulite 2000 auto analyzer kit and Immulite 2000 auto analyzer (BIO-DPC, CA, USA); average ranges were 193-982 pmol/L and 3-17 pmol/L, with a 3.2-5.5% and 4.4-7% intraassay CV, respectively.

Assessment-Insulin resistance (HOMA-IR) was computed by the following formula (17): HOMA-IR = FPG (mg/dL) x Immunoreactive insulin (IRI) (μIU/mL)/405. Dexamethasone late levelswereassayedinserumbyusingacommercially availablekitandImmulite2000autoanalyzer(BIO-DPC,CA,USA);averagerangeswere193-982pmol/Land3-17 nmol/L, with a 3.2-5.5% and 4.4-7% intraassay CV, respectively. DHEAS was measured by RIA using DHEAS Immulite 2000 auto analyzer kit and Immulite 2000 auto analyzer (BIO-DPC, CA, USA); average ranges were 193-982 pmol/L and 3-17 pmol/L, with a 3.2-5.5% and 4.4-7% intraassay CV, respectively. DHEAS was measured by RIA using DHEAS Immulite 2000 auto analyzer kit and Immulite 2000 auto analyzer (BIO-DPC, CA, USA); average ranges were 193-982 pmol/L and 3-17 pmol/L, with a 3.2-5.5% and 4.4-7% intraassay CV, respectively.

The overnight 1-mg or 2-mg dexamethasone suppression test was performed on an outpatient basis. None of the patients were receiving anticonvulsive therapy, rifampin, or estrogen. Patients were randomized to take 1 mg (N=50) or 2 mg (N=50) dexamethasone at 11:00 PM. Between 8:00 AM and 9:00 AM the following morning, blood was drawn from an antecubital vein, and serum cortisol level measured. Suppression of serum cortisol to <50 nM (1.8 μg/dL) after dexamethasone administration was chosen as the cut-off point for normal suppression.

Patients whose serum cortisol after ODST was >50 nM patients underwent a low-dose dexamethasone suppression test (LDDST) as follows: 24-hour urine cortisol was collected for basal urinary free cortisol (UFC); at 8:00 AM, basal serum cortisol was measured; the following day patients started taking 0.5 mg dexamethasone every 6 hours for 2 days; during the last 24 hours urine was collected and UFC was measured at 8:00 AM; 6 hours after the last dose of dexamethasone, cortisol was measured. Suppression of UFC to <27 nmol/24 hour and morning serum cortisol to <50 nM (1.8 μg/dL) was defined as normal suppression. Those who failed to suppress on a LDDST and/or patients whose UFC excretion exceeded cut-off underwent more comprehensive studies to evaluate and localize the source of the hypercortisolism. For positive results after overnight 1-mg dexamethasone suppression test we also performed the overnight 2-mg dexamethasone suppression test. When CS was confirmed by an overnight 2-mg dexamethasone suppression test, its cause was categorized initially by determination of plasma ACTH values. If ACTH levels were not suppressed, ACTH-dependent causes would be investigated. If ACTH levels were suppressed, an adrenocortical computed tomography (CT) or thyroid imaging scan would identify the adrenal lesion responsible for CS. Patients with positive results (cortisol levels were suppressed with high-dose (8-mg) dexamethasone) underwent a pituitary magnetic resonance imaging (MRI). These patients were proven conclusively to have CD based on the following criteria including resolution of hypercortisolism after surgery and requirement for glucocorticoid replacement therapy, confirmation of pituitary adenoma by MRI and/or immuno-histologic confirmation of the presence of ACTH in pituitary tissue.

Results

There was no significant difference in clinical parameters and age between patients in the 1 mg ODST group and 2 mg ODST group (Table 1). In 92 of the 100 obese patients, morning cortisol levels were suppressed to <50 nM (1.8 μg/dL) after the overnight 1-mg or 2 mg dexamethasone suppression test. Five of fifty patients were found to have plasma cortisol levels greater than 1.8 μg/dL following the 1 mg ODST. Three of fifty patients had plasma cortisol levels greater than 1.8 μg/dL following the overnight 2-mg dexamethasone suppression test. Of these, one in five patients in the overnight 1-mg dexamethasone suppression test group and two of three in the overnight 2-mg dexamethasone suppression test had 24-hour UFC levels higher than 248 nmol/d and failed to suppress on a LDDST. The patients’ plasma ACTH levels were not suppressed (greater than 20 μg/mL) such that ACTH-dependent causes were investigated. In patients with Cushing’s disease, endogenous ACTH and cortisol production were suppressed with high-dose (8-mg) dexamethasone. These patients were diagnosed as having CD. Three patients underwent pituitary surgery with excision of
Table 1. Main Characteristics of the Evaluated Subjects: Patients for whom the 1 mg Overnight Dexamethasone Suppression Test Was Applied (Group A) and Patients for whom the 2 mg Overnight Dexamethasone Suppression test Was Applied (Group B)

<table>
<thead>
<tr>
<th></th>
<th>Group A (n = 50)</th>
<th>Group B (n = 50)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Females/males</td>
<td>40/10</td>
<td>39/11</td>
<td>NS</td>
</tr>
<tr>
<td>Age (years)</td>
<td>38.3 ± 12</td>
<td>39.7 ± 11</td>
<td>NS</td>
</tr>
<tr>
<td>BMI</td>
<td>35 ± 6</td>
<td>36 ± 6</td>
<td>NS</td>
</tr>
<tr>
<td>W/H</td>
<td>0.91 ± 0.06</td>
<td>0.89± 0.07</td>
<td>NS</td>
</tr>
<tr>
<td>TSH</td>
<td>2.54 ± 2</td>
<td>2.28± 1.9</td>
<td>NS</td>
</tr>
<tr>
<td>Basal cortisol</td>
<td>15.7±3.4</td>
<td>15.2±3.3</td>
<td>NS</td>
</tr>
<tr>
<td>Free T4</td>
<td>1.2± 0.16</td>
<td>1.1± 0.15</td>
<td>NS</td>
</tr>
<tr>
<td>Free T3</td>
<td>2.1± 0.97</td>
<td>2.6± 0.67</td>
<td>NS</td>
</tr>
<tr>
<td>Fasting blood Glucose</td>
<td>96± 10</td>
<td>101±12</td>
<td>NS</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>3.6± 2</td>
<td>3.7± 2</td>
<td>NS</td>
</tr>
<tr>
<td>LDL</td>
<td>125±37</td>
<td>115±34</td>
<td>NS</td>
</tr>
<tr>
<td>HDL</td>
<td>49±11</td>
<td>52±49</td>
<td>NS</td>
</tr>
<tr>
<td>Triglyceride</td>
<td>189±108</td>
<td>179±110</td>
<td>NS</td>
</tr>
<tr>
<td>T.Cholesterol</td>
<td>212±43</td>
<td>200±42</td>
<td>NS</td>
</tr>
<tr>
<td>ALT</td>
<td>32±1.9</td>
<td>21±1.3</td>
<td>NS</td>
</tr>
<tr>
<td>AST</td>
<td>26±10</td>
<td>20±8</td>
<td>NS</td>
</tr>
<tr>
<td>Úric acid</td>
<td>5.9±1.9</td>
<td>5±1.5</td>
<td>NS</td>
</tr>
<tr>
<td>Creatinin</td>
<td>0.96±0.12</td>
<td>0.82±0.12</td>
<td>NS</td>
</tr>
<tr>
<td>White Blood Cell</td>
<td>6.9±1.6</td>
<td>7±1.3</td>
<td>NS</td>
</tr>
<tr>
<td>Hemotacrit</td>
<td>42±4</td>
<td>40±3</td>
<td>NS</td>
</tr>
<tr>
<td>Thrombocyte</td>
<td>277±48</td>
<td>277±59</td>
<td>NS</td>
</tr>
</tbody>
</table>

Data are expressed as median and range.

* BMI: Body Mass Index, W/H : Waist /Hip ratio

a pituitary adenoma. All of them were corticotrophin microadenomas; hypercortisolism was resolved after surgery in all of them and the presence of ACTH in pituitary tissue was confirmed in immunohistochemistry. Four of five patients in the overnight 1-mg dexamethasone suppression test group were considered to have false positive results in view of normal 24-hour UFC, normal pituitary MRI and normal suppression on a LDDST. Four of five patients demonstrated the positive result of 1 mg DST after the negative result of 2 mg DST. In a fifth of patients, morning cortisol levels were suppressed to 60 nM after the overnight 1-mg dexamethasone suppression test. One in three patients in the overnight 2-mg dexamethasone suppression test group were considered to have false positive results in view of normal 24-hour UFC, normal pituitary MRI and normal suppression on a LDDST. In addition, patients with positive results in the overnight 1-mg dexamethasone suppression test group were distinctly administered the overnight 2-mg dexamethasone suppression test. In these patients, overnight 2-mg dexamethasone suppression test results were found to be the same as the LDDST results. Only three patients with a positive LDDST test had increased urinary cortisol levels. The hormonal values of positive results are given in Table 2.

Overall, 90% of obese patients suppressed serum cortisol to <50 nM after the overnight 1-mg dexamethasone suppression test and 94% of obese patients suppressed serum cortisol to <50 nM after the overnight 2-mg dexamethasone suppression test.
Table 2. Hormonal Values of Patients with Positive Tests in Groups A and B. (A: 1 mg ODST test; B: 2 mg ODST)

<table>
<thead>
<tr>
<th>Patients</th>
<th>1mg ODST</th>
<th>2 mg ODST</th>
<th>UFC</th>
<th>LDDST</th>
<th>8 mg high dose DST</th>
<th>Final diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1</td>
<td>2.2 (3.5)</td>
<td>High</td>
<td>2.1</td>
<td>0.9</td>
<td>CD</td>
<td></td>
</tr>
<tr>
<td>A2</td>
<td>5.6 (1.4)</td>
<td>N</td>
<td>1.1</td>
<td>-</td>
<td>N</td>
<td></td>
</tr>
<tr>
<td>A3</td>
<td>3.4 (1.2)</td>
<td>N</td>
<td>1.2</td>
<td>-</td>
<td>N</td>
<td></td>
</tr>
<tr>
<td>A4</td>
<td>3.8 (1)</td>
<td>N</td>
<td>1</td>
<td>-</td>
<td>N</td>
<td></td>
</tr>
<tr>
<td>A5</td>
<td>4.6 (1.2)</td>
<td>N</td>
<td>1</td>
<td>-</td>
<td>N</td>
<td></td>
</tr>
<tr>
<td>B1</td>
<td>1.5</td>
<td>2.1 High</td>
<td>2.2</td>
<td>1</td>
<td>CD</td>
<td></td>
</tr>
<tr>
<td>B2</td>
<td>7.6</td>
<td>5.1 High</td>
<td>1.9</td>
<td>0.9</td>
<td>CD</td>
<td></td>
</tr>
<tr>
<td>B3</td>
<td>3.4</td>
<td>2.2 N</td>
<td>1</td>
<td>-</td>
<td>N</td>
<td></td>
</tr>
</tbody>
</table>

The false positive rate in the overnight 1-mg dexamethasone suppression test, after using a stricter cut-off of serum cortisol after ODST of 50 nM, was high (8%). Using a cut-off cortisol level of 140 nM, as widely used, would have delayed the diagnosis of one patient (100% of our Cushing’s patients).

The false positive rate in overnight 2-mg dexamethasone suppression test, after using a stricter cut-off of serum cortisol after ODST of 50 nM, was high (2%). Using a cut-off cortisol level of 140 nM, as widely used, would have delayed the diagnosis of one patient (50% of our Cushing’s patients). There was a significant difference between false positive results with 1-mg dexamethasone and 2-mg dexamethasone suppression test (p=0.001).

There was no correlation between the cortisol levels after ODST and other parameters (BMI, WHR, HOMA-IR, fasting plasma levels of insulin, hsCRP, vitamin b 12, folic acid, cholesterol, TSH, free T3, T4, DHEAS, fasting glucose, total homocysteine, vitamin B12, folic acid, anti-thyroglobulin, anti-thyroid peroxidase antibody, uric acid, urea, creatinin, white blood cell count, hemoglobin, hematocrit, thrombocyte, SGOT, SGPT, basal cortisol, and ACTH levels). In both the 1 and 2 mg overnight suppression test groups, there were no significant differences between the above parameters in patients with cortisol levels after suppression <1 μg/dL and in patients with cortisol levels after suppression 1 μg/dL -1.8 μg/dL. In addition, there was no statistically significant difference in regard to these parameters between the patients who had no suppression after ODST and those who had suppression after ODST.

The mean age of the three patients diagnosed with CS was 38.6±10.1 years, and that of the 92 patients that suppressed serum cortisol to <50 nM was 38.8±13.5 years. The mean BMI of the patients with CD was 35.7±2.1 kg/m², which was similar to the mean BMI of the other obese patients (35.6±5.1 kg/m²). Patients with false positive results with overnight dexamethasone suppression tests were evaluated clinically and biochemically and CS was excluded after 10-12 months.

Discussion

The choice of optimal laboratory screening procedures for obese patients is not firmly established. Pasquali et al suggest that, at least in women, abdominal fat distribution may partially counteract the progressively greater suppressibility of the HPA axis that would be expected according to increasing BMI (18). It is now clear that neither the overnight nor the 2-day, low-dose dexamethasone suppression tests (LDDST) are of sufficient reliability to be used to rule out Cushing’s syndrome (19, 20). The majority of previous studies and guidelines have used the 1-mg dose (21, 22). According to one previous report, there appears to be no better discrimination with 1.5 mg or 2 mg of dexamethasone than with 1 mg administration (6). In detail, cortisol suppression by 1 mg dexamethasone yielded the highest diagnostic performance with the 5-μg/dL threshold at 97% specificity, whereas the lower 1.8-μg/dL cutoff resulted in less optimal 80% specificity (22). Ideally, the minimum number of investigations should be employed that allow accurate diagnosis and further management, and if at all possible these should be noninvasive (8). Some patients with Cushing’s disease retain sensitivity to dexamethasone and show suppression of serum cortisol to less than 50 nmol/L on either test (1, 19). Thus, if clinical suspicion remains high, repeated tests and other investigations are indicated (23).

Ness-Abramo et al have used the 1-mg dose in obese patients with a cut-off cortisol level of 80 nmol/L (5). However, Tran and Petrovsky have found that 2 mg ODST offered significant advantages over 1 mg ODST in 27 consecutive patients attending for obesity assessment (24). The great majority of obese patients in the present study (90% of patients in 1 mg ODST group and 94% of patients in 2 mg ODST group) suppressed cortisol levels to <50 nM. We found a very high false positive rate (8%) for the overnight 1-mg dexamethasone suppression test and low false positive rate (2.2%) for the overnight 2 mg dexamethasone suppression test in our obese population, using a strict cut-off of 50 nM. False positive rate in 2 mg ODST was close to the 1% false positive rate in a normal non-obese population (25). Using a cut-off cortisol level of 140 nM, as widely used, would have delayed the diagnosis of one patient (100% of our Cushing’s patients) in the 1 mg ODST group and one patient (50% of our Cushing’s patients) in the 2 mg ODST group.

Our results suggest that even in the obese population, the stricter cut-off cortisol level of 50 nM is adequate for application in the 2 mg overnight ODST. Any patient with results
exceeding this level should be carefully investigated and not assumed to have a false positive result.

As the study was performed in a tertiary referral center, it is possible that the high prevalence of CS in our cohort was due to a referral bias and does not reflect the true prevalence of the disease in obese patients. It should be noted that that none of our patients diagnosed with CS had the classical clinical signs of the disease. A small proportion (3% in this study) of obese patients with no characteristic clinical features of Cushing’s syndrome is likely to eventually suffer from hypercortisolism. Appropriate testing should therefore be performed in simple obese patients.

To reduce the risk of a false-positive test, Arnaldi et al (20) and Mantero et al (26) base their definition of subclinical Cushing’s syndrome on at least two abnormal tests of HPA function in patients without classic clinical stigmata of hypercortisolism (such as high-borderline urinary free cortisol excretion, only partial cortisol suppression with dexamethasone). In our study baseline corticotrophin levels were not suppressed and high-dose (8 mg) overnight DST resulted in a greater than 50% suppression of plasma cortisol levels. Previous reports (20-22) exhibited that plasma ACTH values greater than 20 pg/mL certainly imply an ACTH-dependent cause. According to these findings we did not perform an abdominal CT/MRI scan.

We also did not perform overnight 2 mg dexamethasone suppression test in patients whose 1 mg overnight test was positive but whose urinary cortisol levels were normal. Four of five patients demonstrated the positive result of 1 mg DST after the negative result of 2 mg DST.

As a total of 22 male and 78 female obese subjects were included in this study, one may speculate that this observation may be affected by the greater number of females. However, previous reports by Hunt et al (27) and Grossman et al (28) showed that gender did not have an affect on the percent of cortisol suppression.

In addition, the possible false negative rate of using the 2 mg dose is not known and has not been investigated in this study. Although very rare, false negative results of overnight dexamethasone suppression test have been reported, especially using higher cut-offs (29). However, no evidence of CS was detected after 12 months in obese patients with no suppression.

In our patient population the false positive rate in the overnight 1-mg ODST was higher than and the overnight 2-mg ODST and in simple obese subjects. Overnight 2-mg ODST seems to be more convenient, and accurate as a screening test for excluding CS in subjects with obesity. However, none of these tests is 100% sensitive and specific and further study with 2 mg ODST is required in obese patients. The 2-mg ONDST may prove to be a preferred first-line test for the detection of CS in obese subjects.

References