THE NON ERGOT D2-DOPAMINE AGONIST CV 205-502 DECREASES GROWTH HORMONE CONCENTRATIONS IN ACROMEGALIC PATIENTS

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ABSTRACT

It was the aim of this study to test for a possible effect of the new non ergot dopamine agonist CV 205-502 on plasma growth hormone (GH) concentrations in acromegaly. 10 acromegalic patients received a single oral dose of 150 µg CV 205-502 after an overnight fast. As a control group 7 acromegalic patients undertook the same procedure without receiving any drug. Blood samples were drawn hourly up to 7 hours thereafter for determination of GH.

Plasma growth hormone concentrations decreased by 48.8 ± 8.7 %. The nadir was observed 3 hours after CV 205-502 was administered and GH concentrations remained suppressed throughout the 7 hours of the test period. In contrast GH plasma concentrations in the control group remained stable.

We conclude that acute administration of CV 205-502 suppresses GH secretion in acromegalic patients and thus could serve as an alternative therapy in acromegaly.

INTRODUCTION

CV 205-502 is a potent D2 dopamine receptor agonist (1). It has been introduced recently as a very effective and well tolerated therapy alternative in patients with prolactinomas (2,3). In healthy persons dopamine receptor agonists increase GH secretion (4). In a recent report such a stimulatory effect of CV 205-502 on plasma growth hormone concentrations in healthy persons has been described (5). In contrast, dopamine receptor agonists suppress GH plasma levels in acromegalic
Table I

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<tbody>
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<td></td>
<td>sex</td>
<td>age</td>
<td>duration of disease</td>
<td>number of operations</td>
<td>therapy</td>
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<td>1</td>
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<td>73.9</td>
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<td>8 years</td>
<td>4</td>
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<td>193</td>
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<tr>
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<td>m</td>
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<td>1 year</td>
<td>0</td>
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</tr>
<tr>
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<td>4.6</td>
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<td>2 years</td>
<td>2</td>
<td>5mg bromo.</td>
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bromo=bromocriptine

Ten acromegalic patients with basal plasma growth hormone concentrations ranging from 4.6 µg/L to 193.6 µg/L entered the study after informed consent was obtained. Characteristics of the patients are shown in table 1.

All acromegalic patients had solely GH-producing adenomas with the serum concentrations of PRL being within the normal range.

Eight of them have been treated previously with dopamine agonists or a somatostatin analogue and had stopped this medication either 2 weeks or one day before the test. The patients remained in a supine position and fasted throughout the whole test period. After collecting blood for determination of basal plasma growth hormone concentration, every patient received an oral dose of 150 µg CV 205-502 (Sandoz, Basel, Switzerland) at 8 a.m.

Thereafter blood was drawn every full hour until 3 p.m. In addition 7 acromegalic patients, as a control group, undertook
GH decrease in percent of basal values: after administration of 150 µg CV 205-502 indicated by squares, the asterisk indicates p<0.002 as compared with basal values; acromegalic control persons receiving no drug indicated by triangles.

the same procedure as described above without taking any drug. Samples were centrifuged immediately and the separated plasma was deep frozen until measuring the growth hormone concentration by an immunoradiometric assay (Hybritech, Belgium).

Data are expressed as means of the percent decrease of the initial basal values ± standard error of the mean (S.E.M.). Analyses of variance (ANOVA) was used for statistical evaluation.

RESULTS

CV 205-502 in an oral dose of 150µg decreased plasma growth hormone concentrations in all acromegalic patients. From two hours after administration of CV 205-502 until the end of the observation period, the difference between basal GH
levels and levels measured at the various time points was found to be statistically significant (p < 0.002). The nadir of plasma growth hormone concentration, 51.2 ± 8.6% of basal values, occurred 3 hours after oral administration of 150 μg CV 205-502. No significant changes of plasma growth hormone concentrations occurred in the 7 acromegalic patients who did not receive the drug (figure 1).

DISCUSSION

Surgery is the treatment of choice for acromegaly. Nevertheless growth hormone concentrations remain elevated in a considerable number of patients after surgery (7). Some of these patients may be treated successfully with somatostatin analogues or dopamine agonists. Limiting for the therapy with ergot alkaloids like bromocriptine are the sometimes severe side effects like hypotension and emesis. However, recent studies demonstrate that CV 205-502 has less severe side effects than bromocriptine in patients with prolactinomas.

This study demonstrates for the first time that CV 205-502 is able to decrease effectively plasma growth hormone concentrations in acromegalic patients. This effect and its duration suggest that CV 205-502 could serve as an alternative therapy in acromegaly. It remains to be demonstrated whether prolonged treatment with CV 205-502 will lead to a progressive decrease in GH levels.

REFERENCES


7) Klibanski A, Zervas MT. 1991 Diagnosis and management of hormone secreting pituitary adenomas. 