EFFECTS OF PROLACTIN SUPPRESSION ON HYPOGONADISM IN PATIENTS ON MAINTENANCE HAEMODIALYSIS

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Summary

The effects of prolactin (Prl) suppression by bromocriptine (BC) on impaired sexual function were studied in 47 male patients on maintenance haemodialysis (HD). All patients had normal serum zinc levels. Before treatment, 14 of 47 patients had moderate hyperprolactinaemia (not due to medication), 24/39 patients had elevated LH levels, 13/34 patients had elevated FSH levels, 26/44 patients had decreased serum testosterone levels and 18/24 patients were oligo-/azooospermic.

Bromocriptine was given in doses of 1.25 to 2.5 and 5.0mg/day and each of these doses was maintained for two weeks. Seventeen patients discontinued treatment within the first few days of BC treatment, because of postural hypotension and/or nausea. Fourteen other patients had to be excluded because of poor compliance. On treatment, as little as 1.25mg of BC/day normalised serum Prl, and 2.5mg of BC/day decreased Prl below the lower limit of normal. Neither gonadotrophins nor serum testosterone levels changed significantly during the six weeks of BC treatment.

In conclusion: 1. neither normalisation of moderate hyperprolactinaemia in patients on HD, nor 2. suppression of serum Prl into the subnormal range affects serum gonadotrophin and testosterone levels. 3. These results do not support the hypothesis that moderate hyperprolactinaemia in our patients on HD is an important factor in the development of hypogonadism.

Introduction

Leydig cell and germ cell functions are impaired in most patients on maintenance haemodialysis (HD). One of the possible causes is elevated Prl. Prl can influence the functions of the Leydig cells in a dual way: 1. modulation of gonadotrophin secretion; 2. alteration of LH-receptors and testosterone biosynthesis. In vitro experiments [1] favour a stimulating influence of Prl on the Leydig cells in the
physiological range, whereas the negative influence of severe hyperprolactinaemia is well known.

Therefore we have tested the possible role of mild hyperprolactinaemia as a factor in the development of hypogonadism, by BC suppression of Prol in normo- and hyperprolactinaemic patients on HD.

Patients and methods

Forty-seven adult male patients (23–64 years) who had been on HD for 2–5 years agreed to participate in the protocol shown in Table I.

TABLE I. Protocol of bromocriptine treatment

<table>
<thead>
<tr>
<th>Time weeks</th>
<th>pre-treatment</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>bromocriptine treatment p.o./day</td>
<td>1.25mg</td>
<td>1.25mg</td>
<td>2.5mg</td>
<td>2.5mg</td>
<td>2 x</td>
<td>2 x</td>
<td></td>
</tr>
<tr>
<td>controls</td>
<td>2.5mg</td>
<td>2.5mg</td>
<td>2.5mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>serum</td>
<td>controls</td>
<td>2.5mg</td>
<td>2.5mg</td>
<td>2.5mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prolactin</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td></td>
</tr>
<tr>
<td>LH</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td></td>
</tr>
<tr>
<td>FSH</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td></td>
</tr>
<tr>
<td>Testosterone</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td></td>
</tr>
<tr>
<td>sperm count</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Sperm counts were performed in 24 patients before treatment. All blood samples were taken immediately before HD. The sera were kept frozen (-20°C) until analysis. Commercial RIA kits (IRE, Serono) were used for the analyses of LH, FSH, Prl, and serum testosterone. Reference standards were equivalent to 1.0mg: LH: 66 ± 6.0mg LER 907, FSH: 188 ± 188 ± 15mg LER 907, Prl: 40 IU MRC 71/222. Serum Zn was determined by atomic absorption spectrometry (normal values: 55–150µg Zn/dl serum).

Statistical analysis Wilcoxon's test (paired differences).

Results

Seventeen patients discontinued treatment within a week because of postural hypotension and/or nausea. Fourteen other patients had to be excluded because of poor compliance. Sixteen patients continued the treatment according to pro-
Figure 1. Pretreatment status of hypogonadism in patients on maintenance haemodialysis. 
I= normal range
Figure 2. Effects of Prolactin suppression by bromocriptine in hyperprolactinaemic and normoprolactinaemic patients on maintenance haemodialysis. x---x = normoprolactinaemic patients; x——x = hyperprolactinaemic patients

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tocol (Table I) for 6 weeks; 8 of these patients had moderately elevated Prl levels.

The pretreatment values of Prl (n = 47), LH (n = 39), FSH (n = 34), testosterone (n = 44), sperm counts (n = 24), and Zn (n = 45) are shown in Figure 1; 33/47 patients had normal Prl levels, 14/47 patients had moderate hyperprolactinaemia not explained by drug treatment; 24/39 patients had elevated LH serum values, 13/34 patients had elevated FSH levels, 26/44 patients had decreased serum testosterone levels; 6/24 patients had normal sperm counts, 16/24 had oligospermia, 2/24 patients were azoospermic. All patients had normal serum Zn levels. The pretreatment values of Prl, LH, FSH, and testosterone (means ± SEM) of the patients (n = 16) who continued the treatment are given in Figure 2. The hyperprolactinaemic patients had elevated LH and FSH levels, whereas the levels of testosterone were below the lower limit of normal. The normoprolactinaemic patients (broken lines) showed a similar pattern of LH, FSH, and testosterone.

On treatment (Figure 2), as little as 1.25mg of BC orally, per day normalised serum Prl values (p < 0.01) in all patients (n = 8) with mild hyperprolactinaemia, whereas 2.5mg of BC/day — as well as 2 x 2.5mg of BC — suppressed Prl into the subnormal range. Neither normalisation nor suppression of Prl into the subnormal range induced significant changes of LH, FSH or testosterone. Normoprolactinaemic patients (n = 8) showed a similar pattern, but Prl was suppressed into the subnormal range even by 1.25mg of BC/day. On treatment, all patients suffered more from the side-effects of BC than they gained in libido or sexual activity.

Discussion

The status of primary hypogonadism could be confirmed in most of our patients on HD, whereas there was no evidence of serum Zn deficiency [2] as a causal factor for the development of hypogonadism in these patients. The frequency (20–30%) and the finding of only mild hyperprolactinaemia was in accordance with the results of other authors [3]. The hyperprolactinaemia of patients on HD is said to be due to the prolonged plasma half-time of Prl, chronic stress, and drugs [4]. Evidence of an osmoregulatory action of Prl [5] in humans on HD is lacking. The concept of a pathogenetic role of this mild hyperprolactinaemia in the development of hypogonadism in patients on HD could not be confirmed by our results. Bommer [6] got similar results on 2 x 2.5mg of BC/day. These authors observed increases of libido and sexual activity which they explained by a central dopaminergic effect of BC.

References

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