NOTE

Plasma Concentration of Prolactin during Four-day Osmotic Pump Infusion of Thyrotropin-Releasing Hormone and Vasoactive Intestinal Polypeptide in Rats

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Abstract

Pituitary prolactin (PRL) responses to 4-day continuous infusion of thyrotropin-releasing hormone (TRH) and vasoactive intestinal polypeptide (VIP) were investigated in unanesthetized male rats using Alzet osmotic minipumps. The TRH dose infused was 3.6 μg/day and the VIP dose was 32.8 μg/day. Infusion of TRH with osmotic pumps elevated the plasma PRL level compared to controls over the 4-day infusion period. However, mean levels of PRL tended to decrease during the 4-day infusion. On the other hand, continuous VIP infusion elicited a significant continuous PRL release over the 4-day infusion period. Thus, it may be said that the PRL responses to infused TRH and VIP were maintained during the 4-day infusion.

Both thyrotropin-releasing hormone (TRH) and vasoactive intestinal polypeptide (VIP) are regarded as putative prolactin-releasing factors (PRFs) in rodents because both are found in hypophysial portal blood (Ching et al., 1976; Shimatsu et al., 1981) and can act directly at the pituitary level to evoke the release of prolactin (PRL) (Ruberg et al., 1978; Shaar et al., 1979; Matsushita et al., 1983). The purpose of the present study was to define PRL responses to long-term infusion of TRH and VIP in vivo.

Materials and Methods

Male Wistar rats, weighing 200–250 g were used. They were housed under controlled conditions with constant temperature (22°C) and humidity (50–60%) on a 12:12 h light-dark cycle (lights on at 0600 h) and permitted free access to food and water. Chronic indwelling right atrial cannulae were implanted under pentobarbitone anesthesia as previously described (Brown et al., 1972), and the animals were allowed to recover for 4 days. On the 5th day after catheterization, Alzet osmotic minipumps were implanted beneath the skin of the back under ether anesthesia. Before implantation, the osmotic pumps were filled with a solution of 0.15 mg TRH/ml or 1.37 mg VIP/ml dissolved in 0.01 N acetic acid that would produce a calculated infusion into the rats of 3.6 μg/day and 32.8 μg/day respectively, assuming a pump delivery rate of 1 μl/h. Minipumps filled with 0.01 N acetic acid solution were implanted into the control group. On the next day (Day 1), blood samples were taken from rats housed individually in isolation boxes. Blood samples (0.3–0.35 ml) were taken every 15 min and immediately centrifuged, plasma was frozen until assayed, and red blood cells suspended in normal saline were returned to the animals at the time of the next sampling. Each rat (four control, four TRH
treatment and four VIP treatment) was sampled for 3 h beginning at 1300 h. On Day 4, blood samples for hormone profiles were also obtained.

**Peptides and radioimmunoassay**
Porcine VIP and TRH were purchased from Peptide Institute, Inc. (Osaka). The plasma PRL concentration was measured with a PRL radioimmunoassay kit supplied by NIADDK, and was expressed in ng/ml in terms of the rat PRL-RP-3.

**Analysis of data**
The mean PRL concentration in 12 samples was calculated, and compared with the mean value for the control group using Student's t-test.

**Results**
Occasional episodes of PRL secretion were observed in control animals (Fig. 1). The continuous TRH infusion resulted in a significant elevation of the mean plasma PRL concentration compared to the controls on Day 1 and 4, but mean levels of PRL tended to decrease during the 4-day infusion.
Table 1. Mean plasma PRL levels in male rats

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of Animals</th>
<th>PRL (ng/ml)\textsuperscript{a} Day 1</th>
<th>PRL (ng/ml)\textsuperscript{a} Day 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>4</td>
<td>3.6 ± 0.32</td>
<td>3.5 ± 0.47</td>
</tr>
<tr>
<td>TRH</td>
<td>4</td>
<td>7.8 ± 0.27\textsuperscript{b}</td>
<td>5.3 ± 0.35\textsuperscript{d,e}</td>
</tr>
<tr>
<td>VIP</td>
<td>4</td>
<td>6.4 ± 0.37\textsuperscript{c,f}</td>
<td>6.0 ± 0.87\textsuperscript{d}</td>
</tr>
</tbody>
</table>

\textsuperscript{a} Values represent mean ± SE hormone levels
\textsuperscript{b} P < 0.001 compared to control group
\textsuperscript{c} P < 0.005 compared to control group
\textsuperscript{d} P < 0.05 compared to control group
\textsuperscript{e} P < 0.005 vs Day 1
\textsuperscript{f} Not significantly different from TRH group

(Fig. 1 and Table 1). There was no significant loss in potency of TRH within the minipump during experiments, because plasma TSH was elevated throughout the infusion period (data not shown). VIP infusion, the concentration of which was approximately the same molar basis as TRH, also increased the mean plasma PRL concentration on Day 1. However, the magnitude of the increase in the plasma PRL concentration caused by VIP infusion was smaller than that caused by TRH. On the 4th day, the mean plasma PRL levels in the animals infused VIP were still significantly higher than those in the control group.

**Discussion**

The PRL pattern during TRH infusion observed in the present study was similar to that observed in normal humans. The studies on humans have demonstrated that serum levels of PRL during TRH infusion increase sharply to the maximum level by 40 min, and then, despite continued TRH stimulation, decline gradually to a plateau value after 100 min (Mongioi et al., 1983). Furthermore, Mongioi et al. (1983) suggested that continuous perfusion of the lactotrophs with TRH was associated with desensitization of PRL responsiveness to the releasing hormone, not a result of depletion of pituitary PRL stores.

The response of PRL to VIP infusion was also evaluated in this study. The plasma PRL was elevated in the rats receiving exogenous VIP. PRL response to infused VIP was constant over the 4-day infusion period. This type of hypophyseal response to a hypothalamic releasing factor has previously been reported for TRH and TSH in ewes and normal humans (Klindt et al., 1979; Mongier et al., 1983). The response of PRL to VIP infusion in vivo has not been reported previously and may require further detailed studies.

**References**


Shaar, C. J., J. A. Clemens and N. B. Dininger