Passive Immunisation with Anti-IGF-1 Antibodies Increases Feed Intake during Nutritional Restriction

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Dry-season weight loss is a problematic aspect of cattle growth in the dry tropics. Insulin-like growth factor-I (IGF-I) is a potent stimulator of muscle growth, mediating many of the actions of growth hormone at the cellular level, and is essential for normal growth and development (Jones and Clemmons, 1995). Serum concentrations of IGF-I are typically lowered in catabolic states. Accordingly, anabolic responses to IGF-1 and/or its analogues have been reported during nutritional restriction in several species, including ruminants (Oddy and Owens, 1996; Hill et al., 1999).

However, the cost of administering IGF-1 or its analogues to large animals is prohibitive. Therefore, the possibility of modulating the IGF axis, via antibodies raised against IGF-1, to enhance growth has been investigated. Previously, enhanced growth has been observed in passively immunised dwarf rats and mice (Stewart et al., 1993) and actively immunised cattle (Hill et al., 1998a and b). In the present experiment, the potential of antibodies raised against IGF-1 in cattle to attenuate wasting during nutritional restriction has been investigated by passive immunisation of rats.

After a seven day acclimitisation period, fifteen female JC Lewis rats (4 weeks old, and mean BW 96.90g) were stratified by weight and randomly allocated to three treatment groups. Animals were offered a standard rat chow during acclimitisation, then transferred to an isocaloric, protein deficient (4% protein, ICN Biomedicals, Seven Hills, Australia) diet. For the duration of the experiment, rats were housed individually and allowed ad libitum access to food and water. BW and feed intake (FI) were recorded daily (0900). Rats (n = 5 per treatment) were injected twice daily (0930 and 1630, 1.5ml/day, ip) for 12 d with either saline, non-immune IgG (5mg/ml), or anti-IGF-1 IgG (5mg/ml) and sacrificed between 0900 and 1300 on day 13. BW, change in BW, FI and feed conversion efficiency (FCE) were analysed by analysis of variance. Treatment means were compared using a protected least significant difference test at the 5% level.

Passive immunisation of nutritionally restricted rats with bovine anti-IGF-1 antibodies caused a marked increase in feed intake. Anti-IGF-1 IgG treated animals consumed 39% more feed than saline controls, and 19% more than non-immune treated controls (Table 1). A trend towards increased feed intake was also observed in the non-immune IgG-treated animals (P<0.08). Increased feed intake was reflected by a small, non-significant reduction in BW loss in anti-IGF-1 IgG-treated rats.

Table 1. ΔBW and total FI of protein-restricted rats.

<table>
<thead>
<tr>
<th></th>
<th>Saline</th>
<th>NI IgG</th>
<th>IGF-1 IgG</th>
<th>l.s.d.*</th>
</tr>
</thead>
<tbody>
<tr>
<td>ΔBW (g)</td>
<td>-3.95</td>
<td>-3.65</td>
<td>-1.27</td>
<td>7.71</td>
</tr>
<tr>
<td>FI (g)</td>
<td>119.6</td>
<td>139.8</td>
<td>166.4</td>
<td>22.63</td>
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(*l.s.d. given at P = 0.05)

The large effect of passive immunisation with anti-IGF-1 IgG on feed intake can partially be attributed to the provision of extra protein. This is suggested by the intermediate feed intake of the non-immune IgG treated group, although this accounts for only 17% of the difference (P<0.08). The observed increase in feed intake was not accompanied by a significant retention of body mass during nutritional restriction. To fully elucidate the mechanism in operation, further experiments using rats housed in metabolism cages, with additional replicates, and conducted over a longer period are necessary. This will clarify whether there is a real anti-catabolic effect or possibly a reduction in efficiency of nutrient absorption, and/or an increased metabolic rate in anti-IGF-1 IgG treated rats.


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