A prolonged change in body composition induced by endocrine manipulation of the neonate

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ABSTRACT

The ability of endocrine manipulation of the neonate to effect prolonged changes in body composition was examined. Treatment of lambs with recombinant bovine somatotropin (rbST) at doses of 0.1 or 0.3 mg/kg liveweight/day for 11 weeks from birth elevated circulating ST concentrations ($P<0.01$) but had no effect on circulating concentrations of insulin-like growth factor-1 or on liveweight gain compared with excipient-treated lambs. However, at 8 months of age (5 months after cessation of treatment), ultrasound backfat depths (Mean±SE) were significantly ($P<0.05$) higher in lambs previously treated with excipient (3.4±0.3 mm) than in those treated with rbST at 0.1 mg/kg (2.8±0.3 mm) or 0.3 mg/kg (2.5±0.3mm). In a second study, rats were treated with saline vs. 0.2 µg/g rbST vs. 0.4 µg/g rbST vs. 0.2 µg/g pituitary ovine prolactin (poPRL) vs. 0.4 µg/g poPRL for the first 21 days of life. At 120 days of age they were euthanased, selected fat depots weighed and the carcasses analysed for fat content. Neonatal treatment with rbST or poPRL significantly ($P<0.05$) reduced weight of the subcutaneous scapular fat depot (1.08±0.18 vs. 0.46±0.17 vs. 0.52±0.18 vs. 0.50±0.17 vs. 0.49±0.17 g) and carcass fat content (5.88±0.27 vs. 5.03±0.26 vs. 4.58±0.27 vs. 5.28±0.26 vs. 4.70±0.26%) but did not influence weights of the subcutaneous abdominal, genital or perirenal fat depots. These results suggest that endocrine manipulation of the neonate may offer a means of producing desirable changes in the composition of production animals while avoiding consumer resistance to the use of hormonal growth promotants close to the time of slaughter.

Keywords: Neonate; somatotropin; prolactin; body composition; fat deposition.

INTRODUCTION

It is now well established that the administration of somatotropin (ST) to growing animals decreases carcass fat content, increases carcass lean and, in some cases, increases rate of growth (Boyd and Bauman, 1989). These observations have led to interest in ST as a possible growth-promoting agent. It is also known that galactopoietic responses to ST are abolished shortly after cessation of ST therapy (Bauman and McCutcheon, 1986). The corresponding situation has not been widely studied in the context of body growth and composition, most growing animals experimentally treated with ST being slaughtered at the cessation of treatment. However, two studies (Brumby, 1959; Sandles and Peel, 1987) have provided evidence that growth responses to ST are not maintained for long periods after the end of treatment, possibly due to a suppression of endogenous ST secretion in previously treated animals. Thus if ST were to be used as a growth promotant, treatment would likely be required until the time of slaughter, posing potential problems in terms of consumer acceptability.

Hypophysectomy of fetal lambs increases fat accumulation, an effect which is reversed by ST therapy (Stevens and Alexander, 1986). This suggests the possibility that ST may alter adipocyte proliferation or metabolism in the perinatal period. We report here the results of two studies providing evidence that, in animals with an intact somatotrophic axis, endocrine manipulation in early postnatal life can effect prolonged changes in body composition.

MATERIALS AND METHODS

Experiment 1

This study represented an extension of an experiment reported previously (Sun *et al.*, 1992). Briefly, crossbred lambs (n=11-13 per group) were treated for 11 weeks from the day of birth with either recombinantly derived bovine somatotropin (Somidobove®, Lilly Research Laboratories, Greenfield, Indiana, USA) delivered in a slow release formulation at a daily dose equivalent to 0.1 or 0.3 mg/kg liveweight, or with excipient. Approximately half the lambs in each group were blood sampled by jugular venipuncture for 12 consecutive days in weeks 4 to 5 of treatment. Blood samples were analysed for concentrations of immunoreactive ST (Sun *et al.*, 1992) and (pooled samples) for insulin-like growth factor-1 (using the procedure of Breier *et al.*, 1991). Backfat depths of the lambs were determined by ultrasound (Purchas and Beach, 1981) at 8 and 13 months of age (ie 5 and 10 months after the cessation of ST treatment).

Experiment 2

Female Sprague-Dawley rats were mated to males of the same strain and offered an *ad libitum* complete pelleted diet throughout pregnancy and lactation. At birth, the newborn pups were individually identified and divided at random into 5 groups balanced for litter of origin and sex. Pups in each group (n=10 or 11) were treated from the day of birth by twice daily subcutaneous injection of saline, recombinant bovine somatotropin (rbST, Lot No. AC 6750-48, American Cyana-

mid Company, Princeton, NJ., USA) or pituitary-derived ovine prolactin (poPRL, NIDDK-oPRL-19, NIDDK-NIH, Bethesda, MD, USA). The rbST and poPRL were administered at two daily doses, 0.2 or 0.4 μg/g bodyweight. Treatment continued until day 21 of life when the pups were weaned from their dams. Thereafter the young were separated by sex and offered an *ad libitum* complete pelleted diet. At 120 days of age they were euthanased, the head, feet, tail, skin and visceral contents removed and four fat depots - subcutaneous abdominal, subcutaneous scapular, genital and perirenal - excised from the carcass and weighed. The remaining carcass was then frozen, sliced, ground, mixed thoroughly and a subsample taken for the determination of fat content (in triplicate) by Soxhlet extraction for 8 h (AOAC, 1980) using petroleum ether (B.P. 40 to 60°C).

Statistical Analysis

In Experiment 1, effects of treatment on measured parameters were determined by analysis of variance/covariance (with liveweight at the time of measurement used as a covariate in analysis of backfat depths). In Experiment 2, fat depot weights and carcass fat content were subjected to analysis of covariance after adjustment for any other main effects (litter, sex) or covariate (liveweight at slaughter) found to be significant in preliminary analyses. Comparisons of hormone treatments with controls were made by t-test.

RESULTS

As is shown in Table 1, treatment of lambs with rbST significantly elevated concentrations of immunoreactive ST in plasma, as reported previously (Sun *et al.*, 1992), but did not significantly influence circulating concentrations of IGF-1. At 8 months of age, 5 months after the cessation of rbST treatment, lambs previously treated with rbST had ultrasound backfat depths significantly ($P<0.05$) lower than those previously treated with excipient. At 13 months of age, backfat depths of lambs previously treated with rbST were still 9-14% lower than those in control lambs, but the difference was no longer significant.

Treatment of rats with rbST or poPRL during the first 21 days of life had differential effects on the weights of fat depots (Table 2). Thus while weights of the subcutaneous abdominal, genital and perirenal depots were similar in saline-, rbST-, and poPRL-treated rats, weights of the subcutaneous scapular depot in rats previously treated with rbST or poPRL were approximately half those in rats previously treated with saline ($P<0.05$). Carcass fat content was also significantly ($P<0.05$) lower in rats previously treated with rbST than in those previously treated with saline (Table 2). Rats treated with the 0.2 μg/g/day dose of poPRL did not differ significantly in carcass fat content from those treated with saline, but rats treated with the higher dose of poPRL had lower carcass fat contents than controls ($P<0.05$). Thus, the effect of both rbST and poPRL on carcass fat content exhibited a dose-responsive relationship, and poPRL was less effective than rbST in inducing prolonged reductions in the fat content of the carcass. Liveweight of the rats was not influenced by treatment.

TABLE 1: Effects of rbST treatment (Mean±SE) during the first 11 weeks of life on plasma concentration of ST and IGF-1 at weeks 4-5 of treatment and on ultrasound backfat depth (adjusted to a common liveweight) and liveweight at 8 and 13 months of age.

	rbST treatment (mg/kg/day)		
	Excipient	0.1	0.3
Weeks 4-5 of treatment			
n	7	5	6
Plasma ST (ng/ml)	19.2 ± 2.1^a	65.2 ± 2.8^b	74.7 ± 4.8^b
Plasma IGF-1 (ng/ml)	295.2 ± 46.7	363.2 ± 45.7	379.6 ± 41.1
Ultrasound backfat depth (mm)			
n	12	13	11
8 months of age	3.4 ± 0.3^a	2.8 ± 0.3^b	2.5 ± 0.3^b
13 months of age	3.6 ± 0.3	3.4 ± 0.3	3.1 ± 0.4
Liveweight (kg)			
8 months of age	39.9 ± 1.5	37.7 ± 0.8	41.7 ± 1.4
13 months of age	45.6 ± 1.9	44.3 ± 1.4	46.8 ± 1.9

[a,b] Means with different superscripts are significantly different ($P<0.05$).

DISCUSSION

To our knowledge, these are the only studies reported in which prolonged effects on body composition of elevating circulating concentrations of somatotropin or prolactin during the neonatal period have been examined. In Experiment 1, a three- to four-fold elevation of circulating ST concentrations during treatment did not increase the growth rate of

TABLE 2: Effect of rbST or poPRL treatment (Mean ± SE) during the first 21 days of life on weight of fat depots and on carcass fat content at 120 days of age in rats.

		rbST (μg/g/d)		poPRL (μg/g/d)	
	Saline	0.2	0.4	0.2	0.4
n	10	11	10	11	11
Fat depot weight (g)					
Subcutaneous abdominal	3.58 ± 0.38	3.04 ± 0.35	3.72 ± 0.37	3.13 ± 0.37	3.54 ± 0.37
Subcutaneous scapular	1.08 ± 0.18^a	0.46 ± 0.17^b	0.52 ± 0.18^b	0.50 ± 0.17^b	0.49 ± 0.17^b
Genital	5.01 ± 0.29	5.04 ± 0.26	4.59 ± 0.28	5.38 ± 0.28	5.09 ± 0.28
Perirenal	4.25 ± 0.53	4.79 ± 0.48	4.33 ± 0.52	5.33 ± 0.51	5.02 ± 0.52
Carcass fat content (5%)	5.88 ± 0.27^a	5.03 ± 0.26^b	4.58 ± 0.27^b	5.28 ± 0.26^{ab}	4.70 ± 0.26^b

[a,b] Means with different superscripts are significantly different ($P<0.05$). Least squares means adjusted for other significant effects as follows: subcutaneous abdominal - body weight, litter, sex; subcutaneous scapular - nil (no other effects significant); genital - body weight, litter; perirenal - litter, sex; carcass fat content - nil.

lambs during the treatment period (Sun *et al.*, 1992), nor did it significantly alter circulating concentrations of IGF-1. In a similar study, treatment of newborn bull calves with bST was reported to increase daily gain and reduce carcass fat content without altering circulating concentrations of IGF-1 (Groenewegen *et al.*, 1990). However, the calves in that study were slaughtered at the conclusion of treatment. In the present study, by contrast, backfat depth was measured in the live animals 5 and 10 months after the conclusion of the rbST treatment. The significantly lower ultrasound backfat depth observed at 8 months of age in lambs previously treated with rbST suggests that this treatment had a prolonged effect on the number and/or size of adipocytes in the backfat depot, although the difference was no longer significant at 13 months of age.

The effect of endocrine manipulation of the neonate on body composition 100 days after cessation of hormone therapy was examined more directly in Experiment 2. The results of this study confirm that elevation of circulating bST levels in the neonate effects a prolonged reduction in carcass fat content. The effect on fat accumulation is, however, specific to particular sites, being very marked at the subcutaneous scapular site but absent at the other three sites examined. Furthermore, ovine prolactin had a similar effect to rbST, in terms of both subcutaneous scapular depot weight and carcass fat content, although it was less potent than rbST.

The results of these experiments are consistent with previous reports that hypophysectomy of fetal lambs leads to a substantial increase in subcutaneous fat and a modest increase in internal fat, effects which are eliminated by ST therapy (Stevens and Alexander, 1986). Likewise, treatment of neonatal rats with antibodies to rat ST was shown to decrease the number of adipocytes in the intraperitoneal fat depots, but have the opposite effect in subcutaneous fat depots. Again, all these effects could be prevented by concurrent ST therapy (Flint, 1992). However, neither of those studies examined the effects of ST or PRL therapy in animals with an intact somatotrophic axis.

The mechanism by which rbST and poPRL achieve these effects on composition is not known. Hypophysectomy of fetal pigs leads to increased adipocyte size which implies an involvement of pituitary hormones in the regulation of fat accretion early in life (Hausman *et al.*, 1987). Both somatotropin and prolactin are known to promote lipolysis and suppress lipogenesis in adipose tissue (Bauman and Elliot, 1983) but such effects in the neonate are unlikely to account for the differences in backfat depth (sheep) or subcutaneous scapular depot weight and carcass fat content (rats) observed 150 and 100 days after the cessation of treatment respectively in the present study. For example, although backfat depth was not measured in the lambs at the time treatment ended, lambs of that weight (ca. 20 kg) would be expected to have backfat depths of less than 2 mm (A.Y. Abdullah, pers. comm.). Thus it is most unlikely that the differences observed in backfat depth at 8 months of age reflect differences established during bST treatment (0 to 11 weeks of age) and then maintained for a further 5 months. Rather, we hypothesise that neonatal treatment with rbST (or poPRL) exerts a long-term inhibition of adipocyte formation or the capacity of adipocytes to accumulate fat, rather than just altering composition via classical lipolytic/antilipogenic effects at the time of treatment. While this hypothesis is to some extent consistent with the results of Flint (1992), it does not appear to be consistent with *in vitro* studies showing that ST promotes differentiation of preadipose cell lines (Morikawa *et al.*, 1982) while PRL is without effect.

CONCLUSIONS

This study has demonstrated that treatment of neonates with bST or oPRL can induce favourable changes in body composition which are apparent long after the cessation of treatment and presumably reflect an inhibition of adipocyte number and/or size, particularly in the subcutaneous depots. While the mechanism is as yet unknown, such treatment may provide a means of manipulating body composition in production animals without the need to use hormonal treatments close to the time of slaughter.

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