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Effects of oestradiol on skeletal growth in lambs

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ABSTRACT

Castrate male and female lambs (n = 8) received no treatment (O dose) or a silicone rubber implant containing 3 mg (L dose), 22 mg (M dose) or 52 mg (H dose) of oestradiol, respectively. Implants were placed subcutaneously at 8-10 weeks of age (mean weight 20.4 kg) and the animals slaughtered 180 d later. Oestradiol treatment decreased length of cannon bone but increased length of vertebral column and 12th rib. Cessation of growth in an early maturing bone (cannon bone) appeared to be accelerated by the treatment so that length was reduced. Later maturing bones (rib and vertebrae) showed a dose-dependent stimulation of linear growth. It is concluded that oestrogens accelerate the natural process of skeletal maturation.

Keywords Oestradiol; sex steroids; skeletal growth.

INTRODUCTION

Although exogenous oestrogens are used as growth promotants for farm animals (Galbraith and Topps, 1981), they inhibit linear growth of bones in laboratory animals (Silberberg and Silberberg, 1972). In sheep, oestrogens increased length of carcass and of cannon bones specifically (Wilkinson, *et al.*, 1955) and stimulated growth at the distal end of the femur (Shroder and Hansard, 1958). However, in rats long term oestrogen treatment resulted in animals with shorter body and tail length, shorter and narrower head, smaller thoracic circumference and shorter limb bones than controls (Zondek, 1936). Effects of oestrogens on bone growth in laboratory animals included; inhibition of epiphyseal cartilage cell proliferation, acceleration of maturation of chondrocytes and consequently premature appearance of centres of ossification and hastening of epiphyseal plate closure (Silberberg and Silberberg, 1972). There is no clear understanding of the role of sex steroids in the control of skeletal growth of ruminants, yet it is probable that these hormones are responsible for the growth spurt at puberty in man and for sex-related differences in mature body size in many mammalian species (Short, 1980). The contradictory effects which have been reported in farm and laboratory animals, or in ruminants versus non-ruminants, have been attributed to differences in dose and form of hormone used (Spencer, 1985). However bones of meat animals mature in a differential manner (Hammond, 1932; Pálsson, 1955; Davies, 1979) and the extent to which epipyseal activity may be altered by oestrogens at any time may vary for different bones. This study examined the effects of exogenous oestrogens on skeletal growth of sheep in relation to bones at different stages of maturity.

MATERIALS AND METHODS

Seventy eight Dorset Down x Coopworth (39 males and 39 females) lambs aged 8 to 10 weeks (mean live weight = 20.4 kg) were allocated randomly to 5 treatment groups. One group of lambs (7 males and 7 females) was slaughtered at the beginning of the trial to provide information on initial skeletal measurements of animals. The rest of the animals (32 of each sex) were castrated and 1 group (n = 16) was non-implanted (O dose) whereas the other 3 groups were implanted subcutaneously with 3 sizes of silicone rubber implants containing oestradiol-17β; large implants (H dose) (surface area,-SA 1574 mm^2) medium implants (M dose) (SA 603 mm^2) and small implants (L dose) (SA 75 mm^2) which contained approximately 52, 22 and 3 mg oestradiol respectively. Low dose animals were reimplanted on day 41 to overcome the possibility of exhaustion of hormone from the original implant. During the experimental period (180 d) lambs were grazed on pasture consisting predominantly of perennial rye-grass (*Lolium perenne*) and white clover (*Trifolium repens*). Blood samples were collected at days 1, 41, 42 (L dose group only), 134 and 175 and plasma stored frozen at -20° C until assayed for oestradiol levels. Teat length was measured at days 1, 56 and 175 and length of the fore cannon bone every 3 weeks using vernier calipers with a dial guage. At the end of the trial lambs were slaughtered and the warm carcass weighed, chilled for 2 d, then sawn longitudinally into halves and stored at -20°C. After thawing, the length of the vertebral column was measured, then the 12th rib was exposed and its length measured from the junction with the 12th vertebra at the tubercle along the dorsal surface to the sternal ends.

Experimental data were pooled for both sexes and analysed utilising orthogonal polynomial contrasts (Alvey *et al.*, 1982) for differences between control and treated animals and for linear and quadratic responses to dose level. Means were adjusted by covariance to initial measurements in the case of teat and cannon bone length; to initial body weight in the case of live weight and carcass weight, and to initial radius length in the case of vertebral column and 12th rib.

RESULTS

Oestradiol levels in plasma of implanted wethers were elevated on the day after implantation then decreased to pre-implantation levels (Table 1). Dose of oestradiol, calculated as loss from implants during the trial, was related to size of implants and teat length increased linearly with size of oestradiol implants (Table 2).

Oestradiol-treated animals had higher final live weight, daily gain in weight and warm carcass weight than control lambs, with the values (except carcass weight) increasing directly with dose of the hormone (Table 2). Treated lambs had shorter cannon bones by the end of the experiment and longer vertebral column and ribs than controls (Table 2). These effects were significantly related to dose (determined by size of implant) in the case of vertebral column and ribs but not for cannon bones. In control lambs initial lengths of cannon bone, vertebral column and 12th rib were 134, 692 and 151 mm, respectively (latter 2 values from an initial slaughter group). At slaughter these bones had increased to 147, 812 and 179 mm, respectively with gains of 13, 120 and 28 mm respectively. Oestradiol treatment (H dose) induced a 23% inhibition of elongation in cannon bone and 22% and 43% stimulation of elongation of the vertebral column and 12th rib, respectively.

DISCUSSION

Oestrogen treatment in the present experiment inhibited longitudinal growth of the cannon bones and stimulated that of the vertebral column and ribs at all dose levels. It has been generally accepted that oestrogens cause premature closure of the epiphyseal plates in both man and laboratory animals so that long bones are shorter in treated than in untreated animals (Silberberg and Silberberg, 1972). However, the use of these hormones in farm animals as growth promotants (Galbraith and Topps, 1981) implies that they may have a stimulatory effect on growth of the skeleton. Stimulation on the one hand and inhibition on the other, of bone elongation following administration of oestrogens has been explained by the premise that low doses of oestrogen stimulate longitudinal bone growth while larger doses inhibit it (Suzuki, 1958; Silberberg and Silberberg, 1972; Short, 1980). However, the inhibition of longitudinal growth of cannon bones and stimulation of vertebral column and ribs recorded in the present study occurred at all dose levels of oestradiol. This

TABLE 1 *Mean plasma oestradiol-17 β concentration (pg/ml) ± standard error of wether lambs implanted with silicone rubber implants containing 3 dose levels of oestradiol recorded at different stages of the trial.*

Treatment group		Days of experiment				
	Pre-implantation[1]	1	41[2]	42	134	175
Control	30	-	-	-	-	-
Low dose	-	136±44	25±14	50±20	28± 6	29± 8
Medium dose	43	102±47	28±12	-	28±11	42±12
High dose	30	167±60	43± 7	-	36±23	31±13

[1] Pooled sample
[2] Low dose reimplanted

TABLE 2 Mean and effective standard error (ESE) (n=8) for measured variables of non-implanted lambs (O) and lambs with different sizes of oestradiol (L, M, H) implants. Data pooled for wether and spayed ewe lambs.

Variable	Dose				ESE	Treatment response	Dose response	
	O	L	M	H			Linear	Quadratic
Dose (mg)	0.0	2.7	6.4	12.8	–	1.6	***	NS
Teat length (mm)	9.2	15.2	17.0	17.3	0.7	***	***	NS
Live weight (kg)	39.8	41.5	41.6	43.8	1.0	**	*	NS
Liveweight gain (g/d)	127	138	139	154	6	**	*	NS
Warm carcass wt (kg)	17.0	17.8	17.3	18.3	0.05	†	NS	†
Cannon bone length (mm)	147	143	144	144	0.8	***	NS	NS
Vertebral column length (mm)	812	820	826	838	9.1	*	†	NS
12th rib length (mm)	179	183	187	191	3.4	*	*	NS

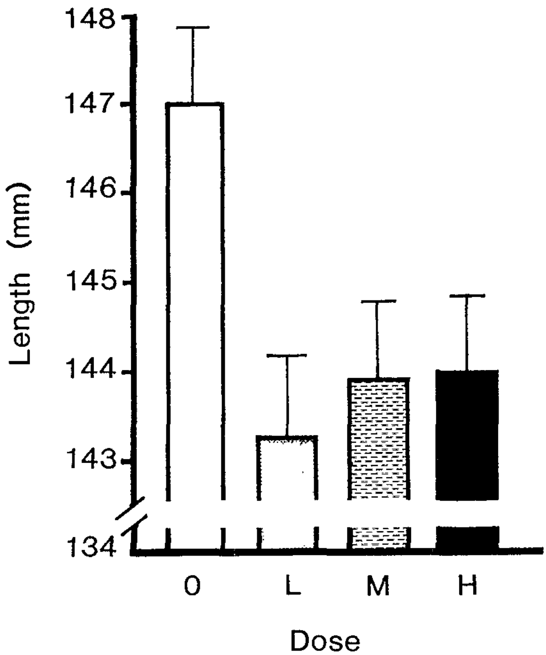

FIG. 1 Cannon bone length in non-implanted lambs (O) and lambs implanted with different sizes of oestradiol (L, M, H) implants. Data pooled for wether and spayed ewe lambs.

indicates that the notion of different effects on bone elongation and shortening arising from different dose levels of oestrogens does not apply in sheep within the range of doses used here.

The influence of exogenous oestrogens on skeletal growth needs to be examined in the light of differential bone growth which gives rise to the normal pattern of maturation of the skeleton. Generally skeletal maturation follows a distoproximal (in the limbs) and craniocaudal (along the axial skeleton) progression (Hammond, 1932; McMeekan, 1943; Wallace, 1948; Pálsson, 1955), although Davies *et al.*, (1984) have suggested that for sheep this craniocaudal pattern is only true prenatally. Postnatally, skeletal maturation in sheep follows an undulating course along the vertebral column. According to these concepts of differential growth, cannon bones are early maturing while ribs are among the last bones of the skeleton to mature. In the present study oestradiol may have accelerated closure of epiphyseal plates of early maturing bones (cannon bones) and consequently further elongation was limited. At the same time it may have stimulated longitudinal growth of the vertebral column and the rib without causing premature closure of the epiphyseal plates of these later maturing bones. In other words, oestrogens accelerate the process that is taking place in the epiphyseal plates whether it be cessation or increased activity, at the time of application of treatment. This process is determined by the stage of maturity of any bone at the time of exposure to oestrogens. It is concluded that the often contradictory effects which have been described for oestrogens on bone growth may be explained by considering the differential pattern by which the skeleton matures.

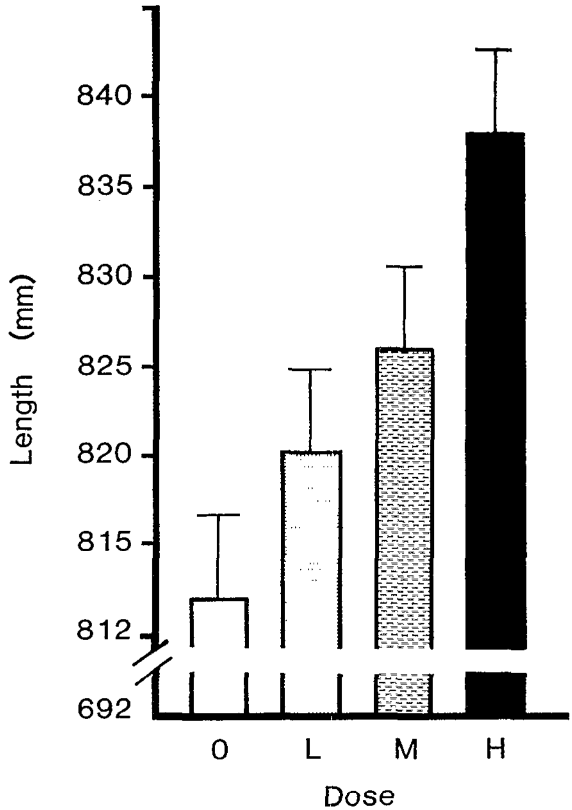

FIG. 2 Vertebral column length in non-implanted lambs (O) and lambs implanted with different sizes of oestradiol (L, M, H) implants. Data pooled for wether and spayed ewe lambs.

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