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Influence of testicular hormones on the somatostatin-GH system during the growth promoted transition to puberty in sheep

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Abstract

The aim of the present study was to investigate whether the growth promoted transition to puberty in lambs involved changes in the effects of testicular hormones on somatostatin in hypothalamic neurons and GH secretion. The study was performed in infants (9-week-old) testis-intact (TEI) and orchidectomized (ORCHX) at the sixth week of age, and pubertal lambs (16-week-old) TEI and ORCHX at the 12th week of age ($n = 20$). In TEI lambs, the changes included a pubertal increase in immunoreactive somatostatin in the periventricular nucleus and median eminence with simultaneous neuropeptide depletion in the median eminence, and a decrease in the percentage of the hypophyseal area (PA) occupied by GH-immunoreactive cells ($P < 0.05$). The mean concentration of GH in the peripheral blood plasma was greater ($P < 0.001$) in early infancy (5 wk), because of the greater ($P < 0.0001$) pulse amplitude, and then uniformly low until puberty. The postnatal increase in the body weight (BW) was prominent ($P < 0.01$) in middle-late infancy (9–12 wk) because of the large daily live-weight gain. After orchidectomy somatostatin was abundant. This effect on nerve terminals in the median eminence was greater ($P < 0.01$) in infancy and lesser ($P < 0.05$) in puberty. Conversely, the PA occupied by GH cells was lower in the ORCHX pubertal lambs compared to TEI lambs ($P < 0.05$). The GH concentration and pulse characteristics were less ($P < 0.05$) in the infantile and pubertal ORCHX lambs compared to the TEI lambs. However, this effect was weak ($P < 0.05$) until middle infancy because of no influence on the GH basal concentration, and strong ($P < 0.001$) after late infancy. The BW did not differ ($P > 0.05$) between TEI and ORCHX lambs. Findings suggest activation of GH negative autofeedback loop in middle infancy. Testicular factors may play an inhibitory role in regulating somatostatin accumulation and a stimulatory role in GH secretion until puberty. The start of puberty is related to an attenuation in the stimulatory role of gonadal factors in regulating somatostatin depletion in nerve terminals associated with an intensification of the stimulatory role of gonadal factors in regulating GH secretion. From a somatic perspective of growth rate, these mechanisms do not seem to be important. Thus, testicular factors modulate mechanisms within the somatostatin-GH system to integrate somatotropic and gonadotropic functions at the time of growth-promoted sexual maturation in sheep.

Keywords: Somatostatin; GH; Orchidectomy; Growth rate; Puberty; Ram lamb

1. Introduction

The sexually dimorphic secretory pattern of GH has been described for adolescent sheep after the onset of puberty [1], suggesting that pubertal sex steroids play an important role in the ovine-GH axis regulation. In fact, the strong association between growth and reproductive maturation in mammals has been demonstrated

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[2–5]. In prepubertal rats, the particular pattern of GH output, pulsatile (male-like) and nearly continuous (female-like) [6], is critical for greater body growth in males and the regulated sex-specific expression of selected genes in GH target cells (for review, see [7]). The anabolic action of estrogens and androgens in male lambs is due, at least in part, to their influence on GH secretion [8]. In this regard, testicular hormones increase GH concentrations in domestic ruminants and pigs [9–12]. However, the gonadal-dependent mechanisms that alter GH secretion during the transition from male infancy to puberty in domestic species are not fully known.

The transition to puberty involves endocrine changes, which lead to the full presentation of physiological readiness to sexual maturation. There is evidence, obtained primarily from rodents and primates, that GH has a permissive role in male sexual maturation (for review, see [3–5]). In rats, GH deprivation markedly affects somatic growth and induces a transient delay in sexual maturation because of a delay in testes growth and differentiation of germinal cells [13]. In lambs, the precise neuroendocrine interactions of somatotropic and gonadotropic factors throughout the transition to puberty remain unknown. In male ruminants, estrogens enhance GH release in early-middle infancy [14], whereas in middle-late infancy low doses of estradiol partly inhibit release of GH without affecting basal concentrations [11]. In this regard, the GH response to GHRH, the stimulus of GH secretory peaks, declines with age in cattle and sheep [15,16]. Circulating GH inhibits its own secretion via feedback (repression) on GHRH and feed-forward (stimulation) on somatostatin in adults. It is possible that this neuroendocrine mechanism in developing domestic ruminants involves the suppressive effect of somatostatin on the GH response to GHRH [17–19]. This effect increases at birth [20]. Growth hormone secretion in the neonate is more sensitive to the inhibitory influence of somatostatin compared to that in the fetus [21,22] and after weaning GH response to GHRH is greatly inhibited during somatostatin challenge [19]. Thus, there is a postnatal decrease in the amplitude of GH pulses and consequently mean concentration, which reflects the ontogenic decline from the high prenatal and neonatal concentrations to the low concentrations characteristic of adult ruminant [10,23,24]. It is hypothesized, therefore, that the transition to puberty in lambs involves changes in the effects of testicular hormones on GH negative autofeedback on somatostatin.

Thus, the aim of this study was to investigate changes in the influence of testicular factors on the development of the somatostatin-GH system with respect to the rate of somatic growth during the transition to puberty. To resolve this issue, histomorphological and functional criteria were used in orchidectomized (ORCHX) and testis-intact (TEI) infantile and pubertal lambs.

2. Materials and methods

2.1. Animals and management

All procedures were conducted in accordance with the EC Directive 86/609/EEC for animal experiments, which were approved by the Local Ethics Committee affiliated to Warsaw Agriculture University (number of opinion 29/2006), according to the Polish Law for the Care and Use of Animals 1997(2, Aug).

The 3- to 4-year-old Polish Longwool ewes (features of the breed in [25]) were mated naturally at a commercial sheep facility (Samoklęski Farm, Poland). The ewes were transported to the Institute of Animal Physiology and Nutrition (Jabłonna, Poland) in September. Sixteen male lambs from twin pregnancy and four from singleton pregnancy were born in February. The lambs were penned with dams indoors in individual pens under natural lighting and temperature conditions at 52° N latitude and 21° E longitude. The animals were fed a diet that provided 100% of the recommendations proposed by the National Research Institute of Animal Production for pregnancy and lactation in ewes and suckling period in lambs [26]. Ten lambs were weaned on the 65th d of age and were fed hay *ad libitum* and complete pelleted concentrate supplemented with vitamins, minerals and containing 17% of protein twice daily (norms for fattening period in lambs; [26]). This diet assured the optimal rate of growth defined by the changes in the slope of the curve of body weight gain, which was detected from the weighing of one-, 39-, 63-, 88- and 112-day-old lambs (Fig. 1).

2.2. Experimental design

It was recently shown by Wańkowska et al [27] that the transition to puberty in this experimental model is a two-step process. The period after the neonatal stage until the time of weaning encompasses the infantile phase of high LH secretion. The period beyond the time of weaning (after 9 wk of age) encompasses the juvenile phase of decrease in the LH secretion associated with the pubertal increase in testosterone secretion and