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Minireview

Growth hormone production and role in the reproductive system of female chicken

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ABSTRACT

The expression and role of growth hormone (GH) in the reproductive system of mammals is rather well established. In birds the limited information thus far available suggests that GH is an endocrine or paracrine/autocrine regulator of ovarian and oviductal functions too. GH and its receptors are expressed in all compartments of the ovary and oviduct and change accordingly to physiological state. The intra-ovarian role of GH likely includes the regulation of steroidogenesis, cell proliferation and apoptosis, the modulation of LH action and the synthesis of IGFs (insulin-like growth factors). In the oviduct, GH is also involved in the regulation of oviduct-specific protein expression. The present study provides a review of current knowledge on the presence and action of GH in the female reproduction, in which it is likely that act in endocrine, autocrine or paracrine mechanisms.

1. Introduction

Growing evidence demonstrates that growth hormone (GH) is produced not only by pituitary gland but also by numerous extra-pituitary tissues including neural (Arámburo et al., 2014), immunological (Luna et al., 2008, 2013) and reproductive ones (Harvey, 2010; Luna et al., 2014; Sirotkin, 2005) in which it can act through paracrine and/or autocrine pathways. In this brief review, based on available literature and the author's own studies, up-to-date discoveries concerning the expression of GH and its receptors in the female reproductive system, mainly of chickens are presented. The possible participation of GH in the local regulation of the avian ovary and oviduct is also discussed.

2. Physiological evidence of growth hormone-controlled avian reproduction

It is well established that pituitary GH is involved in a wide array of reproductive functions in mammals such as sexual differentiation, pubertal maturation, gonadal steroidogenesis, gametogenesis and ovulation as well as pregnancy and lactation (Codner and Cassorla, 2002; Harvey, 2010; Hull and Harvey, 2000, 2001; Sirotkin, 2005). In contrast much less is known about participation of GH in the regulation of reproductive processes in female birds. Involvement of pituitary GH is, however, strongly suggested by the correlated elevation in blood plasma GH concentration in pullets at the onset of lay (Williams et al., 1986) and around the time of oviposition and ovulation in hens (Harvey et al., 1979). Attenuation of GH secretion in chickens, turkey and bantam hens with the cessation of egg laying is also observed (Bedrak et al., 1981; Scanes et al., 1979; Sharp et al., 1979). Moreover, a role for pituitary GH in the function of the ovary is also supported by an increase in the number of small ovarian follicles after GH administration to laying hens (Williams et al., 1992). Similarly, injections of recombinant chicken GH (cGH) to chickens prior to the onset of egg laying resulted in increased ovarian weight (13.5 ± 6.14 g vs 0.89 ± 0.14 g or 7.70 ± 4.17 g vs 1.10 ± 0.12 g, dependently on experiment) about one week before sexual maturity (Hrabia et al., 2011). Moreover, yellow hierarchical follicles were present in the ovaries of most GH treated hens but not in the control hens (Fig. 1), suggesting the involvement of GH in the selection of small prehierarchical follicles into hierarchy of yellow preovulatory follicles (Hrabia et al., 2011). In other experiments Donoghue et al. (1990) found that GH injections for 3 weeks to older egg laying White Leghorn hens did not affect egg production, but significantly improved eggshell quality.

Within the follicle it is also possible that GH is involved in yolk deposition as in the synthesis of yolk proteins in the liver, which are primarily under control of ovarian estrogens (Stevens, 1996), but the liver is also GH responsive organ (Van As et al., 2001). In author's experiment (unpublished data) cGH administration into

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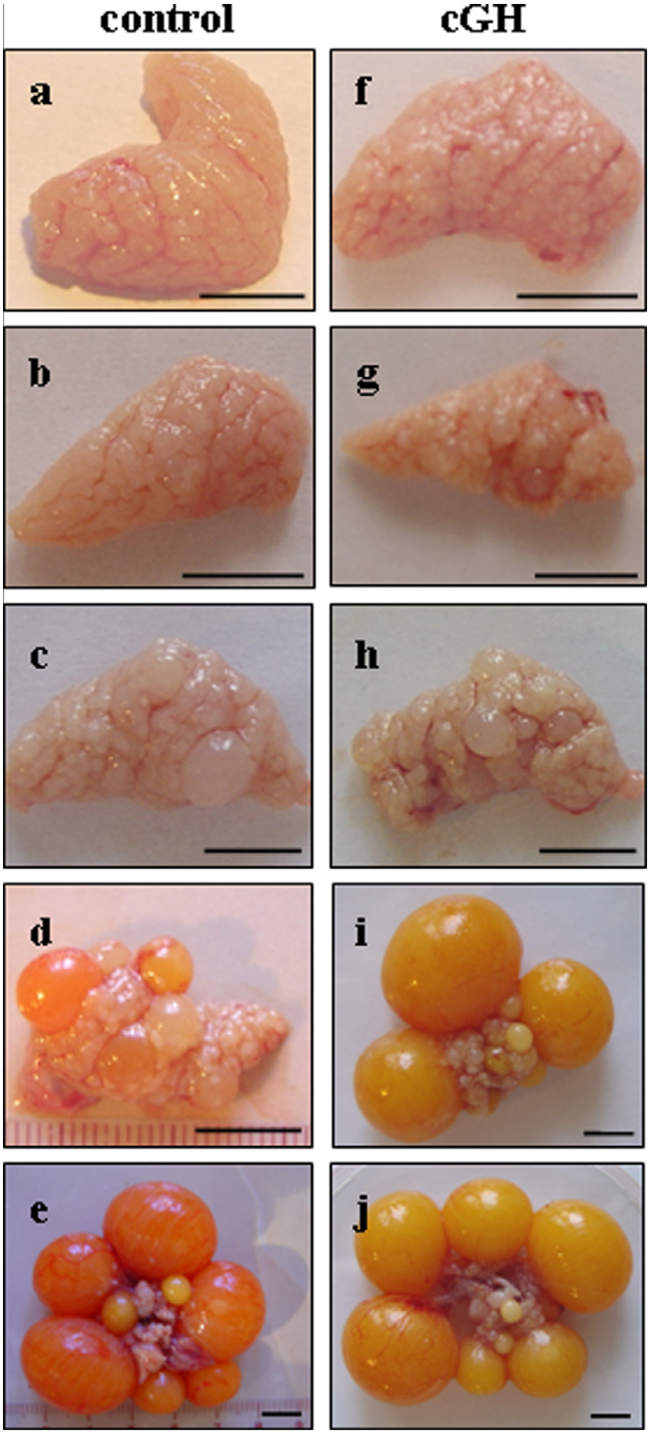

Fig. 1. Effect of cGH administration on morphology of the chicken ovary. cGH (recombinant cGH prepared as described by Paczoska-Eliasiewicz et al. (2006) and purchased from Protein Laboratories Rehovot Ltd (Rehovot, Israel)) was injected three times a week at a dose of 200 µg per kg of body weight from 10 weeks of age. Hens were decapitated at 10 (a and f), 12 (b and g), 14 (c and h) and 16 (d and i) weeks of age and at 17 or 18 weeks (e and j) i.e., just after reaching maturity as evidenced by the first oviposition, and the ovary was weighed, photographed and characterized morphologically. It is of note, that at the age of 16 weeks, in the cGH-treated chickens, large yellow follicles (>8 mm diameter) were present but not in the control group. The mean number of these follicles was 0.8 ± 0.54, 1.0 ± 0.63, 1.8 ± 0.98 and 0.2 ± 0.17, respectively for follicles in diameter 8–12 mm, 12–18 mm, 18–24 mm and 24–30 mm. In other experiment it was 1.7 ± 0.47, 0.8 ± 0.48 and 0.8 ± 0.54, respectively for follicles 8–14 mm, 14–22 mm and 22–30 mm. For more detail see previous publication (Hrabia et al., 2011). Bar = 1 cm.

the chicken during maturation did not change vitellogenin II and apoVLDL mRNAs expression in the liver as examined about one week before and at the time of maturity. Concomitantly, expression of estrogen receptor alpha mRNA was slightly, but not significantly elevated, and expression of estrogen receptor beta was significantly increased just after reaching maturity. Thus it seems possible that GH modulates estrogen-stimulated vitellogenesis in chickens as it was demonstrated in hypophysectomised pigeons (Harvey et al., 1978) and turtles of both sexes (Ho et al., 1982). Moreover, in *in vitro* culture of female eel hepatocytes, the time- and dose-dependent potentiating effect of GH on vitellogenin synthesis induced by estradiol was demonstrated, although, GH alone had no effect on vitellogenin synthesis or secretion (Peyon et al., 1996). On the other hand, in *in vitro* experiment in the frog Rana esculenta, the homologous pituitary homogenate stimulated vitellogenin synthesis in male and female livers, and no cooperation between pituitary homogenate and estradiol was found in the vitellogenin synthesis response (Carnevali and Mosconi, 1992).

3. Expression and localization of growth hormone in the ovary

In addition to pituitary GH, numerous studies have suggested autocrine and/or paracrine actions of GH in reproductive functions, since the mammalian reproductive system has been shown to be an extrapituitary site of GH expression (Abir et al., 2007; Harvey, 2010; Izadyar et al., 1999; Schwarzler et al., 1997). Recent studies have also shown that the chicken ovary expresses the GH gene (Ahumada-Solórzano et al., 2012; Hrabia et al., 2008). Using RT-PCR, a full-length (690 bp) pituitary GH cDNA was, for the first time, detected in chicken ovarian stroma prior to and after the onset of lay, although GH expression was far less than that in the pituitary gland or hypothalamus. GH mRNA was also demonstrated in all classes of ovarian follicles (white, yellowish and yellow) after their ontogenetic appearance in the developing ovary. GH-immunoreactivity was similarly present in the tissues of the ovary and within the follicular wall, and it was more intense in the granulosa than in theca layer, and comparable to that in the epithelium with loose connective tissue. Development of the yellow preovulatory follicles was accompanied by increasing GH immunoreactivity in the granulosa layer, and by a significant reduction of GH staining in the theca layer (Hrabia et al., 2008). Furthermore, GH mRNA identical in nucleotide sequence to that in the pituitary gland and GH protein were detected in the ovarian compartments of laying hen in which stronger expression was in the granulosa cells and lesser in the theca cells (Ahumada-Solórzano et al., 2012). Moreover, by Western blotting, nine moieties of GH proteins were detected in the follicular wall whose relative proportions changed with follicular development. The most abundant variant at all developmental stages of the follicles showed a molecular weight of 17 kDa. It has been proposed that difference in abundance of GH isoforms during development may provide a mechanism to modulate GH activity in the female reproductive system (Ahumada-Solórzano et al., 2012). Additionally, secretion of GH by the granulosa cells of the largest preovulatory ovarian follicles was also revealed (Ahumada-Solórzano et al., 2012). Taken together, these results demonstrate that the ovary of the hen is thus an extrapituitary site of GH gene expression. Folliculogenesis, yolk deposition and ovulation may thus be dependent upon local GH production. The physiological importance of particular isoforms of GH protein in the avian ovary remains unknown.