Regulation of Anti-Mullerian Hormone (AMH) by oocyte specific growth factors in ovine granulosa cells

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BACKGROUND

In addition to gonadotropins, steroidogenesis and proliferation of granulosa cells during follicular development are controlled by a number of intraovarian factors, such as Bone Morphogenetic Proteins (BMPs), Growth Differentiation Factor 9 (GDF9) and Anti-Mullerian Hormone (AMH), all belonging to the transforming growth factors-β (TGF-β) superfamily.

Naturally occurring mutations in sheep for GDF9 and BMPs or their receptors have provided insights into their roles during both the early and terminal stages of follicle development.

On the other hand, Anti-Mullerian hormone (AMH) which is produced by the granulosa cells of growing follicles has been shown to modulate the recruitment of primordial follicles, thereby avoiding the premature exhaustion of the ovarian reserve of follicles. However, the regulation of its production remains poorly understood.

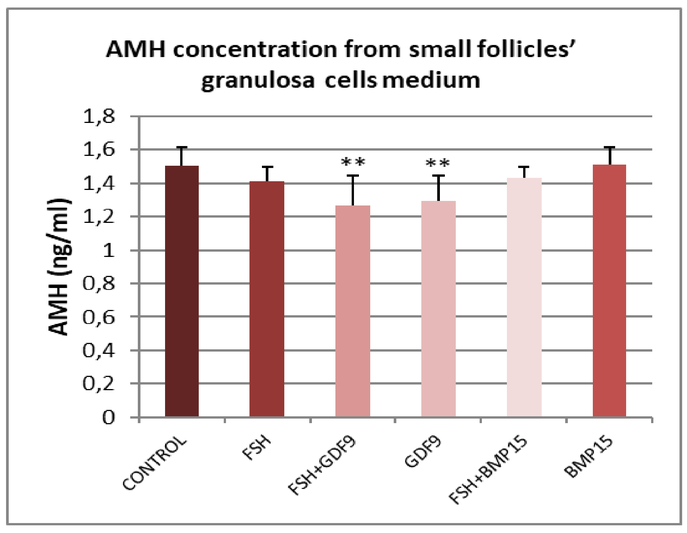
AIM OF THE STUDY

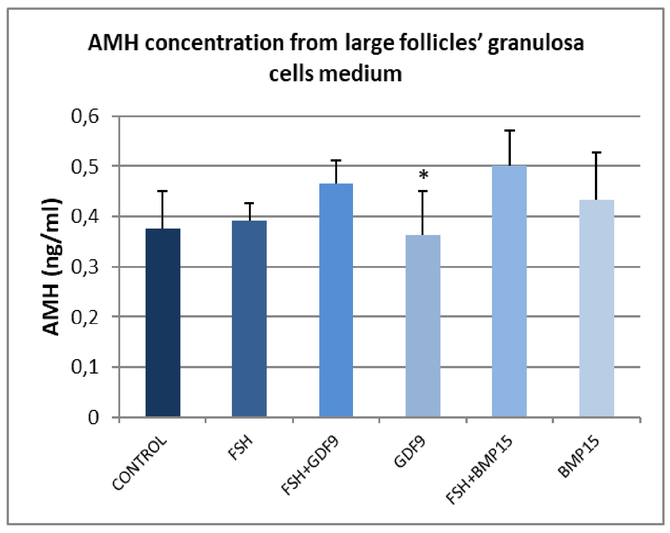
To investigate the role of oocyte-derived factors GDF9 and BMP15 on AMH and estradiol production from ovine granulosa cells, *in vitro*.

MATERIALS & METHODS

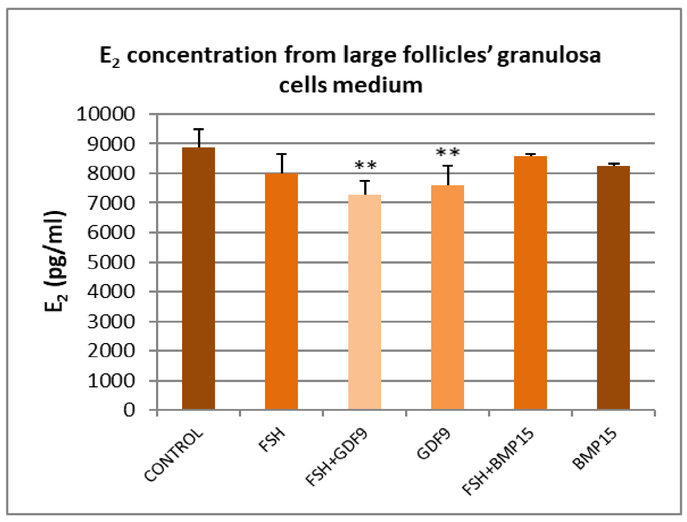
Granulosa cells were harvested from small (1-3 mm diameter) and large (>3 mm diameter) follicles from ovine ovaries and cultured in serum free conditions for 48 hours with or without GDF9 and BMP15 in the presence or absence of FSH. Concentration of 17β-estradiol and AMH in culture medium were determined by RIA and ELISA methods, respectively.

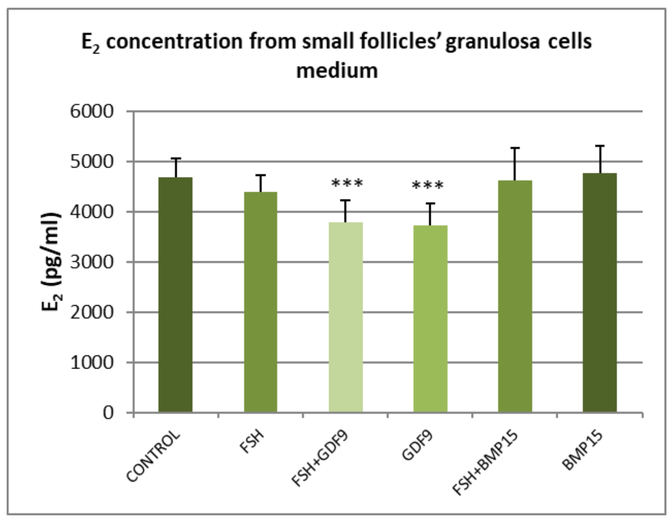
RESULTS





- In small follicles, addition of GDF9, with or without FSH, significantly ($p<0.05$) decreased the production of AMH, compared to control.
- In large follicles, addition of GDF9, significantly ($p<0.05$) decreased the production of AMH, compared to control.





- Estradiol production from granulosa cells from both small and large follicles was significantly ($p<0.05$) decreased by GDF9 alone or in combination with FSH, compared to control.

* Statistical significance difference relative to Control (P<0.05)
** Statistical significance difference relative to Control (P<0.01)
*** Statistical significance difference relative to Control (P<0.001)

CONCLUSIONS

This study shows for the first time that the oocyte-secreted factor GDF9 reduces the production of AMH, thus suggesting an attenuation of its inhibitory action on the progression of small follicles in ewes. The decrease in estradiol production after GDF9 treatment may explain polyovulation in ewes with GDF9 mutations, by earlier maturation and selection of dominant follicles at smaller size.

In conclusion, these findings may contribute to a better understanding of the factors and mechanisms regulating AMH production which may lead to new strategies for managing the ovulation and birth rate.