Review Article

Reproductive Effects of PG600 in Female Pigs

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Abstract

PG600 is a synthetic gonadotropin comprising 400 IU equine chorionic gonadotropin (eCG) and 200 IU human chorionic gonadotropin (hCG). Major responsibilities of PG600 were to stimulate follicle growth and induce ovulation. In replacement gilts, a number of large follicles were found after PG600 treatment. Nevertheless, the number of good quality follicles was not different between treatment and control gilts. In primiparous sows, the number of those returning to estrus within 10 days after weaning from PG600 were higher than those in control group. In addition, the administration of PG600 enhanced the number of piglets born alive per litter in the second parity sows. Considering route of administration, subcutaneous injection contributed to the greater number of gilts expressing estrus than intramuscular injection. In addition to dosage effect, it was found that ovulation rate of the pigs treated with 1.0 dose of PG600 was significantly lower than that of those injected with 1.5 and 2.0 doses of PG600. Moreover, treatment with 1.5 dose of PG600 resulted in more number of large follicles than using 0.5 dose (25.7 vs 19.2 follicles, $p<0.01$). Besides, using 1.5 dose of PG600 contributed to the longest time of estrus (2.7 d, $p<0.05$), comparing with 0, 0.5, and 1.0 doses of PG600. Nonetheless, treatment with 1.5 dose of PG600 led to a high incidence of follicular cyst formation which restricted the ovulation, contributing to low conception rate.

Keywords: estrus, PG600, reproduction, sows

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Introduction

Sexual maturation in the replacement gilts is recognized only when first ovulation and fist estrus take place (Evans and O'Doherty, 2001). Nevertheless, an exact time of ovulation is very difficult to determine since it happens approximately two-thirds of the standing heat period. Age at first observed estrus, consequently, is used to identify puberty attainment in the female pigs since it is apparent to the observers (Tummaruk et al., 2009b). Factors influencing this phenomenon are animal (e.g., age, body weight, backfat thickness) and management (e.g., nutrition, housing, boar contact) factors mediating via endocrine-reproductive axis (Evans and O'Doherty, 2001). In modern swine industry, puberty is one of the crucial indicators to highly focus on since it affects longevity of individuals; those with delayed puberty tended to be removed from the breeding herds prior to those with early puberty (Koketsu et al., 1999; Roongsitthichai et al., 2013). In addition, approximately 50% of replacement gilts in the breeding cycle are removed from the herd from various reasons, such as anestrus, abnormal vaginal discharge, lameness, and so forth (Engblom et al., 2007). Moreover, the most outstanding reasons to remove the replacement gilts, in Thailand, are reproductive disorders: anestrus (44.0%), abnormal vaginal discharge (20.5%), return to estrus (15.5%), not-in-pig (10.0%), and miscellaneous causes (10.0%) (Tummaruk et al., 2009a).

Anestrus is considered one of the significant problems in swine production industry since anestrous pigs cannot deliver production to the farm, contributing to an increase in non-productive day (NPD). This phenomenon is obviously observed in those failing to be in estrus after parturition, entailing prolonged weaning-to-estrus interval (WEI), as well as those with delayed entry-to-service interval (Roongsitthichai et al., 2013). These considerably affect the financial status of the farms as the higher the NPDs, the more the production cost is found (Vargas et al., 2006). Presently, a number of chemicals are used to solve swine anestrus, especially hormones to induce estrus, and solve infertility (Breen and Knox, 2012). An outstanding hormone to resolve those problems is gonadotropin, such as, equine chorionic gonadotropin (eCG) and human chorionic gonadotropin (hCG). These are expected to stimulate follicle development, ovulation, and estrus expression in the female pigs (Knox et al., 2000).

One of the gonadotropins dispersedly used in the modern swine industry is PG600, consisting of 400 IU eCG and 200 IU hCG. This composition mimics endogenous gonadotropins; eCG acts like follicle stimulating hormone (FSH) by stimulating the growth of follicles and the rise of estrogen, meanwhile hCG acts like luteinizing hormone (LH) by inducing the ovulation (Vargas et al., 2006). Nevertheless, the comprehensive information of using PG600 in swine breeding herd has been scant, this review was to demonstrate how PG600 affect follicular and oocyte growth, reproductive performance of the female pigs. In addition, different routes and doses of administration were mentioned.

Effects of PG600 on the growth of follicles and oocytes: PG600 was a synthetic gonadotropin, containing 400 IU eCG and 200 IU hCG; eCG was mainly responsible for activating follicular growth, together with increasing weight and size of follicles to the ovulation, whereas hCG was chiefly in charge of inducing the ovulation (Vargas et al., 2006). According to the real-time ultrasonographic study of intact porcine ovaries, follicles were categorized into three groups on the criterion of diameter: small (1.0-2.9 mm), medium (3.0-6.0 mm), and large (≥6.0 mm) follicles (Van Wettere et al., 2011).

The study on follicular development and oocyte quality using follicle stimulating hormone (FSH), eCG, and PG600 in the replacement gilts revealed that those injected with eCG and PG600 significantly had more large follicles than those in control group (8.3±2.9, 7.5±2.6 vs 2.2±1.1, $p<0.05$). Moreover, those treated with only eCG for 72 h had little number of small follicles, but the number of large follicles increased (Bolamba et al., 1996). In weaned sows, the use of PG600 in high dose contributed to the more number of large follicles as obviously seen between 0.5 and 1.5 doses of PG600 administration (19.2 vs 25.7 follicles, $p<0.05$) (Breen et al., 2006). However, high dose of PG600 (1.5 time of normal dose) treatment could subsequently result in follicular cysts (Breen et al., 2006).

Considering oocyte quality, the good quality oocytes were in the form of cumulus-oocyte complex: those with a great number of cumulus cells. The number of good quality oocytes in those treated with PG600 was not different from those treated with eCG and FSH, including those in control group (Bolamba et al., 1996).

Effects of PG600 on reproductive performance in replacement gilts: The previous study investigating the efficiency of PG600 injection, together with oral progestin (Altrenogest, Matrix, Intervet America, Inc., USA) on reproductive performance in replacement gilts demonstrated that those in treatment group expressed estrus earlier (98.4 vs 110.9 h, $P=0.01$) and ovulated faster (128.6 vs 141.9 h, $P=0.01$) than those in control group. Moreover, those administered with PG600 tended to have higher ovulation rate than those in control group, (14.8 vs 7.5, $P=0.07$) (Horsley et al., 2005). Correspondingly, another study using PG600 injection, along with oral progestin (Regu-mate, Intervet America Inc., Millsboro, DE) demonstrated that those treated with PG600 had higher ovulation rate (26.2±1.8 vs 18.1±1.7, $p<0.01$) than those in control group (Estienne et al., 2001). Nevertheless, estrus duration, estrus onset-to-ovulation interval, conception rate, and survived embryo at 30 days post-mating, of the replacement gilts injected with PG600 were not different from those in control group (Estienne et al., 2001; Horsley et al., 2005).

Effects of PG600 on reproductive performance in weaned sows: Post-weaning anestrus has been one of the foremost causes of reproductive failures in the swine commercial farms. Factors influencing return-to-estrus included parity number, seasons, breeds, lactation length, lactating feed, litter size, and boar

contact. In addition, an increase in WEI contributed to high NPD, which affected financial status of the swine farms (Vargas et al., 2006).

The study of PG600 administration on WEI, estrus duration, ovulation interval, farrowing rate, litter size, and culling rate in the primiparous sows demonstrated that PG600 treatment could increase the higher number of those returning to estrus within 10 days after weaning (94.8% vs 79.7%, $p<0.05$), including longer estrus duration (65.7±13.3 vs 61.0±13.5 h, P $p<0.05$) than those in control group (Vargas et al., 2006). In addition, the use of PG600 effected on estrus expression in weaned sows, especially in the summertime, which was the period with high ambient temperature; the number of those treated with PG600 returned to estrus within seven days after weaning was significantly higher than those in control group (97.1% vs 82.9%, $p<0.05$). Normally, the sows often returned to estrus by more than seven days according to an alteration at the hypothalamic-pituitary axis. In summer, the concentrations of gonadotropin-releasing hormone from the hypothalamus and LH were lower than those in winter (Estienne and Hartsock, 1998). Besides, the release of LH from the sows accommodated within the houses with 30 degree Celsius was lower than those raised in the houses with 22 degree Celsius (Barb et al., 1991). This depressed LH contributed to prolonged anestrus phase of the female pigs.

In primiparous sows, an interval from estrus onset to ovulation of those treated with PG600 was not different from those in control group (46.6 vs 43.3 h, $p>0.05$). As for WEI (Table 1), that of those treated with PG600 was significantly shorter than that of those in control group (5.3±4.1 vs 8.0±7.1 d, $p<0.001$). Nevertheless, WEI, return-to-estrus rate, and farrowing rate, in the sows parity number 2, 3, and 4 were not different between treatment and control group (Vargas et al., 2006). Considering litter size at birth, the sows treated with PG600 delivered the higher number of total piglets born per litter (TB) in the second parity than that in the first parity (11.2 vs 10.4 heads, $p<0.05$). However, PG600 did not affect TB of those in parity number 3 and 4 (Table 2). (Vargas et al., 2006).

Table 1 Weaning-to-estrus interval (WEI) of the sows in parity number 1, 2, 3, and 4 between treatment (PG600) and control groups. (Adjusted from Vargas et al., 2006)

Parity number	Weaning-to-estrus interval (day)		*p* value
	Control group	Treatment group (PG600)	
1	8.0±7.1	5.3±4.1	<0.0001
2	5.7±4.6	5.7±4.3	0.983
3	5.8±4.9	5.7±4.3	0.718
4	5.2±4.1	5.5±4.2	0.445

Table 2 The number of total piglets born per litter in the sows parity number 1, 2, 3, and 4 between treatment (PG600) and control groups. (Adjusted from Vargas et al., 2006)

Parity number	The number of total piglets born per litter (head)		*p* value
	Control group	Treatment group (PG600)	
1	11.7±2.3	11.9±2.3	0.155
2	10.4±3.2	11.2±3.3	0.001
3	11.5±2.9	11.4±3.1	0.663
4	11.2±3.3	11.3±3.0	0.897

Effect of routes of administration on ovulation and estrus expression: The use of PG600 has been proven to induce estrus in the female pigs; as could be lucidly seen in primiparous sows that the percentage of those in estrus within ten days after weaning were higher in PG600-treated pigs than those in control group (94.8% vs 79.9%, $p<0.05$) (Vargas et al., 2006). Moreover, route of administration was investigated to have an effect on their reproductive performance. Basically, the administration of PG600 could be performed via both intramuscular (neck muscle) and subcutaneous (flank) injections. Regarding ovulation in prepubertal gilts, the number of female pigs administered with PG600 via both subcutaneous and intramuscular routes ovulated more than those in control group ($p<0.01$). However, the number of ovulated pigs between intramuscular and subcutaneous injections was not statistically different (77.0% vs 86.0%, $p>0.05$) (Knox et al., 2000).

As for estrus expression, it was found that the higher number of sows showing estrus signs was those treated with subcutaneous PG600 than via intramuscular route (76.0 vs 52.0%, $p<0.01$). Moreover, the pigs expressed estrus signs approximately four to five days after treatment since PG600 was effective only with medium- and large-sized follicles existing at the treatment time. If they presented in adequate number, PG600 would develop them to be mature, produce estrogen, and ovulate eventually. When the pigs possessed enough medium- and large-sized follicles, PG600 would make them produce so adequate amount of estrogen that estrus could be driven (Guthrie et al., 1997). Nevertheless, a long-term administration of PG600 used for estrus induction in prepubertal gilts and superovulation in mature pigs might result in various drawbacks to fertility, such as degenerating embryos, embryo mortality, and high ovulation rate but low litter size (Breen and Knox, 2012).

Moreover, the predomination of routes of administration was not found on the number of corpus lutea, cystic follicles, and pigs developing cystic follicles ($p>0.05$) (Knox et al., 2000).

Effects of different doses on reproductive performance: To induce estrus in replacement gilts and sows with various doses of PG600, no difference was found with injection-to-estrus interval, estrus duration, the number of ovulated gilts, and incidence of follicular cyst formation. Nevertheless, only ovulation rate was noticed; one dose contributed to less ovulation rate than 1.5 and 2.0 doses of PG600 (Breen et al., 2006).

In weaned sows, they were administered with 0, 0.5, 1.0, and 1.5 doses of PG600 on the weaning day. When they were in estrus, size and number of large follicle were investigated via real-time ultrasonography. In addition, conception rate, farrowing rate, and data relevant to the parturition were recorded. WEI of the sows with 0, 0.5, 1.0, and 1.5 doses of PG600 were 4.4, 4.4, 4.3, and 4.1 days, respectively (p>0.05). Nevertheless, estrus duration was the longest in those treated with 1.5 dose of PG600 (2.7 days, p<0.05). Moreover, it was found that the highest number of pigs developing follicular cyst was also those treated with 1.5 dose of PG600 (29.8%, p<0.05). This might be the reason why those injected with 1.5 dose of PG600 showed the longest duration of estrus. Moreover, follicular cyst formation led to several adverse effects to fertility since it inhibited the ovulation and, finally, resulted in low conception rate. However, the conception rate of those treated with 0.5 dose of PG600 was higher than those treated with 0 and 1.5 doses of PG600. Moreover, the use of 1.5 dose of PG600 significantly contributed to higher number of large follicle than that of 0.5 dose (25.7 vs 19.2 follicles, P<0.01). Nonetheless, different doses of PG600 did not influence the number of total piglets born per liter, piglets born alive per litter, stillborn piglets, and mummified piglets even if PG600 could increase the ovulation rate (Breen et al., 2006).

Conclusion

PG600 was one of the beneficial hormones to improve reproductive performance of the female pigs. In replacement gilts, PG600 developed the great number of large follicles; this made the gilts express estrus and ovulate earlier. In weaned sows, PG600 increased the number of sows returning to estrus within ten days after weaning, including prolonged estrus duration. The administration of PG600 via subcutaneous route could induce the more number of pigs expressing estrus than via intramuscular route. Moreover, high dose of PG600 could prolong estrus duration. Nevertheless, follicular cysts were the precautions of this case. As a result, PG600 was one of the decent alternatives to deal with NPD in the swine farm since it could not only reduce anestrus which has been the most universal problem in sow removal, but also improve reproductive performance of the sows in several parity numbers.

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บทคัดย่อ

ผลทางระบบสืบพันธุ์ของ PG600 ในสุกรเพศเมีย

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PG600 เป็นโกนาโดโทรปินสังเคราะห์ที่ประกอบขึ้นจาก equine chorionic gonadotropin (eCG) 400 IU และ human chorionic gonadotropin 200 IU ซึ่งมีหน้าที่หลักในการกระตุ้นการเจริญของฟอลลิเคิลและเหนี่ยวนำให้เกิดการตกไข่ ในสุกรสาวทดแทนพบว่ามีจำนวนของฟอลลิเคิลขนาดใหญ่เพิ่มมากขึ้นหลังจากได้รับการฉีด PG600 อย่างไรก็ตาม จำนวนของโอโอไซต์ที่มีคุณภาพดีไม่มีความแตกต่างกันระหว่างสุกรสาวทดแทนที่ได้รับและไม่ได้รับการฉีด PG600 ในแม่สุกรท้องแรก พบจำนวนของแม่สุกรที่กลับมาเป็นสัดภายใน 10 วันหลังจากหย่านมในกลุ่มที่ได้รับ PG600 มีมากกว่าในกลุ่มที่ไม่ได้รับ PG600 อีกทั้งยังพบว่าจำนวนลูกสุกรทั้งหมดมีจำนวนเพิ่มมากขึ้นเมื่อเป็นแม่สุกรลำดับท้องที่สอง นอกจากนี้ การฉีด PG600 ให้ทางใต้ผิวหนัง ทำให้แม่สุกรแสดงอาการเป็นสัดได้มากกว่าการฉีดให้เข้าทางกล้ามเนื้อ ส่วนขนาดของการฉีด PG600 มีผลต่ออัตราการตกไข่ โดยพบว่าแม่สุกรที่ได้รับการฉีด PG600 ขนาด 1.0 โด๊ส มีอัตราการตกไข่น้อยกว่าแม่สุกรที่ได้รับการฉีด 1.5 และ 2.0 โด๊ส อีกทั้งยังพบว่า การฉีด PG600 ขนาด 1.5 โด๊ส ทำให้แม่สุกรมีจำนวนฟอลลิเคิลขนาดใหญ่มากกว่าการฉีดเพียง 0.5 โด๊ส (25.7 vs 19.2 ฟอลลิเคิล, $p<0.01$) รวมไปถึงทำให้แม่สุกรแสดงอาการเป็นสัดได้ยาวนานที่สุด (2.7 วัน, $p<0.05$) เมื่อเทียบกับการฉีดให้ขนาด 0, 0.5 และ 1.0 โด๊ส อย่างไรก็ตาม การฉีด PG600 ขนาด 1.5 โด๊ส ยังทำให้เกิดถุงน้ำที่รังไข่มากกว่าการฉีดขนาดอื่น ๆ ซึ่งการเกิดถุงน้ำที่รังไข่มีผลไปยับยั้งการตกไข่ และทำให้อัตราการผสมติดลดลงได้ในที่สุด

คำสำคัญ: การเป็นสัด PG600 ระบบสืบพันธุ์ แม่สุกร

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