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Effect of Intrauterine Infusion of Polyvinyl Pyrolidone Iodine on Early Return of Reproductive Function in Postpartum Dairy Cows

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Summary

A commercial polyvinyl pyrolidone iodine (PVP-I) preparation was infused into the uterine cavity in postpartum dairy cows. The effect of this treatment on the early return of reproductive function was evaluated by investigating in changes the uterus and ovaries following infusion and by observing the changes in peripheral blood progesterone.

Using 14 multiparous dairy cows, 50 ml of PVP-I were infused into the uterine cavity using a modified syringe on d 10, 20 or 30 after parturition. The ovarian changes were monitored by palpation per rectum on d 0, 10, 20 and 30 after injection. Blood was sampled from the clavicular vein at intervals of 5 d until 30 d after injection. Blood progesterone extracted with ethyl ether was measured by radioimmunoassay. Intrauterine PVP-I on d 10 to 30 resulted in involution of the uterus within 30 d after injection in 7 of 10 cows. Thus, the effect of PVP-I injection on the early return of reproductive function was demonstrated. Especially in cows treated by PVP-I injection at d 10 postpartum, estrus recurred in 32.3 d (mean), and artificial insemination became possible in 35 d on the average in 3 of the 6 cows. The interval from parturition to artificial insemination was shorter than that (90.0 ± 32.7d) of 60 control cows. It was found that intrauterine infusion of PVP-I induces the early return of reproductive function, the onset of estrus, the development of corpus luteum, the recurrence of estrus after luteal regression, and the realization of artificial insemination within 40 to 60 d after parturition.

Shortening of calving intervals in dairy cows is considered to contribute to the increase in milk production, coordinate recurrence of estrus, and enhance conception rates. Yamauchi *et al.* (1-3) reported that when viscous fluid such as polyvinyl pyrolidone-iodine (PVP-I) was injected into the uterine cavity at the

early luteal phase, the corpus luteum continued to develop for 3 to 4 d after the treatment and was then rapidly atrophied subsequently, and when it was injected at the late luteal phase, its life time was prolonged. Nakahara *et al.* (4-7) found that treatment with Lugol's solution or PVP-I (phlogogenic iodine preparations for uterine mucous membrane) induced an acute inflammatory change locally in the superficial layer of the endometrium, that regeneration of uterine epithelial cells began so soon as within 10 h after the treatment and was almost completed in 3 to 4 d, and that prostaglandin like substances were released from the uterus.

In this experiment, PVP-I was injected into the uterine cavity, and the effect of PVP-I on the early postpartum return of reproductive function was investigated.

Materials and Methods

The number of days from delivery to the next breeding was counted using 60 multiparous cows (Holstein) reared at farms. The experiment was performed using another group of 14 multiparous dairy cows reared at farms. They were housed day and night in cow houses and were fed on rice straw, hay, silage and composite fodder for cattle. Their past deliveries were confirmed to be normal.

At d 10, 20 or 30 postpartum, 50 ml of PVP-I (Fujita Seiyaku K.K.) were infused using a reformed intrauterine injector whose syringe was extended from the normal length of 50 to 62 cm. So, that it could be inserted by the recto-vaginal method or with a vaginal speculum. This improvement was necessary because the cervical canal and uterine angle were enlarged at delivery, that the cervix could not be grasped especially in multiparous cows. PVP-I contained 2.0 g of polyvinyl pyrolidon iodine and 0.2 g of available iodine per 100 ml. This solution is generally used in the treatment of endometritis, poor fertility, abortion, and endometritis caused by retained placenta. Ovarian changes of the cows were monitored by palpation per rectum on 0, 10, 20, and 30 d after infusion of PVP-I. Artificial insemination was attempted when estrus occurred and the follicle was judged capable of ovulation. Subsequently pregnancy was judged by rectal examination. Blood was sampled from the clavicular vein at 5 d intervals of until 30 d after the treatment.

Blood for the measurement of progesterone concentration was collected from the clavicular vein using a vacationer tube and within 1 h after collection, was centrifuged at $1,788 \times g$ for 15 min to collect blood serum. Serum samples were stored at $-20°C$. Serum progesterone concentration was determined by RIA, after extraction with ethyl ether, basically by the method of Taya *et al.* (8). The sensitivity of measurement in this assay was 3 pg/ml. The intra and interassay coefficients of variation were 0.4 to 10.5% and 2% respectively ; $r = 0.95577$ for the calibration curve.

Results

The number of days from delivery to the first estrus was 90.0±32.7 in the 60 multiparous dairy cows that were fed on the same diet as the 14 dairy cows used in the experiment (Table 1).

At the time of intrauterine infusion of PVP-I at d 10 postpartum, the existence of corpus luteum and follicle were found in 1 and 5 cow, respectively. Since the uterus was not involuted sufficiently at d 10 postpartum, the ovarium could not be palpated in some of the cows. Ovulation occurred in 1 cow at d 10 postpartum and in 2 cows at d 15. At d 30, 35 and 40 artificial insemination was carried out in one cow, respectively.

When PVP-I was infused into the uterine cavity at d 20 postpartum, the corpus luteum and follicle were found in 2 cows in both cases. At the time of PVP-I infusion, cows were ovulated in 2 out of the 4. At d 40 postpartum, the second ovulation occurred in only one. Similarly, when PVP-I was infused into the uterine cavity at d 30 postpartum, the corpus luteum and follicle were also found in 2 cows in both cases. Intrauterine infusion of PVP-I at d 30 postpartum induced ovulation were occurred in 2 out of the 4 cows at d 10 after infusion (d 40 postpartum). At d 20 after infusion (d 50 postpartum), ovulation occurred in only one. The second ovulation also occurred in only one at d 60 postpartum.

Figure 1 shows the variations in serum progesterone by intrauterine infusion of PVP-I at d 10 postpartum. The progesterone concentration was found to increase once at d 20 to 30 after infusion (d 30 to 40 postpartum) and then to disappear subsequently.

Figures 2 and 3 shows the variations in serum progesterone by infusion of PVP-I at d 20 postpartum. Figure 2 represents serum progesterone of those cows which had existed the follicle at the time of PVP-I infusion. Consequently, Figure 3 represents serum progesterone of those cows which had existed the corpus luteum at the time of PVP-I infusion. In Figure 2 as in Figure 1, progesterone is seen to increase once after infusion and to disappear subsequently. In Figure 3,

TABLE 1. *Effect of PVP-I infusion on first estrous with 40 days and on first insemination days.*

Treatment		n	First estrous within 40 days	Days of first insemination	Rate of pregnancy
Control (Non-treatment)		60	—	90.0±32.7	87.3%
PVP-I	10th days after calving	5	4/5 32.3±7.6	58.1±9.3	85.7%
	20th days after calving	4	1/4 40		
	30th days after calving	3	1/4 40		

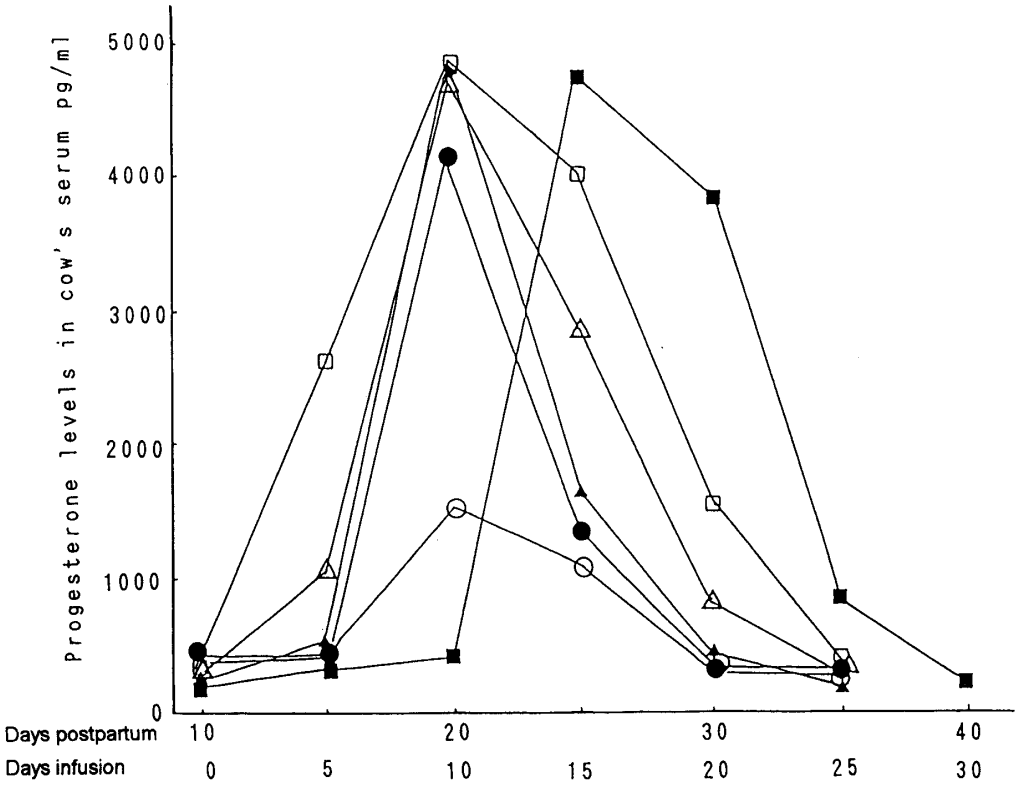

FIG. 1. Progesterone levels in 5 cow's serum, after infusion of iodine solution into the uterus at 10th days of post-partum.

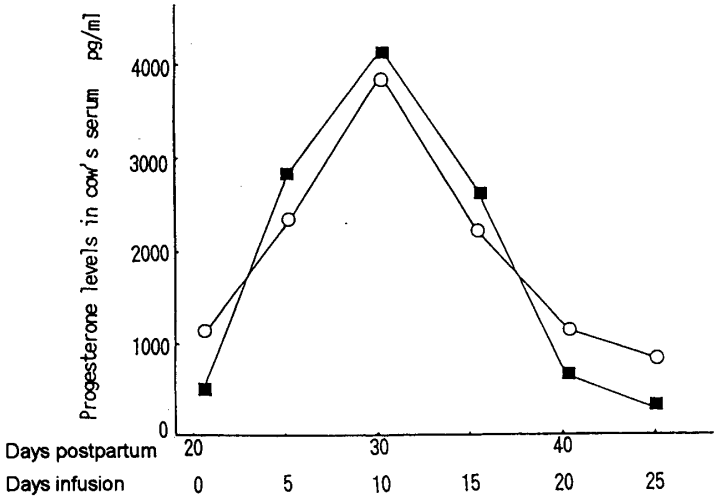

FIG. 2. Progesterone level in cow's serum, after infusion of PVA-I at 20th day of postpartum with follicular stage ovary.

progesterone is seen to decrease once and to increase subsequently.

Figure 4 shows the variations in serum progesterone level by infusion of PVP-I at d 30 postpartum. Progesterone was found to increase immediately after

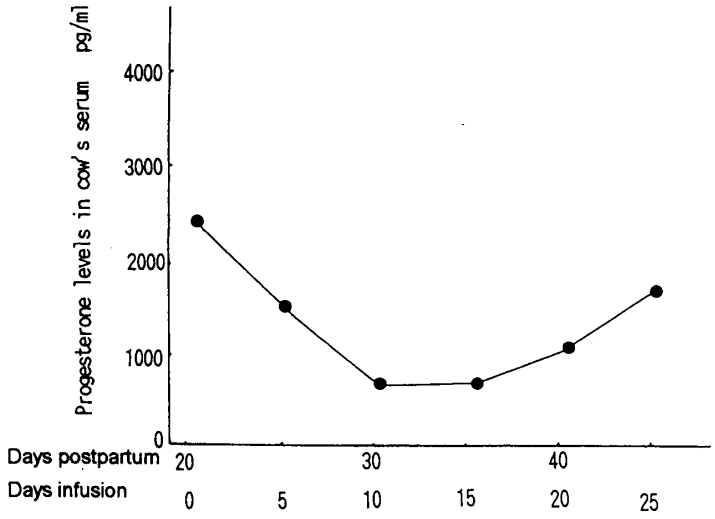

FIG. 3. Progesterone level in cow's serum, after infusion of PVA-I at 20th day of postpartum with luteal stage ovary.

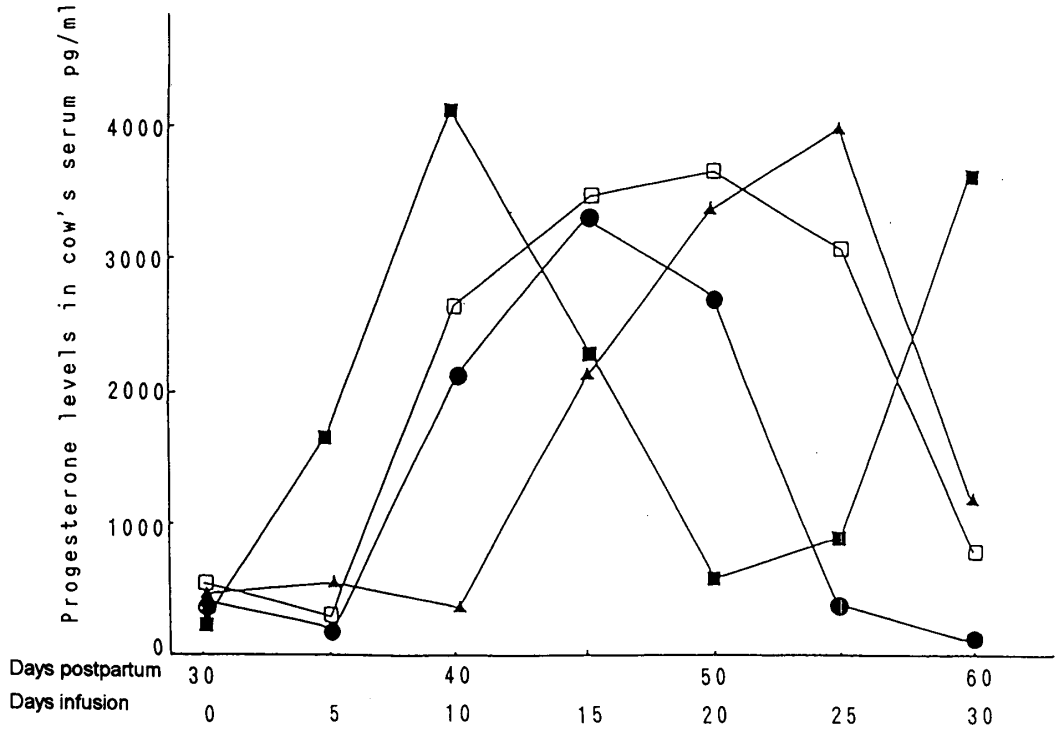

FIG. 4. Progesterone levels in 4 cow's serum, after infusion of iodine solution into the uterus at 30th day of postpartum.

PVP-I infusion in one cow and to increase d 5 to 10 after PVP-I infusion in the other 3 cows.

Table 1 shows the days of first insemination after delivery and conception rates in cows treated by PVP-I infusion. By intrauterine infusion of PVP-I from

d 10 to 30 postpartum, ovulation occurred d 30 after infusion in 12 out of the 14 cows examined. This finding indicates that insemination became possible within d 30 after PVP-I infusion, namely, in 40-60 d (mean 63.6 ± 15.6 d) postpartum. A significant difference was found between the controls (first insemination after delivery 90.0 ± 32.7 d) and the cows treated by PVP-I infusion. In addition, the significant difference was not found in conception rate between the controls (87.3%) and the cows treated by PVP-I infusion (85.7%).

Discussion

Intrauterine infusion of PVP-I from d 10 to 30 postpartum induced the onset of estrus and ovulation within 30 d after injection in 7 out of 10 cows. This treatment was found effective for the early return of reproductive function.

The period required for first insemination after delivery was significantly shortened in the cows treated by PVP-I infusion compared to the untreated controls. The fertilization rates obtained in the cows treated by PVP-I infusion were comparable to those in the untreated controls.

All 6 cows treated by PVP-I infusion at d 10 postpartum had existed the follicle without luteal function. The secretion of progesterone was delayed in a cow which ovulated at d 5 after PVP-I infusion, but the progesterone level was elevated in all 6 cows including the above. This finding indicates that luteinization was induced after PVP-I infusion. Of the 4 cows treated by PVP-I infusion at d 20 postpartum, 2 already had follicle. The progesterone level was elevated at d 10 after PVP-I infusion, representing the development of the corpus luteum. Of the 4 cows treated by PVP-I infusion on d 30 postpartum, one had the corpus luteum. The progesterone level in this cow was likewise increased, representing the development of the corpus luteum. Of the cows treated by PVP-I infusion at d 20 postpartum, luteal regression occurred immediately after PVP-I infusion in the cows which had corpus luteum, indicating the development of the corpus luteum after luteal regression.

Nakahara *et al.* (4, 5, 7) reported that intrauterine infusion of iodine solution during the early luteal phase shortened the life time of the corpus luteum and infusion at the late luteal phase prolonged its life time. Our findings in this study agreed with theirs; namely, the corpus luteum developed in cows which had follicle, and the corpus luteum was atrophied in cows which had corpus luteum at the time (d 20 postpartum) of PVP-I infusion.

On the mechanism of the early return of reproductive function (namely, development and regression of corpus luteum) by intrauterine infusion of PVP-I. Nakahara *et al.* (4) suggested that after infusion of PVP-I, the endometrium undergoes an inflammatory change and produces arachidonic acid and PG ($PGF_{2\alpha}$ or PGE_2). The experiment of intrauterine infusion of the iodine solution sug-

gests that luteal regression by infusion of PVP-I results in production of PG in the endometrium, not during the early stage of inflammatory process but during the process of healing or after completion of the healing process. Inflammation is induced in the endometrium by intrauterine infusion of PVP-I and the inflammation associated production of PG occure 3 to 4 days after inflammation (4).

Prostaglandins are a kind of physiological active substance synthesized from arachidonic acid in animal tissue. Generally, PGE_2 and $PGF_{2\alpha}$ are involved in reproduction. Their major actions are closely related to the release of gonadtropin, ovulation, regression of the corpus luteum, contraction of the uterus, parturition and transport of semen (9). The relation between PG and gonadtropin is still not well understood. PGE_2 and $PGF_{2\alpha}$ are known to induce the release of LH, but the role of PG in the release of gonadtropin still remains unknown. It has been suggested that $PGF_{2\alpha}$ is involved not only in luteal regression but also in ovulation. In fact, $PGF_{2\alpha}$ in ovarian vein increases, as ovulation comes closer. It has been suggested that PG in follicular fluid are increased at ovulation; 13-fold increase in PGE_2 and 18-fold increase in $PGF_{2\alpha}$, and that the action of $PGF_{2\alpha}$ at the time of ovulation is related to the accelerated discharge of ovarian follicle (9).

$PGF_{2\alpha}$ produced in the uterus is transported from the uterus directly to the ipsilateral ovarium (10, 11). It was presumed that since $PGF_{2\alpha}$ induces remarkable luteal regression during the luteal stage except at its early phase (12-14), ovulation was accelerated simultaneously with luteal regression in cows which had corpus luteum.

In this experiment, infusion of PVP-I into the uterine cavity at d 10-30 postpartum seemed to induce luteinization and the subsequent onset of estrus and also ovulation in most of the experimental dairy cows examined. The postpartum onset of estrus usually appears after short term luteinization (15-22). Early weaning of anestrus cows after parturition leads to the appearance of estrous behavior after approximately 4 d of luteinization (23). If the corpus luteum is not formed before the onset of estrus, the consequence is that the corpus luteum ends up in short life. These apply to the initial formation of corpus luteum in dairy cows (24-27). Breuel (28) reported that 88% of ova collected from postpartum estrous cows attained normal growth but were not fertilized when transplanted in postpartum estrous cows. He pointed out that the uterine condition, namely, the environment surrounding the ova but not the condition of the ova was responsible for the non-fertilization. Butcher (29) suggested that the rates of conception and estrus onset could be enhanced, if postpartum cows were treated with norgestomet, a synthetic progesterone preparation, within 12 d before the onset of estrus. Breuel *et al.* (30) also reported a similar finding. From the above, it is noted that the uterine environment which surrounds an ovum is a

problem associated with impregnation of postpartum estrous cows. Hence, luteinization before the onset of estrus was presumed necessary and important.

In conclusion, we observed the effect of PVP-I injection on the early return of reproductive function. It was found that intrauterine injection of PVP-I induces the early return of reproductive function, the onset of estrus, the development of corpus luteum and the recurrence of estrus after luteal regression.

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