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The influence of inflammatory process on prostaglandin $F_2\alpha$ contractile activity in porcine uterus

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ABSTRACT

The aim of this study was to determine the influence of prostaglandin $F_2\alpha$ ($PGF_2\alpha$) on the contractile activity of intact and inflamed porcine uteri. On day 3 of the oestrous cycle, gilts were randomly assigned to group I (control; n = 6) or II (treated with *E. coli*; n = 6). In all gilts median laparotomy was performed and 50 ml of saline or 50 ml of *E. coli* containing 10^9 colony-forming units/ml were injected into each uterine horn in groups I and II, respectively. After seven days (on day 10 of the oestrous cycle) the gilts were slaughtered and uterine horns collected. After macroscopic examination, contractile activity of uterine strips: *endometrium+myometrium* (ENDO/MYO) and *myometrium* (MYO) was examined using noradrenaline (NA), acetylocholine (ACh), $PGF_2\alpha$ alone or together with EP_2, EP_4, EP_1, EP_3 receptor blockers (BEP_2, BEP_4, BEP_1 and BEP_3, respectively). NA decreased ($P<0.01$, $P<0.001$) the intensity of contractions in ENDO/MYO and MYO of the control group but increased ($P<0.05$, $P<0.01$) in the inflamed uterus. ACh at doses 10^{-5}, 10^{-4} and 10^{-3} M increased ($P<0.05$-0.001) the intensity of contractions in ENDO/MYO and MYO from the bacteria group and intact group ($P<0.05$) at doses10^{-4} and 10^{-3} M. ACh at all of the tested doses increased ($P<0.05$-0.001) the frequency of contractions in the control and decreased ($P<0.05$, $P<0.001$) in the experimental group. NA and ACh treatment revealed that uterine strips were living and suitable for further investigations. $PGF_2\alpha$ at a dose of 10^{-7} M increased ($P<0.05$, $P<0.01$) the intensity of contractions in ENDO/MYO and MYO in both control and experimental groups. $PGF_2\alpha$ at doses 10^{-8} and 10^{-7} M used in the presence of BEP_2 or BEP_4 increased ($P<0.05$-0.001) the intensity of contrac-

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tions in both the control and bacterial groups. However, $PGF_2\alpha$ did not significantly influence the frequency of contractions with the exception of the stimulatory effect in ENDO/MYO ($P<0.001$) strips of the control groups. $PGF_2\alpha$ at doses of 10^{-8} and 10^{-7} M administered after BEP_1 and BEP_3 treatment decreased ($P<0.05$-0.001) or did not significantly influence the intensity and frequency of contractions in uterine tissues in both examined groups. The presented findings revealed that $PGF_2\alpha$, besides affecting the contractile activity of uterine tissues, may also act through the PGE_2 receptors. However, thorough interpretation of these results requires determination of the role of other prostanoids in this process.

KEY WORDS: contractile activity, uterus, endometritis, $PGF_2\alpha$, PGE_2 - antagonists, gilts

INTRODUCTION

By acting though specific receptors, prostanoids regulate many physiological processes in different organs: the brain (Cao et al., 1996; Sehic et al., 1996; Resch and Millington, 2001; Moore et al., 2004), kidneys (Harris et al., 1998**)** and gastrointestinal tract (Wallace, 1990; Dubois et al., 1998). Prostaglandins (PGs), mainly from series E and F, control most processes in the reproductive organs, particularly: sperm migration, ovulation, luteolysis, fertilization, egg implantation, foetal growth and the uterine activity in the postpartum period (Herschman, 1996).

The presence of pathogenic microorganisms in the uterus increases considerably PG concentrations in both uterine tissues and venous blood outflow from this organ. Endotoxin (lipopolysaccharide; LPS) released from the bacterial wall, as well as proinflammatory cytokines, stimulate the enzymatic activity of cyclooxygenase-2 (COX-2). The metabolism of mucous membrane phospholipids into PGs is connected with phospholipase A_2 ($cPLA_2$) and phospholipase C (PLC) activity. In the inflammatory changed uterus independent of phospholipase, phospholipid metabolism is more active, and high PG concentrations are the results of intensified COX activity (Chong-Jeh et al., 1996; Gijon and Leslie, 1999).

In veterinary practice, long-lasting uterine inflammatory stages characterized by mucopurulent discharge or pyometra cause long-term problems. Under these conditions the uterine muscular layer loses its contractile ability and the uterus filled with inflammatory exudate hangs in the abdominal cavity. The high $PGF_2\alpha$ concentration in the uterus is caused by the presence of pathogenic microorganisms and should ensure contractile activity of the uterine muscular layer even in long-lasting *endometritis.* During inflammation of the uterus, besides an increase in $PGF_2\alpha$ levels, there is also a rise in concentrations of PGE_2 (Mateus et al., 2003; Jana et al., 2007) and PGI_2 (Kołaczkowska, 2002). In accordance with Jana et al. (2007) after intrauterine *E. coli* infusions the level of PGE_2 was four times higher than of $PGF_2\alpha$ in gilts on day 17. We accept that during development of

endometritis, besides distinctly increasing their concentrations, PGs change their mutual relation (Jana et al., 2007). The concentrations of PGE_2 and PGI_2 increase and the level of $PGF_2\alpha$ decreases. The high PGE_2 and PGI_2 concentrations in the inflamed uterus probably inhibit or delimit the contractile activity of $PGF_2\alpha$. It has been reported that PGE_2 operates on the uterine muscular layer during contraction (though EP_1 and EP_3 receptors) and diastole (though EP_2 and EP_4 receptors) (Myatt and Lye, 2004). Importantly, apart from PGE_2, progesterone is one factor that, under physiological conditions, acts diastolicly on the uterine muscular layer. Moreover, $PGF_2\alpha$ in the human uterus has been reported to act not only by its receptors but also through receptors for PGE_2 (Myatt and Lye, 2004). The literature to date lacks data concerning the influence of $PGF_2\alpha$ on contractile activity in intact and inflamed porcine uteri.

Therefore, the aim of this study was to determine the effect of $PGF_2\alpha$ on the intensity and frequency of uterine contractions in intact and inflamed uteri of gilts. We studied the influence of $PGF_2\alpha$ on the contractile activity of *endometrium+myometrium* (ENDO/MYO) and *myometrium* (MYO) uterine strips and the effect of $PGF_2\alpha$ on the contractile activity of the uterine tissues in the presence of PGE_2 receptor antagonists (EP_2, EP_4, EP_1 and EP_3).

MATERIAL AND METHODS

Animals

Twelve crossbred gilts (Large White × Landrace) 7-8 months old, weighing 100-120 kg and with at least two regular oestrous cycles were used in this study. The animals originated from a herd with no abnormal discharge or fertility disorders and were not treated with antibiotics before, during or after surgery. The gilts were individually housed in stalls under conditions of natural light and temperature. They were fed a commercial grain mixture and tap water *ad libitum.* All experimental procedures followed the principles of animal care (NIH publication No 86-23, revised in 1985) and were approved by the Local Ethics Commission for Animal Experiments (Agreement No 20/N). On day 3 of the oestrous cycle the gilts were randomly assigned to one of two groups: group I (n = 6) control receiving saline and group II (n=6) treated with *E. coli*. In all the gilts median laparotomy was performed under general anaesthesia using Stresnil (Janssen Pharmaceutica, Belgium) at a dose of 1 ml/10 kg BW and Vetbutal (Biowet, Poland) at a dose 30-40 ml/100 kg BW. Next, group I had 50 ml of saline injected into each uterine horn (10 ml in five places). Group II received 50 ml of an *E. coli* (strain O25:K23/α/:H1; National Veterinary Research Institute, Department of Microbi-

ology, Puławy, Poland) suspension containing 10^9 colony-forming units (cfu)/ml, the same way. The animals were slaughtered seven days after surgery (on day 10 of the oestrous cycle) and the uteri were collected. The uterine horns were then cut off and a macroscopic examination was performed. Fragments of the uterine horns were transferred on ice, transported to the laboratory within 20 min and immediately processed for examination of contractile activity.

Determination of contractile activity

Strips 3 × 5 mm were prepared (in an identical way and from the same site) from two kinds of uterine wall fragments: *endometrium* with *myometrium* (ENDO/MYO) and *myometrium* (MYO) from the middle part of the uterine horns. They were separated, washed in saline and mounted between two stainless steel hooks in 5 ml organ bath (Schuler Organ bath type 809; Hugo Sachs Electronic, Germany) under conditions of resting tension of 5 mN. The strips were kept in Krebs-Ringer solution of the following composition (mM/l): NaCl, 120.3; KCl, 5.9; $CaCl_2$, 2.5; MCl_2, 1.2; $NaHCO_3$, 15.5; glucose, 11.5; and pH 7.4. The solution was maintained at 37°C and continuously saturated with a mixture 95% O_2 and 5% CO_2. After equilibration the contractile activity of the strips was recorded for at least 60 min. Contraction intensity and frequency were measured using a Hugo Sachs Electronic force displacement transducer (HSE F30 type 372), and recorded with HSE-ACADW software for Windows 2000 (Germany). At the beginning of the study the strips were incubated (7 min) with noradrenaline (NA) (Polfa, Poland) at a concentration of 10^{-7} and 10^{-6} M and acetylocholine (ACh) (Sigma) at concentrations of 10^{-5}, 10^{-4} and 10^{-3} M to determine the strips′ contractile activity and their qualification for further study. Afterwards, the influence of increasing (10^{-8} and 10^{-7} M) doses of $PGF_2\alpha$ was examined. $PGF_2\alpha$ was tested alone or after two min of preincubation with AH 6809 (Cayman Chemical, USA), BEP_2; ONO-AE_2 (Sigma), BEP_4; ONO-AE_3-240 (Sigma), BEP_1; and SC19220 (Sigma), BEP_3; selective antagonists of EP_2, EP_4, EP_1 and EP_3 receptors, respectively. BEP_2, BEP_4 and BEP_1 were used at a dose of 10^{-6} M, while BEP_3, at a dose of 10^{-7} M. The effective dose of each substance was tested in pilot studies on uterine tissue collected at a local slaughterhouse from gilts in the luteal phase of the oestrous cycle. At the end of the study NA and ACh were administrated in the same doses as at the beginning to assess the contractile activity of the strips.

Statistical analysis

For the statistical analyses, the numerical values of the contraction activity (intensity and frequency) of tissues before the application of the biologically ac-

tive substances were calculated for seven min and taken as 100%. The results calculated for the seven min period after treatments were expressed as a percentage (mean ± SEM) of the contraction intensity and frequency before drug administration. The Bonferroni test was applied for calculating the statistical significance of mean differences (ANOVA, InStat Graph Pad, San Diego, CA) and P value of < 0.05 was considered statistically significant for all tests.

RESULTS

Macroscopic examination of uteri. Macroscopically, inflammatory changes were not observed in the *endometrium* of the gilts receiving saline. The administration of *E. coli* into the uterus induced inflammation involving the entire organ. The *endometrium* was red**,** swollen with distinctly visible blood vessels. The uterine horns were enlarged and a grey-white mucosal exudate was found inside them.

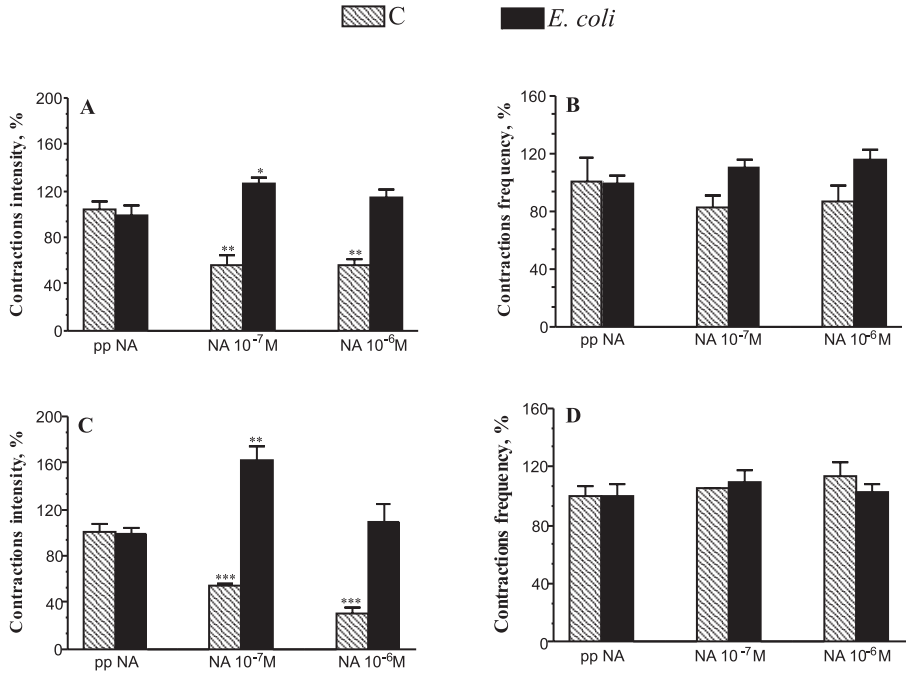

Figure 1. Influence of noradrenaline (NA) on the intensity of contractions (A, C) and frequency of contraction of *endometrium* and *myometrium* (A, B) and *myometrium* (C, D) strips collected from the control and *E. coli*-treated gilts. Values (mean±SEM; n=6) are presented as percentage in the relation to the basal (before treatment, pp) intensity and frequency of contractions. * $P<0.05$, ** $P<0.01$, *** $P<0.001$

Effect of NA and ACh on the contractile activity of uteri. NA at doses of 10^{-7} and 10^{-6} M decreased the intensity of contractions of ENDO/MYO ($P<0.01$) and MYO ($P<0.001$) from the control group. In the animals receiving bacteria, NA at a dose of 10^{-7} M increased the intensity of contractions in ENDO/MYO ($P<0.05$) and MYO ($P<0.01$) as compared with the period before treatment. The frequency of contractions in response to NA was similar in the two kinds of uterine tissue from both groups of gilts and insignificant ($P>0.05$) as compared with the period before treatment (Figures 1 A-D).

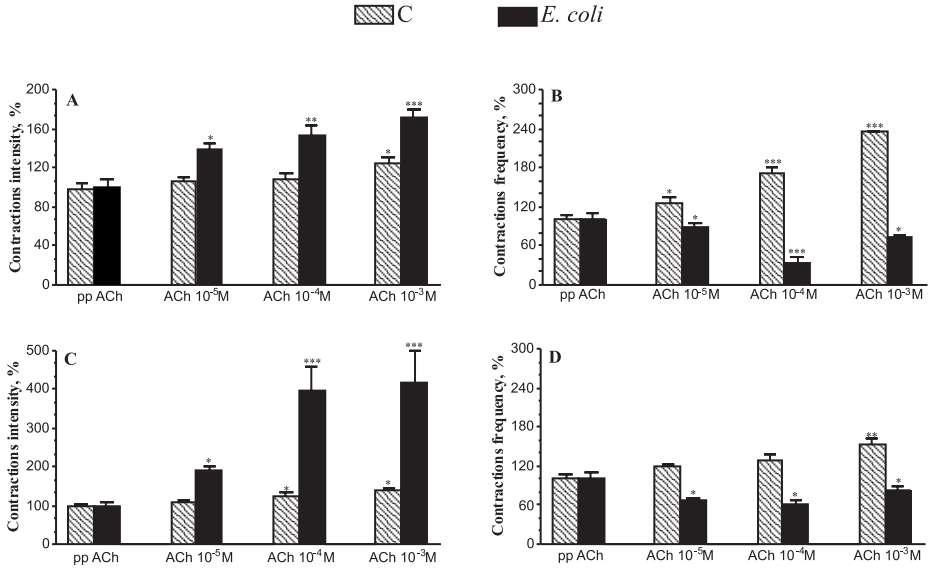

Figure 2. Influence of acetylocholine (ACh) on the intensity of contractions (A, C) and the frequency of contraction (B, D) of *endometrium* and *myometrium* (A, B) and *myometrium* (C, D) strips collected from the control and *E. coli*-treated gilts. Values (mean±SEM; n=6) are presented as percentage in the relation to the basal (before treatment, pp) intensity and frequency of contractions. * $P<0.05$, ** $P<0.01$, *** $P<0.001$

In the control group ACh elevated ($P<0.05$) the intensity of contraction in ENDO/MYO at a dose of 10^{-3} M and in MYO at doses of 10^{-4} and 10^{-3} M. In the strips from the inflamed uterus, ACh increased the intensity of contractions in both ENDO/MYO ($P<0.05$, $P<0.01$ and $P<0.001$ after dose of 10^{-5}, 10^{-4} and 10^{-3} M, respectively) and in MYO ($P<0.05$, $P<0.01$ and $P<0.001$ after dose of 10^{-5}, 10^{-4} and 10^{-3} M, respectively). Moreover, in the control group ACh increased the frequency of contractions in ENDO/MYO in a dose-dependent manner ($P<0.01$, $P<0.001$) and at the highest dose ($P<0.01$) in MYO strips. In contrast, in the strips collected from the *E. coli*-treated group, a decrease was observed ($P<0.05$) in the frequency of contractions after all tested doses of ACh (Figures 2 A-D).

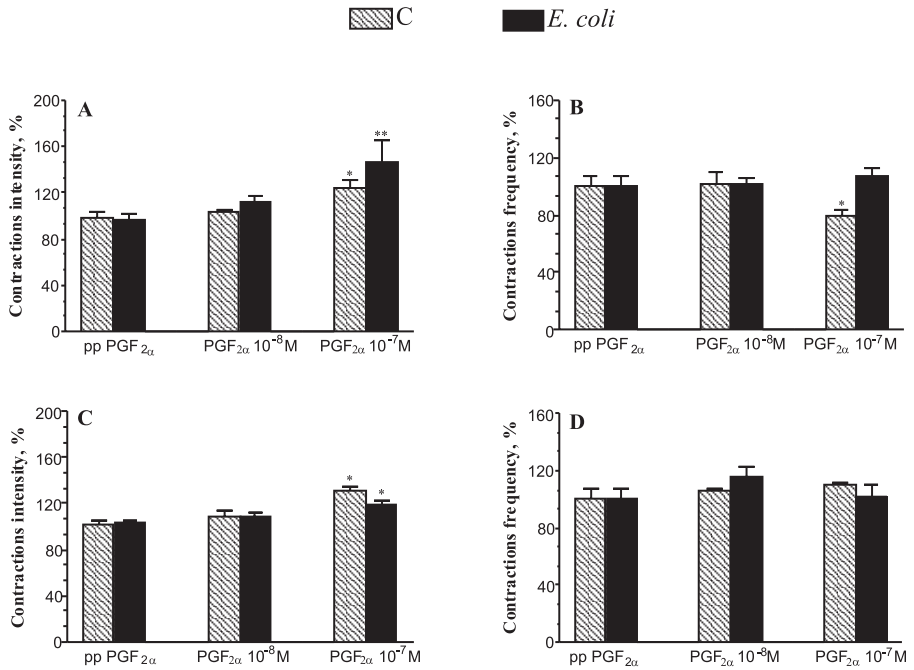

Figure 3. Influence of prostaglandin $F_2\alpha$ ($PGF_2\alpha$) on the intensity of contractions (A, C) and frequency of contractions (B, D) of *endometrium and myometrium* (A, B) and *myometrium* (C, D) strips collected from the control and *E. coli*-treated gilts. Values (mean±SEM; n=6) are presented as percentage in the relation to the basal (before treatment, pp) intensity and frequency of contractions. * P<0.05, ** P<0.01

Effect of $PGF_2\alpha$ on the contractile activity of uteri. $PGF_2\alpha$ at a dose of 10^{-7} M increased the intensity of contractions in both ENDO/MYO and MYO strips of the control (P<0.05) and *E. coli*-treated (ENDO/MYO-P<0.01, MYO-P<0.05) gilts. Instead, $PGF_2\alpha$ at a dose of 10^{-8} M did not significantly influence the intensity of contractions in the uterine tissues in both examined groups. The frequency of contractions in ENDO/MYO decreased (P<0.05) in the control group after treatment of $PGF_2\alpha$ at a dose of 10^{-7} M. In the MYO, $PGF_2\alpha$ did not significantly influence the frequency of contractions (Figures 3 A-D).

Effect of $PGF_2\alpha$ on the contractile activity of uteri in the presence of BEP_2 and BEP_4. BEP_2 employed alone increased (P<0.01) the intensity of contractions in ENDO/MYO of the intact group but decreased (P<0.01) the frequency of contractions in ENDO/MYO of the bacteria group. $PGF_2\alpha$ at a dose of 10^{-7} M in the presence of BEP_2 increased (P<0.05) the intensity of contractions in both uterine tissues of the control croup. At doses of 10^{-8} and 10^{-7} M $PGF_2\alpha$ increased (P<0.001) the frequency of contractions in the ENDO/MYO of the control group. In contrast, in the ENDO/MYO of the bacteria group and also in the MYO of both examined

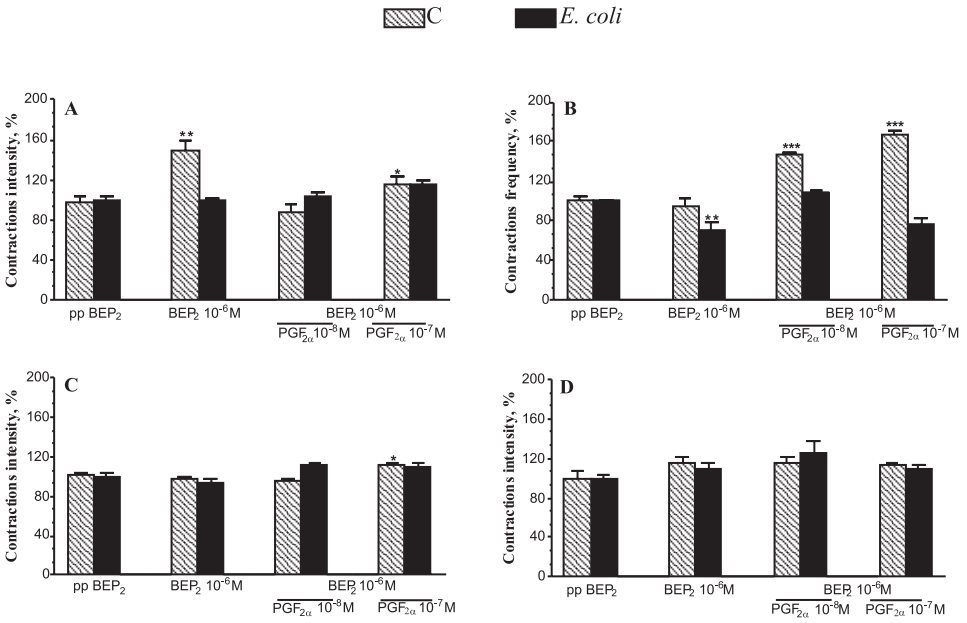

Figure 4. Influence of prostaglandin $F_2\alpha$ ($PGF_2\alpha$) on the intensity of contractions (A, C) and the frequency of contractions (B, D) of *endometrium* and *myometrium* (A, B) and *myometrium* (C, D) strips collected from the control and *E. coli*-treated gilts in the presence of BEP_2. Values (mean±SEM; n=6) are presented as percentage in the relation to the basal (before treatment, pp) intensity and frequency of contractions. * P<0.05, ** P<0.01, *** P<0.001

groups, $PGF_2\alpha$ did not significantly influence the intensity and frequency of contractions in the presence of BEP_2 (Figures 4 A-D).

BEP_4 applied alone did not significantly influence the intensity and frequency of contractions in uterine strips of both healthy and inflamed uteri. $PGF_2\alpha$ at a dose of 10^{-8} M in the presence of BEP_4 decreased (P<0.05) the intensity of contractions in ENDO/MYO of the control group. Inversely, $PGF_2\alpha$ given at a dose of 10^{-7} M increased (P<0.01) the intensity of contractions in MYO of the control group. In the MYO of the bacteria group, $PGF_2\alpha$ dose dependently (10^{-8} or 10^{-7} M) increased (P<0.05 and P<0.001) the intensity of contractions. However, in the ENDO/MYO of the bacteria group, $PGF_2\alpha$ caused no significant changes. $PGF_2\alpha$ did not significantly influence the frequency of contractions in uterine tissues in both examined groups in the presence of BEP_4 (Figures 5 A-D).

Effect of $PGF_2\alpha$ on the contractile activity of uteri in the presence of BEP_1 and BEP_3. BEP_1 applied alone decreased (P<0.05) the intensity and frequency of contractions in MYO of the bacterial group and the frequency of contractions in ENDO/MYO in both examined groups. $PGF_2\alpha$ at a dose of 10^{-8} and 10^{-7} M used in the presence of BEP_1 decreased (P<0.05) the intensity of contractions in the

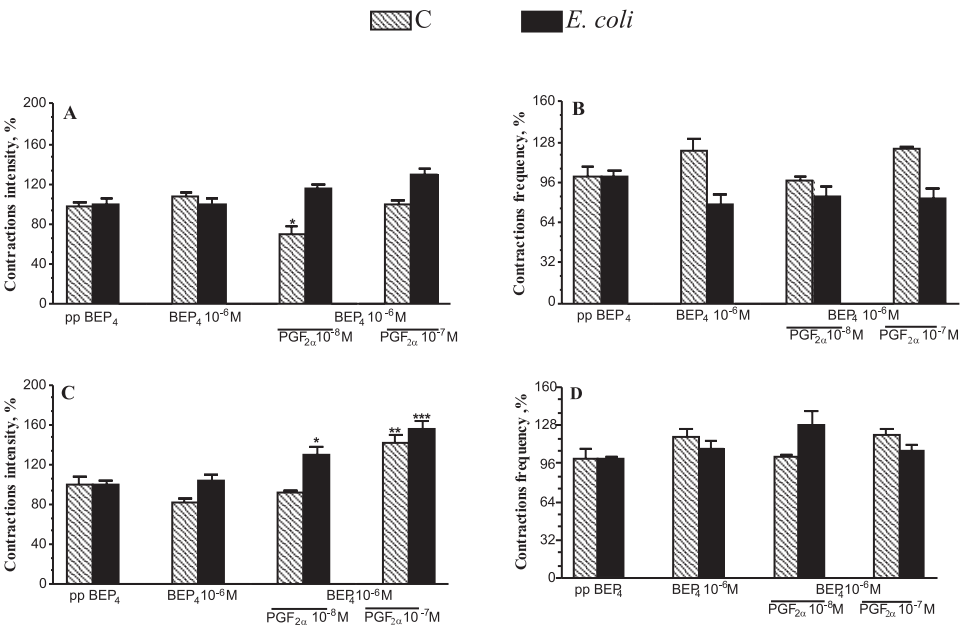

Figure 5. Influence of prostaglandin $F_2\alpha$ ($PGF_2\alpha$) on the intensity of contractions (A, C) and the frequency of contractions (B, D) of *endometrium* and *myometrium* (A, B) and *myometrium* (C, D) strips collected from the control and *E. coli*-treated gilts in the presence of BEP_4. Values (mean±SEM; n=6) are presented as percentage in the relation to the basal (before treatment**,** pp) intensity and frequency of contractions. * P<0.05, ** P<0.01, *** P<0.001

ENDO/MYO of the control group, whereas it did not significantly influence the intensity of contractions in both ENDO/MYO and MYO of the *E. coli*-treated group. $PGF_2\alpha$ at a dose of 10^{-8} M in the presence of BEP_1 reduced the frequency of contractions in ENDO/MYO in both intact (P<0.001) and bacterial (P<0.01) groups. However, in the MYO strips in both examined groups such changes were not observed (Figure 6 A-D).

BEP_3 administered alone decreased the intensity and frequency of contractions in ENDO/MYO (P<0.05, P<0.01) and MYO (P<0.01, P<0.001) of the intact group. In the group after *E. coli* infusions such changes were not observed. $PGF_2\alpha$ at a dose of 10^{-8} M used in the presence of BEP_3 decreased the intensity of contractions in MYO of the control (P<0.05) and experimental (P<0.01) groups. Instead, $PGF_2\alpha$ at a dose of 10^{-7} M decreased (P<0.01) the intensity of contractions in MYO of the control group. In ENDO/MYO, $PGF_2\alpha$ did not significantly influence the intensity of contractions in both examined groups. $PGF_2\alpha$ at a dose of 10^{-8} M in the presence of BEP_3 reduced the frequency of contractions in the ENDO/MYO of the control (P<0.05) and experimental (P<0.01) groups. Instead, $PGF_2\alpha$ at a dose of 10^{-7} M decreased (P<0.01) the frequency of contractions in the

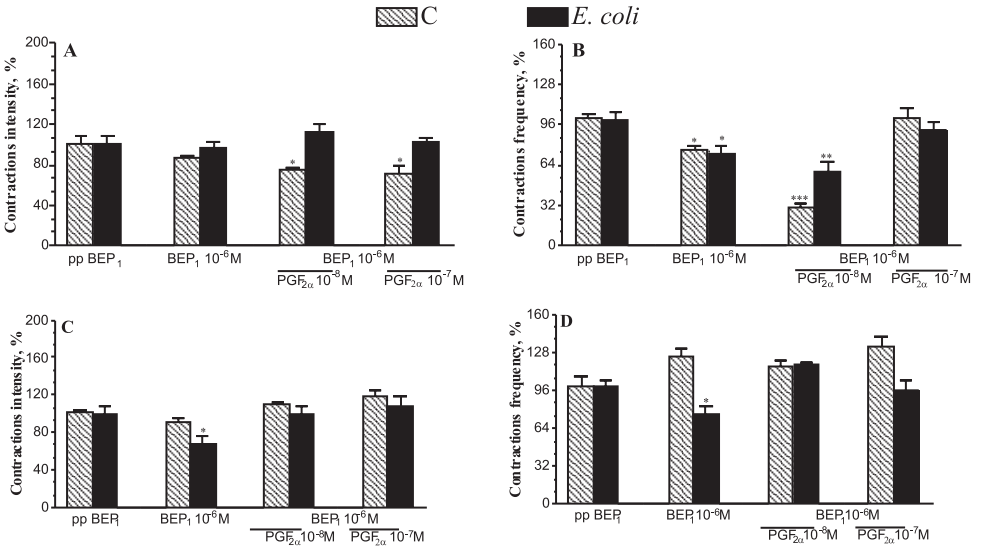

Figure 6. Influence of prostaglandin $F_2\alpha$ ($PGF_2\alpha$) on the intensity of contractions (A, C) and the frequency of contractions (B, D) of *endometrium* and *myometrium* (A, B) and *myometrium* (C, D) strips collected from the control and *E. coli*-treated gilts in the presence of BEP_1. Values (mean±SEM; n=6) are presented as percentage in the relation to the basal (before treatment, pp) intensity and frequency of contractions. * P<0.05, ** P<0.01, *** P<0.001

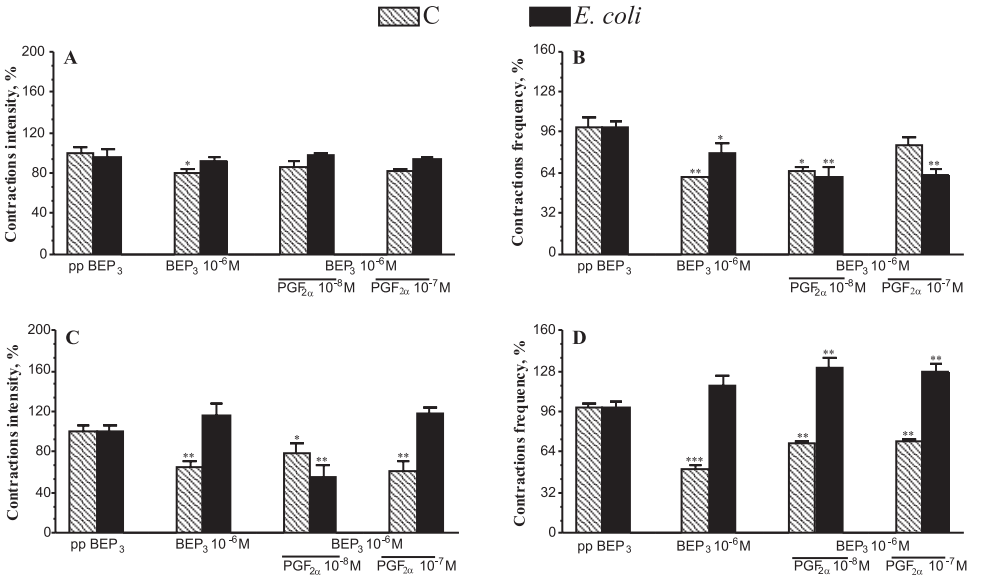

Figure 7. Influence of prostaglandin $F_2\alpha$ ($PGF_2\alpha$) on the intensity of contractions (A, C) and the frequency of contractions (B, D) of *endometrium* and *myometrium* (A, B) and *myometrium* (C, D) strips collected from the control and *E. coli*-treated gilts in the presence of BEP_3. Values (mean±SEM; n=6) are presented as percentage in the relation to the basal (before treatment, pp) intensity and frequency of contractions. * P<0.05, ** P<0.01, *** P<0.001

ENDO/MYO of the bacterial group. In the MYO strips the influence of $PGF_2\alpha$ on the frequency of contractions in the presence of BEP_3 differed. Both doses of $PGF_2\alpha$ decreased ($P<0.01$) the frequency of contractions in the healthy group and increased ($P<0.01$) this indicator in the inflamed uterus group (Figures 7 A-D).

DISCUSSION

Whereas according to the generally held assumption, NA should relax the uterine tissues in both intact and inflamed uteri of gilts, it actually decreased contraction intensity only in healthy uterine tissues. Inversely, in the inflamed uterus, NA caused a significant increase in the contraction intensity of the uterine strips. Such NA activity in the inflamed porcine uterus has been unknown to date. Generally, we can accept that NA activity leads to inhibition in uterine contractile activity, which is probably connected to the numerical superiority of β- over α-adrenergic receptors (Williams and Leffkowitz, 1977; Garbuliński, 1984; Kitazawa et al., 2001) and also with the lower threshold excitability for β-receptors (Kubikowski and Kostowski, 1983). In this study, increased uterine contractile activity may result in increased expression of β-receptors or lower threshold excitability for α-adrenergic receptors. Moreover, NA did not significantly influence uterine contraction frequency in either control or experimental groups.

ACh, as was to be expected, increased the contractile intensity of uterine tissues in both intact and inflamed uteri. However, the intensity of contractions was greater in *E. coli*-treated gilts in comparison with control animals. It is difficult to explain this difference in activity of ACh in healthy and inflamed uteri. We suppose that during the inflammatory process expression of muscarine receptors probably increases in uterine tissues. Finally, we can add that besides a contractile reaction in the smooth uterine muscles (Dynarowicz, 1987; Fogel and Maśliński, 2000), ACh may act diastolicly and dilatate pulmonic lumen and coronal vessels and decrease the intensity of contractions of the cardiac muscle (Fogel and Maśliński, 2000). The application of NA and ACh as control substances in healthy and inflamed uteri revealed that uterine sections were living and suitable for further investigation.

$PGF_2\alpha$ added to the uterine tissues increased the intensity of contractions in both control and experimental groups. The contractile activity of $PGF_2\alpha$ in healthy uterine tissues is generally known and accepted by different authors (Kindahl et al., 1982, 1996; Lindell and Kindahl, 1983; Slama and Vaillancourt, 1991; Cao et al., 2002, 2005). On the other hand, high $PGF_2\alpha$ contractile activity in the inflamed porcine uterus requires explanation. One reason may be the short period (seven

days) between intrauterine *E. coli* infusion and investigation. The inflammatory stage created in the uterus probably was incapable of causing changes in the distribution and expression of $PGF_2\alpha$ receptors in uterine tissues. Because of this the intensity of contractions of the uterine tissues in both control and experimental groups was similar. Moreover, in comparison with cows we can accept that the uterine muscular layer loses its contractile activity only in heavy and prolonged *endometritis*.

$PGF_2\alpha$ treated in the presence of EP_2 and EP_4 receptor blockers whose stimulation leads to uterine relaxation caused increased contractile activity in the uterine muscular layer of the healthy gilts. In the gilts with inflamed uteri, only in the presence of EP_4 blocker did $PGF_2\alpha$ have a stimulatory effect on the intensity of contractions in the *myometrium*. In terms of uterine strip contraction frequency, $PGF_2\alpha$ acted differently in the presence of the blockers. In the presence of BEP_2, the frequency of contractions increased in the *endometrium* of the control group. The use of BEP_4 did not significantly influence the frequency of contractions in the examined groups. The stronger activity of $PGF_2\alpha$ in the *myometrium* after prior BEP_4 treatment is certainly caused by the increased concentration of contractile receptors in this tissue. The ineffective reaction or lack of response in the intensity of contractions of the uterine tissues in the *E. coli*-infused gilts to $PGF_2\alpha$ treatment in the presence of BEP_2 was probably caused by the presence of the inflammation in this organ.

$PGF_2\alpha$ administered in the presence of EP_1 and EP_3 receptor blockers decreased the intensity of contractions or failed to evoke a response in uterine tissues in both examined groups. However, stronger $PGF_2\alpha$ activity was observed in the *myometrium* after prior of BEP_3 blocker treatment. Similarly, the contraction frequency decreased except for the *myometrium* of the bacterial group where this parameter increased. The presented findings revealed that $PGF_2\alpha$ may act on the uterine muscular layer through non-specific PGE_2 receptors. However, thorough interpretation of these results requires determination of the role of other prostanoids in contractile activity in pathologically-changed uterine tissues. This study is one of the first to deal with this problem.

CONCLUSIONS

NA and ACh used as control substances in healthy uterine tissues acted consistently as expected; NA caused relaxation and ACh contraction of the uterine wall. However, in the gilts with inflamed uteri both substances caused strong contraction of the uterine tissues. $PGF_2\alpha$ in both healthy and inflamed uteri increased contraction intensity. The application of PGE_2 (EP_2 and EP_4) receptor blockers

prior to $PGF_2\alpha$ treatment caused an increase in contractile activity in the *myometrium* of the healthy gilts and in EP_4 of *E. coli*-infused gilts. The application of $PGF_2\alpha$ in the presence of PGE_2 (EP_1 and EP_3) receptor blockers caused a significant decrease in the intensity of contractions or no reaction in the uterine tissues of both healthy and inflamed-uterus gilts.

The investigations revealed that $PGF_2\alpha$ contractile activity in uterine tissues was present in both healthy and inflamed uteri. However, its ability to contract uterine tissues is probably dependent on the intensity of the inflammatory process. The application of PGE_2 receptor blockers demonstrated that $PGF_2\alpha$ in uterine tissues may act in a non-specific manner through PGE_2 receptors.

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