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# Effect of xylazine, isoxsuprine, and lidocaine on Doppler sonographic uterine and umbilical blood flow measurements in cows during the last month of pregnancy

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ABSTRACT

The maternal portion of the bovine placenta receives blood mainly from the uterine arteries (AUT) and the fetal portion from the umbilical arteries (AUM). Placental perfusion is crucial for fetal development and undergoes adaptive changes during pregnancy according to the fetal requirements. One goal of this study was to investigate changes in Doppler sonographic measurements of blood vessels that supply blood to the placenta in cows during the last 4 weeks of pregnancy. Another goal was to examine how these measurements are affected by three drugs commonly used in cows at the time of parturition. Nine cows underwent Doppler sonographic examination of the AUT ipsilateral and contralateral to the pregnant horn and one AUM three times per week during the last 4 weeks of gestation. This was followed by the randomized administration of one of the three following experimental drugs per day: isoxsuprine (200 mg/cow, iv), xylazine (2 mg/100 kg, iv), and lidocaine for epidural anesthesia (100 mg/cow). Doppler sonographic examination was repeated 30 minutes after medication. Maternal pulse rate increased during the study period ($P < 0.001$), and the diameter of the contralateral AUT was smaller in the last week before birth than in the two preceding weeks. The resistance index (RI) of the ipsilateral AUT was smaller in the last week than in the first 2 weeks of the study period. Uterine blood flow volume increased after isoxsuprine by 5% and after epidural anesthesia by 6% (both $P \leq 0.05$) and decreased after xylazine by 10% ($P < 0.001$). Isoxsuprine was the only drug that elevated the blood flow volume in the AUM ($P \leq 0.05$). Xylazine increased the RI of both AUT (both $P < 0.001$) and significantly reduced maternal and fetal pulse frequencies, whereas isoxsuprine significantly reduced the RI of both AUT and the AUM and increased maternal and fetal pulse frequencies. The results reported that Doppler sonographic measurements of uterine and AUM change little in the last month of pregnancy in the cow. Isoxsuprine and epidural anesthesia with lidocaine have the potential to improve uterine perfusion.



## 1. Introduction

Color Doppler sonography has become the diagnostic technique of choice in human medicine for assessing placental function and fetal well-being. This imaging modality has been used routinely for years for monitoring pregnant women and to establish a prognosis in conditions such as fetal growth restriction [1]. Doppler sonography is noninvasive and provides information pertaining to pulse waves, vascular resistance, blood flow volumes, and changes in blood flow [2–5]. For example, analysis of blood flow velocity and blood flow resistance in the umbilical arteries (AUM), uterine arteries (AUT), and fetal blood vessels aids in the identification of morphologic changes in the fetoplacental vascular bed.

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Doppler sonography has also been used to study uterine perfusion in cows during normal pregnancy [6–8]. Because the AUT provide the major portion of blood supply to the bovine uterus, changes in blood flow in these vessels reflect changes in uterine perfusion [9]. The cranial half of the uterus also receives blood from the uterine branch of the ovarian artery [10]. Time-averaged maximum blood flow velocity (TAMV) increased, and resistance index (RI), which measures vascular resistance in tissues distal to the point of examination, decreased during pregnancy [6]. Another study reported a massive increase in blood flow volume during the second half of gestation as a function of the birth weight of the calf [8]. The increase was mainly on the basis of an increase in the diameter of blood vessels rather than on an increase in blood flow velocity.

Changes in fetal blood supply through the umbilical vessels have been investigated in several animal species. There has been one study on umbilical blood flow in calves during parturition using sonographic transducers fixed to the umbilical vessels [11], and several others in canine, equine, and ovine fetuses [12–16].

Transabdominal Doppler sonographic examination of an AUM in pony mares at the 5th, 8th, and 10th month of pregnancy revealed a progressive decrease in the ratio between systolic and diastolic blood pressure [12]. In contrast, transrectal Doppler sonographic examination of the AUM in pregnant mares starting at week 19 reported an increase in RI in the last few weeks of gestation [13]. In the pregnant bitch, a progressive increase occurred in the time-averaged maximum velocity in the AUM and a decrease in RI between the 4th and 9th weeks of gestation [14].

Toward the end of gestation, both the placenta and fetus undergo profound maturation processes [15]. One goal of this study was, therefore, to examine the effects of vascular changes in placenta and fetus on Doppler sonographic measurements of the AUT and AUM in the last month of gestation in cows.

In human medicine, a variety of measures are used to determine and prevent fetal hypoxia. These not only include prepartal and peripartal monitoring of uterine, placental, and fetal perfusion but also pharmacologic interventions to improve uterine perfusion in pregnant women and women giving birth [16]. These steps are referred to as intrauterine resuscitation and may include the administration of tocolytic agents to control excessive uterine contractions, in cases of fetal growth restriction or chronic asphyxia [17]. To our knowledge, analogous studies investigating the positive and adverse effects of commonly used drugs on uterine perfusion in pregnant cows have not been published. The drugs most commonly used in bovine obstetrics are lidocaine for epidural anesthesia and isoxsuprine and xylazine. Isoxsuprine, a $\beta_1$- and $\beta_2$-adrenomimetic drug, is used to relax the uterus to facilitate fetal mutations or to exteriorize the uterus during cesarean section. Isoxsuprine relaxes the smooth musculature of the uterus and blood vessels and has a peripheral vasodilatory effect [18,19]. It stimulates $\beta_2$-receptors to activate adenylyl cyclase, which results in an increase in myometrial cAMP and, thus, a decrease in uterine contractility. Isoxsuprine also affects phosphodiesterase, which converts cAMP to AMP [20,21].

Xylazine has the opposite effect. A study in pregnant goats reported that it stimulates postsynaptic uterine $\alpha_2$-receptors causing an increase in uterine tone and a decrease in uterine arterial blood flow [22]. It is used for sedation of fractious animals and also has analgesic and muscle-relaxant properties [23].

Epidural anesthesia with a local anesthetic drug is used mainly during conservative or surgical obstetrical procedures to block the Ferguson reflex and the evacuation reflex. With an appropriate dose of local anesthetic, the anogenital region, the pelvic area, and the proximal part of the udder can be desensitized without inducing recumbency [24]. Epidural anesthesia is used in women for pain control during labor [25] and for cesarean sections because it has fewer adverse effects on uterine and fetal perfusion compared with general anesthesia [26]. Lidocaine is a commonly used local anesthetic and has intermediate efficacy and duration of action compared with other similar drugs. It affects the permeability of the sodium and potassium channels in the cell membrane of neurons, thus blocking the action potential [27]. By blocking $Na^+$ and $K^+$ channels in the dorsal horn neurons of the spinal cord, it stops the transmission of pain-induced stimuli [28].

It is conceivable that isoxsuprine, xylazine, and lidocaine also affect uterine and fetal perfusion in cattle and, thus, are involved in fetal hypoxia. Another goal of this study was, therefore, to examine the effects of these drugs on the hemodynamics of uterine and AUM in cows during the final 4 weeks of gestation.

## 2. Materials and methods

### 2.1. Animals

Seven Braunvieh and two Red Holstein cows, which ranged in age from 3 to 17 years and weighed between 720 and 866 kg, were used. Parity ranged from 2nd to 14th. The cows were brought to our clinic 4 weeks before the calculated due date. They were kept in tie stalls, bedded with straw, and fed hay, grass silage, and water ad libitum. They had daily access to pasture. The cows were moved to a straw-bedded pen on the first signs of calving and remained there until after delivery of the placenta.

The cows underwent daily clinical examination and transrectal manual and sonographic examinations to identify which uterine horn was pregnant and to confirm that the fetus was alive. The sonographic appearance of the amniotic and allantoic fluid was monitored. The calves were examined clinically immediately after birth.

### 2.2. Study design

The cows were placed in a chute and were allowed to eat and drink during sonographic examinations. Before the first examination, the right lower flank was clipped from the ventral midline to the level of the stifle. The examinations, which lasted from 1.5 to 3 hours, started 30 minutes after clipping. During the 4 weeks before the