Ultrasound Studies of the Effects of Certain Poisonous Plants on Uterine Function and Fetal Development in Livestock

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ABSTRACT: Ingestion of locoweed (Astragalus spp. and Oxytropis spp.) by pregnant livestock may result in fetal malformations, delayed placentation, reduced placental and uterine vascular development, hydrops amnii, hydrops allantois, abnormal cotyledonary development, interruption of fetal fluid balance, and abortion. Ultrasonography of pregnant sheep fed locoweed demonstrated that abortion was first preceded by changes in fetal heart rate and strength of contraction and structural changes of the cotyledons, followed by increased accumulation of fetal fluid within the placental membranes and death of the fetus. During pregnancy the toxic agent in locoweed (swainsonine) apparently passes through the placental barrier to the fetus and during lactation through the milk to the neonate. Poison-hemlock (Conium maculatum), wild tree tobacco (Nicotiana glauca), and lunara lupine (Lupinus formosus) all contain piperidine alkaloids and induce fetal malformations, including multiple congenital contractures and cleft palate in livestock. Ultrasonography studies of pregnant sheep and goats gavaged with these plants during 30 to 60 d of gestation suggests that the primary cause of multiple congenital contractures and cleft palate is the degree and the duration of the alkaloid-induced fetal immobilization.

Key Words: Livestock, Poisonous Plants, Fetus, Cleft Palate, Ultrasound

Introduction

Toxic agents from poisonous plants can dramatically affect the embryo, fetus, and neonate in ways that are economically important to the livestock industry. Poisonous plants are ubiquitous on rangelands and pastures and livestock are exposed to toxic agents during critical reproductive periods. Thousands of species of plants in the United States, Canada, and Australia are hazardous when ingested by cattle, sheep, goats, horses, and other animals (Kingsbury 1964; Everist 1974).

Research during the past 40 yr has implicated many plants as causes of embryonic death, abortion, or teratogenesis in livestock. Many of these malformations are undiagnosed and/or unreported because they are attributed to genetic factors and might reduce the value of breeding stock. However, it is now apparent that many livestock losses due to embryonic death, abortion, and teratogenesis are induced by poisonous plants. Estimates of a 1% reduction in calf and lamb crop due to poisonous plants resulting in losses of over $65 million annually in the 17 western states have been reported (Nielsen et al., 1988).

This review discusses the use of ultrasound imaging to describe the fetotoxic effects of the locoweeds and the effects of a group of piperidine and quinolizidine alkaloid-containing plants belonging to the Conium, Nicotiana, and Lupinus genera, which induce similar contracture and palate defects in livestock.
Plants Causing Fetotoxicity

The ingestion of certain poisonous plants during critical periods of gestation alters uterine function and interferes with normal fetal development. The locoweeds of the genus Astragalus and Oxytropis are a large, diversified group of noxious plants that adversely affect livestock reproduction. Locoweed can cause fetal malformations, delayed placentation, reduced placental and uterine vascular development, interruption of fetal locoweed ingestion and include aberrant behavior, that adversely affect livestock reproduction. Locoataxia, weakness, emaciation, rough hair coat, and interferes with normal fetal development. The et al., 1967, 1969, 1981; Van Kampen and James, lar development, hydrops amnii, abnormal high elevations apparently contributes to the onset and incidence of High Mountain Disease (James et al., 1983; Panter et al., 1988b). High Mountain Disease may result from increased vascular resistance and(or) vasoconstriction, thereby leading to right ventricle hypertrophy, cardiac insufficiency, edema, hydrothorax, ascites, and, eventually, death. Similar conditions occur in fetuses of dams that had ingested locoweed. Locoweed-induced vascular resistance or vasoconstriction is thought to be the major cause of fetal heart hypertrophy, dilation, cardiac insufficiency, fluid accumulation, fetal death, and abortion.

Many poisonous plants cause fetal malformations. Species of plants from the Conium, Nicotiana, and Lupinus genera contain piperidine and quinolizidine alkaloids that are toxic and teratogenic to livestock. Conium maculatum (poison-hemlock) (Keeler, 1974; Keeler and Balls, 1978; Keeler et al., 1980; Panter, 1983, Panter et al., 1985a,b), Nicotiana glauca (tree tobacco) (Keeler, 1979; Keeler and Crowe, 1984, 1985; Keeler et al., 1984), Nicotiana tabacum (Burley tobacco) (Crowe, 1969; Menges et al., 1970; Crowe and Pike, 1973; Crowe and Swerczek, 1974), Lupinus caudatus (tail cup lupine) (Shupe et al., 1967; Keeler, 1973a,b, 1976), Lupinus sericeus (silky lupine) (Shupe et al., 1967; Keeler, 1973a,b, 1976), and Lupinus formosus (lunara lupine) (Keeler and Panter, 1989; Panter et al., 1990c) induce congenital birth defects in livestock.

Ultrasound Studies of Locoweed-Induced Fetotoxicity

Until the mid 1980s, studies on the fetotoxic effects of locoweeds required that pregnant females be killed and examined postmortem. The use of real-time ultrasound imaging by Bunch et al. (1986) and Panter et al. (1987) provided a noninvasive approach to observing effects of poisonous plants on fetal growth and development and showed that locoweed induced a series of events that often led to abortion (Panter et al., 1987). Feeding locoweed (Astragalus lentiginosus) to pregnant ewes during gestation d 60 to 100 caused cotyledons, which were normally donut-shaped, to become irregular, solid masses, and they often became atretic and diminutive. Excessive fluid also accumulated within the placenta (hydrops allantois) and was accompanied by irregularities of fetal heart beat. Initially (60 to 70 d of gestation), an affected fetus had a heart rate of 222 beats per minute (bpm) and its heart often fibrillated. As the severity of locoweed intoxication increased in the dam, the fetal heart rate slowed to 63 bpm. Three days later the heart beat ceased and abortion occurred within 40 to 72 h. Fetal heart rate abnormalities seemed to occur concomitantly with cotyledon diminution and hydrops allantois. All affected fetuses exhibited cardiac insufficiency and upon necropsy had enlarged hearts, dilation, and rounding of the right ventricle. None of the fetuses in the control groups exhibited anatomical irregularities.

Ultrasound Studies of Poisonous Plants on Fetal Development

The piperidine alkaloid-containing plants from the Conium, Nicotiana, and Lupinus genera are toxic to livestock and interfere with normal fetal development. Conium maculatum (Panter et al., 1985a,b, 1990a,c) and Nicotiana glauca (Keeler et al., 1984; Panter et al., 1990a) induced cleft palate in pigs and goats and multiple congenital contractures in pigs (Keeler et al., 1984, Panter et al., 1985b), goats (Panter et al., 1990a), sheep (Keeler et al., 1986; Keeler and Crowe, 1984; Panter et al., 1990a), and cattle (Keeler, 1974; Keeler and Balls, 1978; Keeler et al., 1980). Nicotiana tabacum induced multiple congenital contractures in pigs (Crowe, 1969; Menges et al., 1970; Crowe and Pike, 1973; Crowe and Swerczek, 1974). Lupinus caudatus, L. sericeus, and L. formosus induced cleft palate and multiple congenital contractures in cattle (Shupe et al., 1967, 1968; Keeler, 1976; Keeler and Panter, 1989). All of these plants contain teratogenic piperidine alkaloids except L. caudatus and L. sericeus, both of which contain a quinolizidine alkaloid, anagyrine, believed to be the teratogen (Keeler, 1978). Keeler and Balls (1978) hypothesized that teratogenic piperidine alkaloids require a certain molecular structure to be teratogenic. Teratogenic piperidines must contain an
alpha-substituted piperidine ring with an alpha side chain of three carbons or larger. The plants containing piperidine alkaloid are teratogenic in cattle, sheep, and goats, whereas the lupines containing quinolizidine alkaloids are only teratogenic in cows. Keeler and Panter (1989) hypothesized that the cow, through either ruminal metabolism or enzymatic degradation, alters the quinolizidine teratogen to a complex piperidine, thus meeting the proposed structural requirement for teratogenic piperidines. If this proposed metabolic conversion is correct, then the metabolically altered quinolizidines should be teratogenic in sheep and goats also.

Many plant genera contain piperidine alkaloids that meet these teratogenic structural requirements (Keeler and Crowe, 1985). Some of these include Conium, Nicotiana, Lupinus, Lobelia, Pinus, Punica, Duboisia, Sedum, Withania, Carica, Hydrangea, Dickroa, Cassia, Prosopis, Genista, Amondendron, Liparia, Collidium, and others. Their structural similarity to known piperidine teratogens indicates that some of the piperidine alkaloids in these plants may be teratogenic (Keeler and Crowe, 1985).

Plants containing piperidine alkaloid with structures associated with teratogenicity cause a variety of multiple congenital contracture-type skeletal malformations and cleft palate. Conium maculatum contains eight known piperidine alkaloids, of which coniine and gamma coniceine seem to be teratogenic in cattle, pigs, sheep, and goats (Keeler, 1974; Keeler et al., 1980; Panter, 1983). Nicotiana glauca and N. tabacum contain numerous piperidine alkaloids including anabasine, a proven teratogen (Keeler et al., 1984; Keeler and Crowe, 1985). Lupinus formosus contains the piperidine alkaloid ammodendrine believed to be the teratogenic alkaloid (Keeler and Panter, 1989; Panter et al., 1990b). The quinolizidine alkaloid, anagyrine, believed to be teratogenic in cattle is not teratogenic in sheep and goats (Keeler, 1984; Panter et al., 1990a). Teratogenic effects include multiple congenital contractures resulting in fixed extension or flexure of the carpal, tarsal, or fetlock joints, enlargement of these joints, lateral deviation of the forelimbs, scoliosis, torticollis, lordosis, and cleft palate (Shupe et al., 1967, 1968; Keeler, 1974, 1976; Keeler and Balls, 1978; Keeler and Crowe, 1984; Keeler et al., 1984; Panter et al., 1985a,b, 1990a,c; Keeler and Panter, 1989).

Cleft palate and multiple congenital contractures are associated with the inhibition of fetal movement (Panter et al., 1990a). Panter (1983) associated sedation and relaxation in pregnant sows fed Conium to cleft palate and multiple congenital contractures in their offspring. Later, Panter et al. (1985a,b) stated that Conium alkaloids may cross the placenta and elicit a similar sedative and anesthetic effect on the fetus. Panter et al. (1988a) gavaged Conium maculatum (5.4 to 6.0 g/kg) to pregnant ewes twice daily during d 30 to 60 of gestation. Conium had been previously reported to cause multiple congenital contractures in cattle and cleft palate and multiple congenital contractures in pigs (Keeler and Balls, 1978; Panter et al., 1985a,b). Real-time ultrasound showed a significant reduction in fetal movement in Conium-treated ewes, although the lambs were born with normal palates and with only slight to moderate carpal flexure of the front legs, which was resolved by 8 wk of age. Because the sedative and anesthetic effects on fetal movement did not persist between gavages, Panter et al. (1988a) suggested that the duration of reduced fetal movement may be the most critical factor leading to cleft palate and permanent limb, spine, and neck deformities.

Panter et al. (1990b) observed fetal movement in normal sheep and goats with ultrasound to determine normal movement patterns beginning 3 wk after mating until 110 d of gestation. Fetal movements were recorded for 5 min once a week. Increased fetal activity occurred between d 38 and 50 and there was a second, more prolonged, increase between d 65 and 90. Panter et al. (1990b) hypothesized that the early rise in activity is important for palatal plate closure and normal skeletal development. Immobilization of the head and neck muscles that may obstruct the tongue may prevent palate closure. They also hypothesized that the lack of fetal movement could result in postural or uterine molding of the skeletal system.

The correlation of cleft palate and multiple congenital contractures and inhibition of fetal movement has been further substantiated by Panter et al. (1990a,c). Palate closure in goats occurs near d 38 when fetal movement is initiated. Fetal movement peaks between d 40 to 60, which is concomitant with rapid musculoskeletal development. Pregnant goats were gavaged during d 30 to 60 of gestation with Conium maculatum seed (3.5 g/kg) and fall growth (10.8 g/kg), Nicotiana glauca (6.3 g/kg), and Lupinus caudatus (13.1 g/kg). Fetal movement was inhibited in dams receiving Conium or Nicotiana but not in those given Lupinus caudatus. Conium (seed) and Nicotiana also resulted in 100% cleft palate and multiple congenital contractures, which indicates that both types of malformations are probably caused by the inhibition of fetal movement. Lupinus caudatus did not reduce fetal movement in intoxicated dams, and their offspring had normal palate closure and skeletal development.
Implications

Poisonous plants cause substantial loss to the livestock industry through altered reproductive function. Until recently, the mode of action of many of these plants on reproductive processes was poorly understood. Ultrasound imaging provides a method of observing fetal development and reproductive processes in the live animal, thus increasing our understanding of these physiological processes and the manner in which poisonous plants affect them. Through increased understanding of the mode of action and diagnosis, methods of management and treatment may be developed or improved to reduce losses to the livestock industry.

Literature Cited


