Reserpine toxicosis in an aged gelding

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Keywords: horse; fasciculations; gelding; phimosis; priapism; reserpine; toxicosis

Introduction

Reserpine is an indole alkaloid obtained from the root of Rauwolfia serpentine (Oates 1996). It is prescribed in human medicine to treat high blood pressure and calm severely agitated mental health patients and acts by decreasing heart rate, decreasing cardiac contractility and relaxing blood vessels (Benowitz 1995). Reserpine is not approved for use in horses; nevertheless, this drug is sometimes administered for prolonged tranquillisation. Reserpine has also been reported useful for treatment of agalactia in mares associated with fescue toxicosis, although the current treatment of choice is domperidone, a DA2 dopamine receptor antagonist that does not cross the blood-brain barrier, thus resulting in fewer side effects (Evans et al. 1999).

In this article we report on a Thoroughbred gelding who received reserpine for intended prolonged sedation and was subsequently admitted for further examination following onset of clinical signs.

Case details

History

A 26-year-old Thoroughbred gelding weighing 475 kg presented to the Michigan State University Veterinary Teaching Hospital 12 h after receiving 10 mg of a compounded formulation of reserpine i.m. Reserpine was administered as a long-term sedative to reduce excitement produced by nearby construction. Approximately 5 h after injection, clinical signs were noted prior to referral, which included agitation (stall walking), hyperexcitability, muscle fasciculations, sweating over the entire body, priapism, upper respiratory sounds associated with nasal congestion, diarrhoea and apparent abdominal discomfort.

At presentation, hyperexcitability, muscle fasciculations involving skeletal muscle groups over the entire body, nasal congestion, sweating and priapism persisted but colic signs were no longer observed. When stimulated, agitation and fasciculations increased and the horse appeared to tremble. Further examination revealed an elevated heart rate of 52 beats/min, respiration rate 16 breaths/min, rectal temperature 38.2°C and mild dehydration (estimated at 5%). Rectal examination was normal and passage of a nasogastric tube did not yield reflux of gas or stomach contents. No evidence of small intestinal distension was detected on transabdominal ultrasonographic examination and motility was subjectively assessed as normal.

Diagnostic procedures

A complete blood count revealed a mature neutrophilia (6.51 x 10⁹/l; hospital reference range [hrr] 3.04 x 10⁹–6.36 x 10⁹/l), consistent with stress, but no other abnormalities. Serum biochemistry results revealed a slightly elevated creatinine (19 mg/l; hrr 8–18 mg/l) and elevated total bilirubin concentration (31 mg/l; hrr 1–21 mg/l). Venous blood gas results were within normal limits. Fluid obtained from an abdominocentesis was translucent yellow and had an estimated total protein concentration (via refractometry) of less than 25 g/l; consequently further cytological evaluation was not pursued.

Treatment

An i.v. catheter was placed into the jugular vein and isotonic fluid administered at a rate of 2–3 l/h for the initial 12 h. The referring veterinarian had administered flunixin meglumine (1 mg/kg bwt, i.v.) 2 h prior to admission. Signs of abdominal pain were no longer apparent at admission so additional analgesic medication was not deemed necessary. When the horse exited the trailer on admission, a full skin thickness laceration resulted over the palmar aspect of the right front metacarpus. The wound sustained during the trailer ride was cleaned and bandaged during the initial work-up. The horse was current on tetanus prophylaxis; thus no other treatments were administered at that time. Due to historical signs of abdominal pain, food was withheld for the initial 12 h. Water...
was available but the gelding did not drink during this period. Clinical signs did not change markedly during the initial 8 h of hospitalisation. Muscle fasciculations were continuous and increased with stimulation (physical examination or activity in his stall) and sweating was localised to the areas under the mane, chest, flank and under the tail. The penis remained prolapsed over the initial 12 h of hospitalisation. There were no signs of oedema and the penis was not placed in a sling during this period.

Twenty-four hours after reserpine administration, vital parameters were within normal limits. The gelding had intermittent muscle fasciculations but sweating and nasal oedema resolved and the priapism had improved. Soft faeces were produced rather than fluid diarrhoea and the gelding ate a flake of hay. There were no signs of abdominal discomfort at this time. The gelding's upper eyelids were slightly drooped and there was an appearance of mild sedation. Stimulation with noise or quick movements produced transient excitement, increased alertness, stall walking and more prominent muscle fasciculations. The laceration over the right front leg was sutured in a mattress pattern and bandaged at this time. Local anaesthesia and a twitch were used for restraint.

Approximately 30 h after reserpine administration, the gelding appeared to be having periods of altered consciousness (mildly base-wide stance and lack of response to the observer) accompanied by swaying and sudden movements as if startled in the absence of external stimuli. The gelding appeared to be focusing on a location on the stall wall but would readily respond to visual stimuli. Muscle fasciculations had resolved by this time, although stimulation would initiate transient fasciculations. Partial penile prolapse was now accompanied by paraphimosis; therefore towel clamps were used to maintain the penis in the sheath and a sling was used for additional support. Intravenous fluids were discontinued after 24 h. Further treatments for the laceration included administration of flunixin meglumine (1 mg/kg bwt i.v. q. 24 h) and procaine penicillin (22,000 units/kg bwt i.m. q. 12 h) for 3 days starting 12 h after presentation.

Formed faeces were being passed 30 h after presentation and food and water intake was normal. Clinical signs resolved within 48 h except for occasional muscle fasciculations (when excited) and paraphimosis. By the fourth day, the horse appeared normal. The gelding was sent home 5 days after admission.

Discussion

Reserpine is an indole alkaloid obtained from the root of Rauwolfia serpentina (Oates 1996). It is prescribed in human medicine to treat high blood pressure and calm severely agitated mental health patients and acts by decreasing heart rate, decreasing cardiac contractility and relaxing blood vessels (Benowitz 1995). These effects are obtained by depletion of catecholamines and serotonin stores in many organs (particularly norepinephrine in the heart) and by reducing the uptake of catecholamines by sympathetic neurons (Moss and Craigo 1994). Diminished sympathetic tone can also relax capacitance vessels (veins), which reduces total peripheral resistance, resulting in an additional decrease in blood pressure (McEvoy 1999). Reserpine is not approved for use in horses; nevertheless, this drug is sometimes administered for prolonged tranquillisation. Reserpine has also been reported useful for treatment of agalactia in mares associated with fescue toxicosis, although the current treatment of choice is domperidone, a D2 dopamine receptor antagonist that does not cross the blood-brain barrier thus resulting in fewer side-effects (Evans et al. 1999).

Adverse effects observed with administration of reserpine in man include sympathoplegia, sedation, nightmares, depression, Parkinsonian symptoms, bradycardia, increased airway resistance and gastrointestinal disturbances (diarrhoea, cramps and increased gastric acid secretion). Adrenergic inhibition produces increased gastrointestinal motility, increased gastric acid secretion and miosis (Moss and Craigo 1994; Benowitz 1995; Oates 1996; McEvoy 1999). In horses, these effects may cause clinical signs of colic. Large doses produce respiratory depression and decreased body temperature. Sympathetic inhibition produced by the drug may result in vasodilation, an effect that results in hypotension as well as nasal congestion (McEvoy 1999). The resulting hypotension can be particularly troublesome in anaesthetised horses.

The effects of reserpine are prolonged due to inactivation of catecholamine storage granules. Reserpine detection can be difficult due to the rapid clearance from circulation after a single dose (Benowitz 1995). Therefore, this drug has become an enigma in competitive performance as trainers can administer a single dose of the drug prior to a competition or sale and often escape detection by blood tests. Reserpine can be detected by high-performance liquid chromatography (HPLC; Chapman et al. 1991) and this technique is more sensitive when combined with an ionspray or ion trap method, although detection is variable beyond 48 h (Anderson et al. 1997). The United States Equestrian Federation (USEF) tests for reserpine administration using an HPLC/mass spectroscopy ion trap method. Reserpine is detectable in blood, but not urine, and can remain detectable for longer periods of time depending on the dose administered and if multiple doses have been given. The USEF recommends a 90 day withdrawal period prior to competing after reserpine administration. The penalty for a horse testing positive for reserpine at a USEF recognised/governed competition is at the discretion of the hearing committee and can result in up to 9 months of suspension from competition and $8000 in fines (J. Lengel, USEF Equine Drug Medication Director, personal communication).

Suggested doses in human medicine range from 0.05–0.25 mg/day and are normally administered orally (Benowitz 1995; Oates 1996). A report from 1956 suggested administering 1 mg/450 kg bwt parenterally in horses for sedation but discouraged doses greater than 5 mg orally due to resulting signs of colic (Earl 1956). In 1978 a study examining reserpine pharmacokinetics reported that 10 mg of...
reserpine administered i.v. caused sweating, flatulence, miosis, upper eyelid ptosis and depression in horses (Tobin 1978). A 0.25% solution for i.m. administration is formulated by compounding companies. The horse in this case was administered 10 mg, which is more than 4 times the suggested dose (Earl 1956).

Reserpine is considered a safe drug for treatment of mild to moderate hypertension in man if dosed appropriately. However, in human patients there is a concern that at any time during treatment, despite months of uneventful treatment, the side effects discussed earlier may be seen (Benowitz 1995). A similar case of reserpine toxicosis in a horse was reported in 1985. Findings included colic-like behaviour, depression, bradycardia, upper airway noise, paraphimosis, miosis and ptosis. This horse was administered 12.5 mg reserpine and 200 mg xylazine i.v. as sedation for blistering. Clinical signs improved in approximately 72 h with supportive care. High performance liquid chromatography was used to detect reserpine in the blood from the reported case at 72 h but no reserpine was detectable 9 days post administration (Lloyd et al. 1985). Because of the deficiency of studies involving dose, safety and efficacy of reserpine in equine patients and its restrictions by competitive governing organisations, this drug warrants caution when considering its use.

**References**


