Pferdeheilkunde 32 (2016) 6 (March/April) 103-109

Clinical findings, treatment and resolution of Simplex® toxicity in three horses

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Summary: Three horses were presented two hours after accidental ingestion of plants contaminated with Simplex®. Simplex®, containing aminopyralid (30 g/l) and fluroxypyr (100 g/l), is an herbicide used against common ragwort. The toxic effect of both ingredients is probably induced by free acid, but an effect of dissociated fluoride ions of fluroxypyr is conceivable, too. At presentation, all horses showed a moderate impairment of their general condition, appeared sedated with intestinal hypomotility and showed symptoms of marked conjunctival irritation. A mild ataxia and cardiac arrhythmia were observed in one horse. Within one day, all horses revealed a slight decrease in plasma calcium concentration, two horses developed a mild oral ulceration and one horse a mild skin irritation in the area of the mouth. The initial treatment consisted of minimising absorption from the gastrointestinal tract and increasing urinary excretion. To counteract any damage induced by dissociated fluoride ions, calcium gluconate was administered as a continuous rate infusion. Initially, an irrigation of the stomach with 1% calcium gluconate was performed, and the horses received a resuscitative intravenous fluid therapy with Ringer`s solution and 23% calcium gluconate. Subsequently, a lavage of the eyes was performed. Over 36 hours Ringer s solution was administered, and sucralfate (40 mg/kg bwt/tid p.o.) was given over three days. On day five and day six two horses and one horse, respectively were discharged without abnormal clinical or laboratory findings. Follow-up enquiries after 3 months with the owners indicated that the horses were healthy, sound and had returned to their previous level of work. To our knowledge, these are the first documented clinical cases of Simplex® toxicity in horses.

Keywords: horse / Simplex® / fluroxypyr / aminopyralid / toxicity / calciumgluconate

Citation: Michutta J.-I., Cavalleri J.-M., Ohnesorge B. (2015) Clinical findings, treatment and resolution of Simplex® toxicity in three horses. Pferdeheilkunde 32, 103-109

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Introduction

Simplex® is a widely used herbicide to eradicate broad-leaf weeds, especially creeping thistle (Cirsium arvence), spear thistle (Cirsium vulgare) and dock (Rumex longifolius) (Norwegian Scientific Committee for Food Safety 2010). It is applied to established grassland; forage, pasture and grass during the first year of sowing. Additionally, Simplex® is frequently used to eradicate common ragwort (Senecio jacobaea) on pasture grazed by horses. According to the producer's instructions, it is possible to reuse the pasture for horses after a grazing restriction of seven days. Up until now no side effects in horses have been reported in literature after applying Simplex® according to the instructions. This case report illustrates the clinical signs, the possible treatment and the outcome of accidental ingestion of stinging nettles contaminated with Simplex® in three horses.

The Norwegian Scientific Committee for Food Safety (2010) emphasised that exposure to the product poses a risk to human and animal health, for example if swallowed, risk of serious damage to the eyes and skin irritation. Simplex® contains the active substances aminopyralid (30 g/l) and fluroxypyr (100 g/l). Aminopyralid (4-amino-3,6-dichloropyridine-2-carboxylic acid) is a growth regulator herbicide that mimics the action of the plant hormone auxin. By binding to auxin receptor proteins, aminopyralid disrupts physiological processes and leads to plant death (*Hartzler* 2006). According to an evaluation report of Simplex® (Norwegian Scientific Committee for Food Safety 2010), aminopyralid was characterised by a low acute toxicity after oral, dermal and inhalation administration. In addition, no evidence for a genotoxic or teratogenic potential was observed, but carcinogenic effects based on an increased number of uterine sarcomas in mice were proposed (The Norwegian Food Safety Authority 2010). Furthermore, the United States Environmental Protection Agency (2005) described an absorption rate of 77–86% in rabbits, with the highest distribution concentration in the skin of rats, detectable levels in the gastrointestinal tract and low concentrations in the kidneys, liver and spleen. Aminopyralid was mainly excreted unchanged through the urine with no evidence of it having any detrimental effects on the metabolism in rabbits and rats (United States Environmental Protection Agency 2005; The Norwegian Food Safety Authority 2010). Access to specific data concerning the effects and cell mechanisms after intoxication with aminopyralid was restricted.

The second active substance of Simplex®, fluroxypyr (1-methylheptyl-4-amino-3,5-dichloro-6-fluoro-2-pyridyloxyacetic acid), also induces auxin-type responses in plants to control their growth mechanism (Washington State Department of Transportation 2006). However, fluroxypyr is classified as a substance with low acute toxicity, having no potential for genotoxicity, teratogenocity or reproductive toxicity (European Food Safety Authority 2011). Therefore, it is not likely to be a human carcinogen (*Tao* 2011). In contrast, acute oral, dermal and inhalation toxicity were observed in a series of studies on laboratory animals (United States Environmental Protection Agency 1998, Washington State Department of

Transportation 2006). In the context of high-dosage toxicity studies, laboratory animals were affected by gastric ulceration, caecal enlargement, skin and eye irritation, ataxia and renal dysfunctions after administering one or both substances (United States Environmental Protection Agency 2005, The Norwegian Food Safety Authority 2010). According to a review of pesticide risk assessment, the oral absorption of fluroxypyr was estimated to be higher than 90% with no evidence for accumulation (European Food Safety Authority 2011). Similar to aminopyralid, data on the exact toxicological effects are lacking. To the authors' knowledge, no case report documenting the clinical signs, treatment and outcome of horses after accidental ingestion of aminopyralid and fluroxypyr has previously been written.

Case report

History

A 21-year-old Arabian-Berber gelding (475 kg, BCS 6/9, horse 1), a 17-year-old mixed breed mare (412 kg, BCS 7-8/9, horse 2) and an 11-year-old mixed breed gelding (398kg, BCS 7/9, horse 3) were presented at the clinic after being fed a bunch of stinging nettles that had been treated with 1L of Simplex® solution two hours earlier. This amounts to a potential ingestion of 100 g fluroxypyr and 30 g aminopyralid in total. As the horses were kept on a paddock together, the amount of toxin ingested per horse could not be determined.

Clinical findings

Upon presentation the horses were moderately depressed (Fig. 1). The mucous membranes were injected with a prolonged capillary refill time of 3–4 seconds. In all three horses a moderate tachycardia (60–72 beats/min) and intestinal hypomotility in all quadrants detected by abdominal auscultation were present. Horse 1 showed mild ataxia and cardiac arrhythmia. All of the three horses showed slight to marked bilateral conjunctival redness, epiphora and a mild to moderate chemosis without corneal lesions (Fig. 2). Initial laboratory investigations revealed mild hyperlactataemia in two horses (horses 1, 2) and mild azotemia in one horse (horse 1).

Treatment

As initial treatment, irrigation of the stomach in all horses was performed with 1% calciumgluconate. After irrigation, 5L 1% calciumgluconate was left in the stomach to further protect the gastrointestinal tract. Unilateral intravenous jugular catheters were placed and resuscitative intravenous fluid therapy was initiated with a bolus of lactated Ringer`s solution and 23% calciumgluconate solution. Subsequently, an exhaustive lavage of the eyes with isotonic saline, followed by application of calcium gluconate drops was performed. After initial treatment all horses received a continuous rate infusion with Ringer s solution (60 ml/kg bwt/day i.v.) for the first 36 h to induce diuresis. Additionally, due to the risk of gastrointestinal lesions, the horses received sucralfate (40 mg/kg bwt/tid p.o.) for 3 days. For five days an eye ointment containing panthenol was administered six times a day until signs of conjunctivitis had subsided.

Over the course of the first day all horses developed a slight decrease in ionised calcium concentration, two horses (horses 1, 3) showing mild oral ulceration (Fig. 3) and horse 1 developing a mild irritation in the area of the mouth (Fig. 4). On day five two horses (horses 1, 3) and on day six horse 2 were discharged without clinical or laboratory findings. Follow-up enquiries with the owners indicated that the horses were sound and had returned to their previous level of work 3 months later.

Discussion

To the authors' knowledge, these are the first documented clinical cases of Simplex® toxicity in horses. Therefore, no existing data were available concerning the effect, the pathological mechanism and sensitivity to aminopyralid and fluroxypyr in horses. In comparison, a large number of studies in

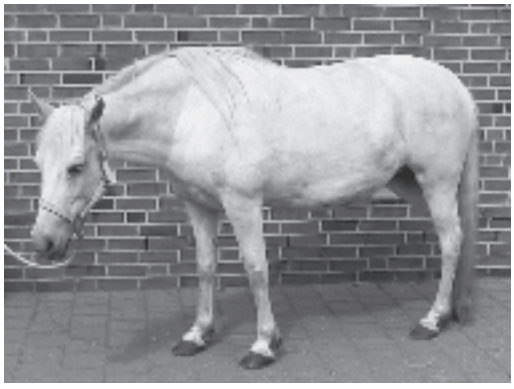

Fig. 1 Horse 1 after initial presentation to the clinic, 2 hrs after accidental ingestion of Simplex® contaminated plants with a sedated appearance at the time of presentation with lowered head and marked lethargy.
Pferd 1 zum Zeitpunkt der Erstuntersuchung ca. zwei Stunden nach Aufnahme von mit Simplex® kontaminierten Pflanzen. Das Pferd zeigt ein deutlich reduziertes Allgemeinbefinden einhergehend mit einer Lethargie und einer gesenkten Kopf-Hals-Haltung.

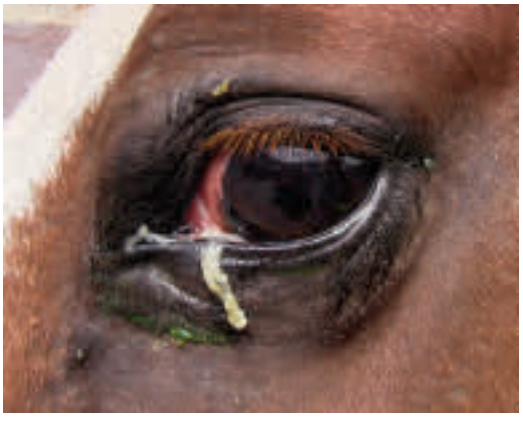

Fig. 2 Marked scleral and conjunctival redness, epiphora and a mild to moderate chemosis without corneal defect (fluorescein-test negative) 2 hrs after exposure to Simplex®.
Deutliche konjunktivale und sklerale Rötung, Epiphora, sowie gering- bis mittelgradige Chemosis ohne Hinweis auf einen cornealen Defekt (Fluoreszein-Test negativ) zwei Stunden nach dem Kontakt mit Simplex® kontaminierten Pflanzen.

laboratory animals have been conducted in the context of licence processes of different products. Similar to the presented horses, laboratory animals developed gastrointestinal side effects, exhibited ataxia, hind limb weakness, skin and eye irritation after high dosages of one or both substances (United States Environmental Protection Agency 1998).

After exposure to a total dosage of 100 g fluroxypyr and 30 g aminopyralid, the patients revealed clinical signs such as a sedative appearance, this being the case in all horses and mild ataxia in one horse. These signs were consistent with the clinical findings in laboratory animals. Especially in aminopyralid toxicity studies, behavioural alterations are documented. According to an evaluation report (The Norwegian Food Safety Authority 2010), transient incoordination was a consistent finding in pregnant rabbits after high dosages of aminopyralid. The authors suggest that the bioavailability of aminopyralid in late-stage pregnant animals is greater than in non-pregnant or early stage pregnant individuals. However, in this previous report evidence or suspected mechanism of the mode of action was given, but in contrast the authors stated that aminopyralid did not result in any neurotoxic effects (The Norwegian Food Safety Authority 2010). Concerning the potential for neurotoxicity of fluroxypyr, the literature is also contradictory: A study in dogs observed exhibited ataxia and hind limb weakness after dosages of 500 mg/kg/d fluroxypyr (United States Environmental Protection Agency 1998). Nevertheless, in a more recent toxicity study no potential for neurotoxicity was documented (European Food Safety Authority 2011). Similar to aminopyralid, the mechanism of action was unknown. An additional finding in a recent evaluation report describes drowsiness and dizziness caused by vapours after application of the co-formulation Simplex® (European Food Safety Authority 2011). In this research evidence of the mechanism of action is again lacking. Thus, in these patients not only the ingestion of the afore-mentioned herbicide, but also the effects thereof due to inhalation should be taken into consideration.

In human medicine, skin contact with fluroxypyr is one of the major routes for systemic exposure. Therefore, the metabolism of fluroxypyr methyl ester (FPM), fluroxypyr methylheptyl ester (FPMH) and fluroxypyr (FP) in the skin has been well documented (*Hewitt* 2000a, *Hewitt* 2000b). In a human and rat skin in vitro study, *Hewitt* et al. (2000b) demonstrated that only the hydrolysis product FP penetrates the skin and induces a systemic exposure after skin contact. However, after diffusion through the stratum corneum into the underlying layers, FPM and FPMH were rapidly metabolised to the acid metabolite FP by an active enzyme system including carboxylesterasen (*Hewitt* 2000b). While systemic exposure with fluroxypyr via the skin is possible, no systemic toxic effects in rats after administering aminopyralid in a 28-day toxicity study were observed (United States Environmental Protection Agency 2005). Otherwise, for the co-formulation Simplex® a dermal absorption of 80% was set (The Norwegian Food Safety Authority 2010) so that systemic exposure is most likely. Besides systemic exposure via skin also local skin irritations have been observed. Similar to laboratory animals, one horse revealed mild dermal affections 24 hours after skin contact in the area of the mouth. In an acute toxicity study with fluroxypyr, rabbits also developed slight skin irritation that subsided after 48 hours (United States Environmental Protection Agency 1998). Comparable reports exist for aminopyralid. After skin exposure, dermal desquamation (The Norwegian Food Safety Authority 2010), slight erythema that subsided after seven days (rabbits), and an epidermal hyperplasia (rats) were detected (United States Environmental Protection Agency 2005). Consistent with the findings in laboratory animals, in the affected horse the skin irritation subsided after 3 days without treatment. For both substances, no evidence for skin

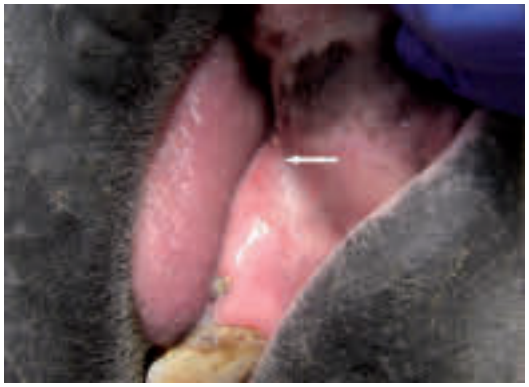

Fig. 3 Mild oral ulceration (arrow) 24 hrs after accidental ingestion of Simplex® contaminated feed
Milde Maulschleimhautulzeration (Pfeil) 24 Stunden nach der Aufnahme von mit Simplex® kontaminierten Pflanzen

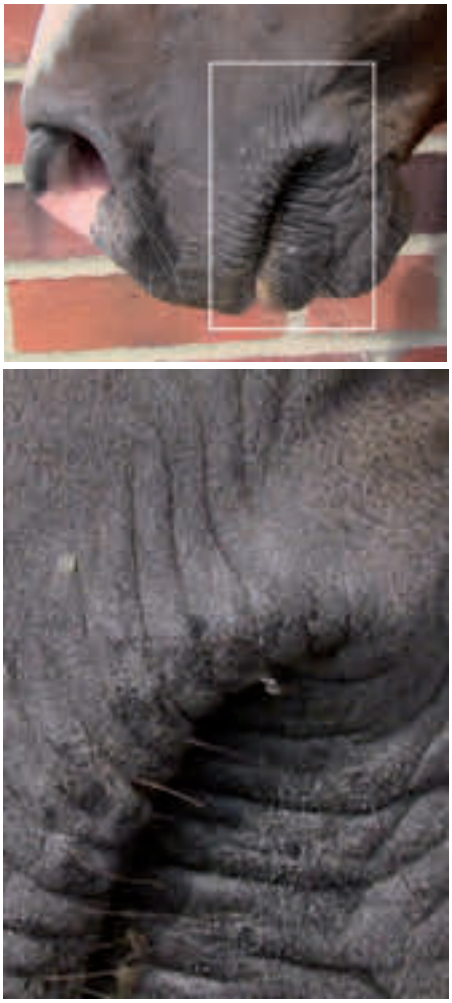

Fig. 4 Dryness, cracking and a slight desquamation of the skin in the area of the lips 24 hrs after contact with Simplex®
Trockenheit, Rissbildung und leichte Schuppung der Haut im Bereich der Maulspalte 24 Stunden nach Kontakt mit Simplex®

sensitisation was observed (The Norwegian Food Safety Authority 2010).

After administering aminopyralid, laboratory animals developed gastric ulcers and erosions (rats, rabbits), slight diffuse hyperplasia and hypertrophy of the mucosal epithelium of the stomach (dogs), and hyperplasia of the mucosal epithelium of the ileum and caecum (rats) (United States Environmental Protection Agency 2005, The Norwegian Food Safety Authority 2010). In chronic aminopyralid feeding studies, also a caecal enlargement (rats) and a thickening of the stomach wall (dogs) were observed (United States Environmental Protection Agency 2005). Additionally, in rabbits a decreased faecal volume and dark watery caecal contents were recognised after high dosages of aminopyralid (The Norwegian Food Safety Authority 2010). In fluroxypyr toxicity studies, a slight to moderate acute gastroenteritis (dogs), emaciation and decreased food intake (rats, dogs) were noticed (United States Environmental Protection Agency 1998). Similar to the studies in laboratory animals, all presented horses showed signs of intestinal hypomotility, but none of gastrointestinal inflammation or abdominal discomfort. Furthermore, two horses developed mild oral ulcerations over the first 24 hours after exposure. While the gastrointestinal reaction to aminopyralid is likely to be mainly induced by the free acid effect, in fluroxypyr an additional effect of dissociated fluoride ions is conceivable besides the acidic effect. In human medicine, acute toxicity after ingesting fluoride has been well described. Especially in children, dental products are a common source for fluoride intoxication and induce temporary gastrointestinal effects, like nausea, vomiting of blood and diarrhoea after overexposure (*Whitford* 2011). Based on the strong affinity of fluoride for calcium, muscular and cardiovascular dysfunction related to electrolyte imbalances occurred after a severe overexposure (*Whitford* 2011). Consistent with these findings, the presented horses developed mild hypocalcaemia after accidental ingestion of Simplex®. Consequently, one could speculate that the hypocalcaemia was a result of an effect of fluoride ions binding to calcium. In horses fluorosis is a rare condition and only a few older reports exist. In one previous report, *Shupe* and *Olson* (1971) described the clinical aspects of chronic fluorosis in several horses. These horses were presented with a rough coat appearance, lameness and stiffness, thickening of the skull bones, hyperostotic lesions and excessive abrasion of the teeth after unknown dosages of fluoride. The authors also describe that horses show a relatively high tolerance for fluorine, in contrast to cows. In the report a tolerance value of 60 ppm for sodium fluoride or other fluorides with the same toxicity for breeding or lactating animals was given (*Shupe* et al. 1971). In addition, *Damman* et al. (1904) noticed an acute fluorine toxicity in horses after consuming 100 mg sodium fluoride (*Damman* et al. 1904). In the presented cases the amount of dissociated fluoride ions was unknown so that an effect based on this pathomechanism is only speculative. One should also take into account that fluroxypyr shows only a low solubility in water so that a release of a large amount of fluoride ions was most unlikely. Otherwise, other studies observed an effect of a small amount of fluoride ions, especially that of local irritation. *Whitford* et al. (2011) demonstrated that not the total amount of fluoride ions but in fact the fluoride concentration in the solution in the stomach influenced the severity of gastric damage. Therefore, it cannot be completely ruled out that gastric ulceration may have occurred here in this case series. However, since gastroscopic examination was not performed, there is no evidence supporting this hypothesis. Likely, for horses, the development of gastrointestinal side effects due to local mucosal damage was one of the major risk factors after accidental ingestion of Simplex®.

Comparable with laboratory animals, the horses developed slight to marked eye irritation, presumably caused by the substances containing vapours rather than direct contact. Initially, at the time of referral the horses showed marked conjunctival redness, bilateral epiphora and chemosis concordance with the findings in rabbits, where Simplex® was characterised as being a "risk to serious damage eyes" (The Norwegian Food Safety Authority 2010). Without clear evidence for the mechanism of action, eye irritation is most likely caused by the acidic effect of both substances. In addition, an effect of dissociated fluoride ions originating from fluroxypyr is conceivable. Therefore, an initial local treatment with an exhaustive lavage with isotonic saline followed by application of calcium gluconate drops was performed. Additionally, over five days an eye ointment containing panthenol was administered six times a day. In all horses the signs subsided over the course of three to five days.

The initial treatment in these patients was undertaken to minimise ongoing absorption of toxins from the gastrointestinal tract and to increase their urinary excretion. Based on the potential risk of damage induced by dissociated fluoride ions, the initial irrigation of the stomach was performed with 1% calcium gluconate. Subsequently, 5 L 1% calcium gluconate solution were instilled into the stomach to prevent further absorption and mucosal damage. This procedure is consistent with the guidelines for fluoride toxicity in human medicine. Following acute toxicity of ingested fluoride, administering 1% calcium chloride or calcium gluconate or, alternatively milk orally is recommended (*Whitford* 2011). In human medicine several studies indicate the ameliorative effect of calcium for reducing fluoride-induced damage (*Vance* et al. 1986, *Chinoy* et al. 1993, *Graudins* et al. 1997, *Roblin* et al. 2006, *De Capitani* et al. 2009, *Yu* et al. 2013). Recently, *Wang* et al. (2014) described the different injury mechanism of fluoride ions after hydrofluoric acid burns. The authors stated that the calcium- and magnesium-binding effect of fluoride ions resulted in an increased permeability of the cell membrane for potassium ions. Following calcium depletion, also nerve stimulation is induced by the cellular release of potassium, in bone tissue decalcification and necrosis have been observed, and after absorption into the blood circulation major electrolyte imbalances resulted which induced arrhythmias and coagulation disorders (*Wang* et al. 2014). Administering calcium gluconate has a neutralising effect by binding fluoride ions, forming insoluble salts and blocking the fluoride ions from infiltrating into tissues (*Sheridan* et al. 1995, *Wang* et al. 2014). Additionally, a marked electrolyte imbalance could be avoided. In the presented cases, only one horse showed arrhythmia at presentation, but there was no incident of hypocalcaemia. Over the course of one day, the arrhythmia subsided. None of the horses developed a marked hypocalcaemia, and only a slight decrease in the calcium concentration was observed. Otherwise, the alteration in the calcium level could be evidence for the existence of free fluoride ions in the presented cases. It should also be considered that the fact

that the horses did not develop hypocalcaemia was presumably due to the treatment regime of administering calcium gluconate orally and intravenously. Furthermore, treatment was directed at increasing diuresis. In laboratory animals the kidney is one target organ of both substances (European Food Safety Authority 2011). In chronic toxicity studies in laboratory animals, an increased severity of chronic progressive glomerulonephopathy after fluroxypyr administration was observed (United States Environmental Protection Agency 1998). Therefore, the presented horses received Ringer s lactate solution (60 ml/kg bwt/day i.v.) for 36 h after initial treatment. None of these horses developed clinical or laboratory signs of renal dysfunction. Follow-up enquiries with the owners indicated that the horses were healthy, sound and had returned to their previous level of work 3 months later.

Due to the occurrence of these cases of intoxication as a last step it should be discussed whether or not alternative preventive measures and methods for using chemical herbicides such as Simplex® for eradicating common ragwort are preferable. In particular, pasture management plays a crucial role in establishing and spreading ragwort. Due to the fact that horses selectively eat certain areas of pasture and urinate and defaecate only in other areas vegetation redistribution occurs. The poisonous plants are able to grow particularly in the areas which have been eaten. Additionally, the destruction of the sward by hooves on wet ground leads to more favourable growth conditions for common ragwort. For this reason the upkeep of sward to prevent ragwort from establishing is one of the most important factors. This can be realised by avoiding under- and overgrazing, by regular removal of faeces, by removing poisonous plants before they flower, as well as by the upkeep of an intact sward by not allowing the animals for example to graze on softened ground (Department for Environment, Food and Rural Affairs 2004).

If there has already been an increased occurrence of ragwort in the case of moderate contamination it is recommended to remove individual plants including the roots before seed production. In the case of stronger contamination mowing the pasture could be an option. However, here the production of seeds can occur later and additionally, there is a risk of exposure of the animals to parts of poisonous plants left behind (Department for Environment, Food and Rural Affairs 2004).

As a long-term strategy additionally biological eradication methods are discussed. This includes the use of natural predators of the plants such as the cinnabor moth (Tyria jacobaea), the ragwort flea beetle (Longitarsus jacobaea) and the ragwort seedfly (Pegohylemia seneciella). Also various fungal pathogens (rust diseases) are used. Nevertheless, through these measures a signficant reduction in the ragwort population is seldom achieved (Department for Environment, Food and Rural Affairs 2004).

In conclusion, the authors recommend that the treatment of horses with Simplex® intoxication after accidental ingestion should be based on the elimination of the substances fluroxypyr and aminopyralid by gastric irrigation, and, if necessary, eye or skin lavage. Furthermore, the facilitation of diuresis is important, and the protection of the intestinal mucosa, for example with sucralfate might be advantageous. Finally, based on the likelihood of fluoride ions occurring after fluroxypyr intoxication together with the involved risk, the authors also recommend the usage of calcium gluconate in the treatment for neutralising fluoride ions.

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Erweiterte Zusammenfassung

Symptomatik, Behandlung und Krankheitsverlauf nach Intoxikation mit dem Herbizid Simplex® bei drei Pferden

Simplex® ist ein Herbizid welches zurzeit hauptsächlich zur Bekämpfung von Jakobskreuzkraut und Brennesseln auf Weiden eingesetzt wird. Das Produkt beinhaltet die Wirkstoffe Aminopyralid und Fluroxypyr, zwei Substanzen die eine Inaktivität des pflanzlichen Wachstumshormos Auxin bewirken und so zum Absterben der Pflanze führen. Wird das Produkt gemäß den Herstellerangaben auf einer Pferdeweide verwendet, sollte die Fläche für 7 Tage nicht beweidet werden. Bisher sind nach Wissen der Autoren keine Intoxikationsfälle beim Pferd mit Simplex® nach unsachgemäßer Verwendung publiziert. Auch gibt es annähernd keine toxikologischen Daten der beinhalteten Substanzen für das Pferd.

Ein 21-jähriger Araber-Berber Wallach, eine 17-jährige Kleinpferdstute und ein 11-jähriger Kleinpferdwallach wurden nach Verfütterung einer Schubkarre mit frisch Herbizid-kontaminierten Brennesseln in der hiesigen Klinik vorstellig. Vorberichtlich wurden die Brennesseln zwei Stunden vor Verfütterung mit 1l Simplex®-Lösung behandelt, woraus eine Gesamtaufnahmemenge der drei Pferde von 100g Fluroxypyr und 30g Aminopyralid resultiert. Zum Zeitpunkt der Erstuntersuchung zeigten die Pferde ein gering- bis mittelgradig gestörtes Allgemeinbefinden einhergehend mit einer Depression (Abb. 1), geröteten Schleimhäuten, einer verlängerten kapillaren Wiederfüllungszeit, einer moderaten Tachykardie sowie einer intestinalen Hypomotilität. Weiterhin zeigte Pferd 1 eine milde Ataxie, eine kardiale Arrhythmie und labordiagnostisch eine milde Azotämie. Bei allen Pferden wurde eine geringgradige bis deutliche bilaterale Rötung der Konjunktiven, Epiphora und eine gering- bis mittelgradige Chemosis ohne Hinweise auf korneale Beteiligung festgestellt. Pferd 1 und 2 zeigten labordiagnostisch zusätzlich eine milde Hyperlaktatämie. Initial wurde bei allen Pferden eine Magenspülung mit 1%iger Calciumgluconat-Lösung durchgeführt. Nach erfolgter Spülung wurden 5l Calciumgluconat-Lösung im Magen belassen. Aufgrund des Risikos einer bereits erfolgten gastrointestinalen Schleimhautirritation erhielten die Pferde Sucralfat (40mg/kg KM/tid p.o.) über insgesamt drei Tage. Weiterhin wurden die Tiere zur Unterstützung der Diurese initial mit einer Bolusinfusion mit Ringer-Lösung und 23%iger Calciumgluconat-Lösung versorgt. Im Anschluss wurde die Infusion mit Ringerlösung (60ml/kg KM/Tag i.v.). über den Zeitraum von 36 Stunden fortgeführt. Aufgrund der beobachteten Augenirritation infolge einer wahrscheinlich erfolgten Exposition der Augen durch direkten bzw. indirekten Kontakt mit den Substanzen wurde initial eine Augenlavage mit physiologischer Kochsalzlösung durchgeführt sowie einmalig Calciumgluconat-haltige Augentropfen eingegeben. Nach fünf Tagen wurden Pferd 1 und 3, und nach sechs Tagen Pferd 2 aus der Klinik entlassen. Zu diesem Zeitpunkt waren die Tiere klinisch und labordiagnostisch unauffällig. Nach abschließender Rücksprache mit den Besitzern drei Monate später zeigten die Pferde unauffälliges Allgemeinbefinden und wurden alle ihrem ursprünglichen Leistungsniveau entsprechend gearbeitet.

Der genaue toxikologische Wirkungsmechanismus von Aminopyralid und Fluroxypyr ist bisher unbekannt, jedoch sind die meisten ausgelösten Symptome vermutlich auf die primäre Säurewirkung der Substanzen zurückzuführen. Da in den vorliegenden Fällen eine Dissoziation der Fluoridionen als möglich angesehen wurde, basierten die durchgeführten Therapiemaßnahmen hauptsächlich darauf, eine lokale Schädigung, sowie eine mögliche Resorption der Fluoridionen zu verhindern. Aus diesem Grund wurde als Spüllösung für den Magen und die Augen eine Calciumgluconat-Lösung gewählt. Fluoridionen besitzen eine starke Affinität zu Calcium, was zu einem Ausfällen von schwerlöslichen Salzen führt. In der Folge kommt es zur Neutralisation der Fluoridionen, jedoch sind ebenfalls gravierende Elektrolytstörungen durch eine Hypocalcämie möglich.

In der Humanmedizin ist die akute Intoxikation nach Aufnahme von Fluoriden vielfach beschrieben. Insbesondere bei Kindern führt die exzessive Aufnahme von fluroridhaltigen Zahnpflegeprodukten zu schwerwiegenden gastrointestinalen Symptomen. Basierend auf den bereits beschriebenen Elektrolytverschiebungen, bedingt durch die Affinität der Fluoridionen für Calcium, werden regelmäßig kardiovaskuläre und muskuläre Symptome beobachtet. Bezogen auf die drei betroffenen Pferde, die innerhalb von 24 Stunden trotz Substitution von Calciumgluconat eine geringgradige Senkung des ionisierten Calciumwertes entwickelten, ist somit ursächlich eine systemische Wirkung der Fluoridionen in Erwägung zu ziehen. Beim Pferd wurde bisher sowohl die akute, als auch die chronische Fluorose beschrieben. Chronisch betroffene Tiere zeigten ein stumpfes Haarkleid, Lahmheit, ein steifes Gangbild, Knochenzubildungen im Bereich der Schädelknochen und eine exzessive Abrasion der Zähne. Im Gegensatz zum Rind jedoch beschrieben die Autoren die Spezies Pferd als relativ tolerant. Im Rahmen dieser Veröffentlichung geben die Autoren einen Toleranzwert von 60mg für Natriumfluorid und Fluoride mit ähnlicher Toxizität an. Ein älterer Einzelfallbericht beschreibt zudem eine akute Fluorose eines Pferdes nach Aufnahme von 100mg Natriumfluorid. Abschließend bleibt jedoch im vorliegenden Fall die Menge von dissoziierten Fluoridionen unbekannt. Da jedoch eine Wirkung, die gravierende Folgen haben kann, nicht vollständig auszuschließen ist, plädieren die Autoren für den Einsatz von Calciumgluconat in der Therapie.

Schlüsselwörter: Pferd / Simplex® / Fluroxypyr / Aminopyralid / Toxizität / Calciumgluconat / Vergiftung / Intoxikation