

Treatment rationale for dogs poisoned with aldicarb (carbamate pesticide)

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ABSTRACT

The treatment rationale for dogs poisoned by aldicarb is reviewed from a pharmacological perspective. The illegal use of aldicarb to maliciously poison dogs is a major problem in some parts of the world. In South Africa, it is probably the most common canine poisoning treated by companion animal veterinarians. Aldicarb poisoning is an emergency and veterinarians need to be able to diagnose it and start with effective treatment immediately to ensure a reasonable prognosis. Successful treatment depends on the timely use of an anti-muscarinic drug (e.g. atropine). Additional supportive treatment options, including fluid therapy, diphenhydramine, benzodiazepines and the prevention of further absorption (activated charcoal) should also be considered. Possible complications after treatment are also briefly discussed.

Keywords: aldicarb, carbamate, malicious poisoning, supportive treatment, Temik[®].

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INTRODUCTION

Malicious poisoning of dogs, especially with aldicarb (carbamate pesticide), has become an increasingly common emergency faced by companion animal veterinarians in some parts of the world^{20,43,64}. To date, there have been very few published articles discussing the treatment of aldicarb poisoning in dogs^{2,64}, with most published reports focusing on human cases^{9,31,66}. Aldicarb poisoning is an emergency^{2,51,64} and patients may die within minutes after ingestion due to respiratory failure^{22,31,51}. Therefore, veterinarians need to be able to promptly diagnose aldicarb toxicity and start with effective treatment immediately to offer a reasonable prognosis. The main focus of this article is to review the treatment options for veterinarians dealing with accidental or malicious aldicarb poisonings.

BACKGROUND INFORMATION TO THE PROBLEM IN SOUTH AFRICA

The malicious use of aldicarb in South

Africa to poison dogs is of major concern and it is arguably the most common intoxication treated by veterinarians⁶⁴. The Onderstepoort Veterinary Academic Hospital (OVAH), Faculty of Veterinary Science, University of Pretoria, South Africa, treats between 50 and 100 clinical aldicarb cases per annum (L F Arnot, OVAH, unpubl. data.) giving some indication of the magnitude of the problem. The number of cases seen depends on criminal activity within the area⁶⁴. The use of aldicarb to poison animals is, however, not only restricted to South Africa, with reports indicating large-scale intentional malicious poisoning of dogs and other species from the United States of America^{2,20} and Spain⁴³.

The extensive use of aldicarb in agriculture, and resultant easy accessibility, has been suggested as 1 of the reasons why the malicious use of aldicarb in recent years has increased, in preference to the more traditional poisons such as strychnine^{43,57,59,62}. Criminals use aldicarb to eliminate dogs within residential areas with the intention of gaining access to these properties for malicious activities. Cats are generally not intentionally targeted, but are assumed to be incidentally affected⁶⁴.

Bayer CropScience (Bayer CropScience, Isando, South Africa) is the sole distributor of aldicarb in South Africa. Aldicarb is marketed world wide under the trade name of Temik^{®7}. It is an agricultural insecticide and nematicide^{7,24,26}, contain-

ing 15 % aldicarb and is usually formulated as small black granules (Fig. 1). Temik[®] is registered for agricultural use in South Africa under the Fertilizers, Farm Feeds, Agricultural and Stock Remedies Act (Act 36 of 1947) and the sale of it to farmers within South Africa is tightly controlled. Only certified farmers are legally able to purchase the product and strict control is enforced regarding the use and storage of the product on farms (Act 36 of 1947) (P Fourie, Bayer CropScience, pers. comm.).

In 2001, Bayer CropScience began adding an extremely bitter substance (denatonium benzoate) to Temik[®] in order to prevent its use for suicides or homicides in humans (P Fourie, Bayer CropScience, pers. comm.). Unfortunately most animal species do not possess the specific taste receptors found in humans that detect the bitter taste sensation and this protective measure therefore does not absolutely guarantee that animals would not ingest aldicarb treated with denatonium benzoate¹⁹.

It is estimated that at least 60 % of the aldicarb-containing pesticides used in South Africa for the malicious poisoning of dogs are illegally smuggled across the border into South Africa from neighbouring countries such as Mozambique and Zimbabwe, where strict agricultural product control is lacking (G H Verdoorn, Griffon Poison Information Centre, pers. comm.). In South Africa Temik[®] is sold illegally by informal street traders as a rodenticide called 'Two Step'⁵⁶ and it is often the cause of accidental poisoning in children and intentional poisoning in adults⁶³. Similar problems are experienced in the United States of America with aldicarb sold illegally as a rodenticide under the name *Tres Pasitos* (3 little steps), and is sometimes used in human suicide attempts^{9,45,66}. It has also been reported that aldicarb is illegally used as a household rodenticide in Brazil and the Caribbean Islands and that humans are sometimes poisoned⁵¹.

Criminals in South Africa wishing to gain access to a property where dogs are present typically insert aldicarb granules into cheap meat baits, such as viennas, sausages or polony, to kill the resident dog(s) (Fig. 1). Pieces of bait are clandest-

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Fig. 1: Meat-based product used to maliciously kill dogs. Aldicarb appears as tiny black granules, somewhat resembling gun-powder, in the bait.

tinely thrown over property fences for the dogs to consume, with criminals gaining access to the property once the dogs have been eliminated.

ALDICARB (CARBAMATE) POISONING: DESCRIPTION AND DIAGNOSIS

Chemistry of aldicarb

Aldicarb (2-methyl-2-(methylthio)propionaldehyde-*o*-methylcarbamoyloxime) is an extremely toxic substance^{7,20,24,45} and is classified as an 'extremely hazardous pesticide' (class 1a) according to the World Health Organization classification of pesticides⁶⁷. The rat oral LD₅₀ varies between 0.46 mg/kg²¹ and 0.93 mg/kg⁶². In humans it is 0.80 mg/kg⁶⁶. The canine oral LD₅₀ for Temik[®] is about 6.5 mg/kg and it contains 15 % aldicarb (G H Verdoorn, Griffon Poison Information Centre, pers. comm.).

Mode of action of aldicarb in dogs

Both the carbamate and organophosphate pesticides are classified as cholinesterase inhibitors^{24,60,61}. Carbamates, such as aldicarb, cause inhibition of the activity of acetylcholinesterase (AChE), an enzyme responsible for the hydrolysis of the neurotransmitter acetylcholine (ACh) into choline and acetic acid^{21,30,33}. The ingestion of a carbamate results in the inactivation of AChE activity by carbamylation of the serine hydroxyl group located at the active site of AChE^{31,52,59}. The carbamylation of the active site on the AChE is temporary and rapidly reversible, and AChE activity is restored when spontaneous hydrolysis of the carbamylated enzyme occurs (often within an hour), resulting in the release of AChE^{26,31,34,59}.

Exposure to organophosphates results in the phosphorylation of the same active site of AChE, but a stable and irreversible bond is formed after 24–48 hours. This process is referred to as 'aging'^{15,21,25,31,34,60}.

Once AChE has been inactivated, ACh accumulates at muscarinic and nicotinic cholinergic receptors in the sympathetic and parasympathetic nervous systems, as well as at neuromuscular junctions resulting in continuous stimulation of these receptors^{10,15,31,33}. Central nervous system (CNS) toxicity is less common in carbamate poisoning because many carbamates do not readily cross the blood-brain barrier (BBB)^{35,55}.

Clinical signs

The clinical presentations of carbamate and organophosphate poisonings are clinically indistinguishable from each other^{14,57,61}. If a dog presents with clinical signs indicating possible organophosphate or carbamate toxicity, unless there is a clear history that an organophosphate was used (for example, history that the dog was recently dipped by the owner with an organophosphate ectoparasiticide), the clinician should assume carbamate poisoning, due to the very high prevalence of malicious misuse of aldicarb in South Africa.

The clinical signs of aldicarb poisoning are associated with muscarinic, nicotinic and central effects^{33,57,60}. Muscarinic receptors are located in the smooth muscle of glands, intestine, cardiac muscle, CNS and the iris. The nicotinic cholinergic receptors are located at the neuromuscular junctions of striated muscle and the ganglionic synapses of the autonomic ganglia²⁵.

Muscarinic signs are often very pronounced and include bradycardia,

miosis, bronchospasm, bronchorrhea, hypersalivation, lachrymation, urination and diarrhoea. Nicotinic signs include muscle tremors, fasciculations, muscle stiffness, weakness and paralysis^{8,16}. Prolonged muscle activity finally results in exertional rhabdomyolysis⁴¹. Central effects include apprehension and seizures, followed by CNS depression and coma³¹.

Hyper-stimulation of the nicotinic receptors may cause tachycardia, mydriasis and hypertension, instead of the bradycardia, miosis and hypotension that are seen when muscarinic stimulation predominates⁶⁶. Tachycardia may also be due to hypoxia. This is an important consideration when a patient is initially examined and subsequently treated. When using atropine as an antidote, it is important to remember that the endpoint for atropinisation is when secretions have dried up, not the presence of tachycardia or dilated pupils⁶⁶.

In dogs, the clinical signs most often reported by veterinarians include muscle tremors and hypersalivation, followed by emesis, miosis, bradycardia, seizures and dyspnoea⁶⁴. Excessive urination, paresis and paralysis have only been occasionally recorded. Death is caused by respiratory failure, due to bronchospasm, paralysis of the diaphragm and intercostal muscles, and depression of the respiratory centre^{16,22,31}. In a study undertaken in humans the most common muscarinic effect was diarrhoea, the main nicotinic sign was muscle fasciculations and CNS depression occurred in about 50 % of patients⁵¹.

Diagnosis

At the Outpatients clinic of the OVAH, most aldicarb emergencies are diagnosed on the basis of the presenting clinical signs and a history of a very acute onset. Owing to the fact that in a clinical emergency there is little time to confirm a definite diagnosis of aldicarb poisoning before treatment commences, a positive response to initial anti-muscarinic treatment can assist in confirming a preliminary diagnosis.

Some owners may report that the dog vomited up unfamiliar food in which the aldicarb granules were concealed or that they found pieces of meat products containing small black granules in the vicinity of the animal.

Measurement of decreased cholinesterase concentrations in the blood may be considered to confirm the diagnosis of aldicarb toxicity^{1,5,24}. However, due to the fact that the temporary AChE-carbamate bond is rapidly reversed, this test must preferably be performed immediately, seeing that the diagnostic test results could become inconclusive if the test is

Table 1: Proposed treatment protocol for dogs poisoned with aldicarb. The treatment protocol may need to be adjusted on a case by case basis, depending on the severity of the case. Refer to text for specific references.

Action	Additional information
Treatment must be implemented immediately due to the rapid deterioration of the patient.	The canine oral LD50 of Temik® is about 6.5 mg/kg. Temik® contains 15% aldicarb.
Establish a patent airway. Weigh the dog. Insert an IV catheter and administer fluids.	Administer intravenous fluids at 1½ maintenance if emesis is severe.
If the dog has not vomited yet and the dog is not convulsing, administer apomorphine to induce emesis. An apomorphine tablet can be placed on the conjunctival sac mucosa or inject 0.08 mg/kg IM or SC.	Never induce emesis in a convulsing patient, as this will predispose to aspiration of ingesta. Always rinse the eye if apomorphine was administered in the eye.
Administer atropine sulphate, 0.2–0.5 mg/kg. Give a quarter of the dose IV and the balance SC. Keep the dog atropinised – important for the control of excessive bronchial and oral secretions.	Atropine antagonises the muscarinic effects caused by accumulation of the neurotransmitter (ACh) at the receptor sites. If one cannot place an IV catheter (due to dog convulsing for example), one could administer <i>via</i> the IM route.
Administration of oximes is not indicated! 2-PAM and other oximes are ineffective in carbamate poisoning cases.	In the case of some carbamates, such as carbaryl and carbofuran, 2-PAM therapy may accentuate the toxicity.
If the dog is convulsing, give diazepam at 0.5–1 mg/kg IV.	Some anticonvulsant drugs, such as barbiturates, may aggravate the toxicity.
Administer diphenhydramine at a dose of 1–4 mg/kg q8 hours, per os, to antagonise the nicotinic effects.	Diphenhydramine may cause severe sedation in patients.
Administer activated charcoal powder <i>per os</i> at a dose of 0.5–2 g/kg. The activated charcoal powder is mixed with water to form a slurry (0.5 mg/kg charcoal into 5 ml/kg water) and this is administered <i>per os</i> .	Activated charcoal adsorbs aldicarb within the gastrointestinal tract. Activated charcoal can cause constipation, impaction, obstruction and faeces to appear black in colour.
It is advisable to substitute some of the water used to form the slurry with lactulose at 1 ml/4.5 kg body mass.	Lactulose will help prevent constipation and will assist with intestinal emptying.
If the dog is convulsing, insert a naso-oesophageal tube to prevent aspiration if medication is administered <i>per os</i> .	Activated charcoal could cause fatal aspiration pneumonia if aspirated.
Once emergency treatment has been completed, ongoing monitoring of the patient is necessary (heart rate, respiration, pupillary size, etc.).	Atropine can be administered again if the patient continues to exhibit hypersecretions, bradycardia and miotic pupils. Atropine treatment can be slowly tapered off once the heart rate and pupil size have normalised.
Continue to administer activated charcoal and diphenhydramine for at least 3 days after aldicarb ingestion.	Activated charcoal has no taste or smell, so once the dog is stable and eating, the charcoal can be mixed with food. Diphenhydramine can be stopped earlier if sedation is severe, but patient is otherwise stable.
Confirmation of the diagnosis.	If a blood sample was collected to determine the AChE concentration, it should be tested immediately to avoid false negative results. Send vomitus or stomach contents (dead animal) to analytical laboratory for pesticide analysis. Bait could also be analysed.
Discuss with the dog owner.	Dog owner must remove left-over bait in garden – owner must use gloves. Report the incident to the police. Criminal activity is highly likely after the poisoning of dogs in a specific neighbourhood.

not performed within a few hours²⁷. A blood sample may be collected prior to initiating the treatment and the AChE concentration determined as soon as possible.

THERAPEUTIC OPTIONS

Due to the highly toxic nature of aldicarb, dogs presented to a veterinary clinic with the 'classic' clinical signs indicative of aldicarb toxicity, or a relevant history, should always be handled as an emer-

gency. At the OVAH it is generally accepted that without prompt treatment most malicious cases will die within 20–30 min of ingestion, leaving little time for the attending veterinarian to perform additional tests to confirm the diagnosis.

A proposed treatment protocol for dogs poisoned with aldicarb is summarised in Table 1. The sequence of the different recommended procedures detailed in the table is only a guide and the treatment protocol may need to be adjusted on a

case by case basis depending on the severity of the poisoning. However, it is essential to administer atropine as soon as possible.

The mortality of clinical cases is high, with a mortality rate of 25–50 % recorded even after prompt treatment⁶⁴. Treatment is directed towards reversing or preventing over-stimulation of the muscarinic receptors by the accumulation of ACh in the junctions^{31,33,66}. Effective therapy can be expensive, often requiring intensive

care and monitoring with a guarded prognosis, which may cause some owners to elect for humane euthanasia instead of treatment⁶⁴.

Immediate action and fluid therapy

Initially, an intravenous catheter should be placed, as intravenous access is crucial for the administration of drugs and fluids³³. At the OVAH, if the patient is convulsing, a naso-oesophageal tube is inserted to reduce the risk of aspiration of medication requiring administration *per os*.

Intravenous crystalloid fluids should be administered to all patients⁵⁵. If the patient is vomiting or exhibiting severe diarrhoea, the fluid rate should be increased to accommodate these losses. Otherwise, fluid therapy should be sufficient to maintain hydration and prevent hypovolaemia^{33,55}.

Muscarinic receptor antagonists

The administration of an antimuscarinic drug as soon as possible is critically important in all cases. Constant over-stimulation of the muscarinic receptors results in severe and fatal consequences. Severe bradycardia and bronchospasm are often life-threatening and need to be treated immediately⁵⁵. Muscarinic receptor antagonists compete with ACh for a common binding site on the muscarinic receptors³³. Two specific muscarinic receptor antagonists that may be considered are atropine sulphate and glycopyrrolate⁵⁰.

Atropine sulphate

Atropine is the drug of choice in the treatment of acute aldicarb toxicity. It is a competitive muscarinic receptor antagonist at postganglionic parasympathetic neuroeffector sites⁵⁰. Atropine administration reverses the severe bronchospasm, bronchorrhoea, bradycardia and circulatory depression associated with over-stimulation of the muscarinic receptors^{31,33,61}. Atropine activity is, however, specific to muscarinic receptors and has no effect on the nicotinic receptors or the AChE-carbamate complex^{50,55}. Atropine administration will therefore not counteract the muscle tremors, weakness and paralysis associated with aldicarb toxicity^{8,16,51}. Atropine may lower the cerebral glucose threshold and thereby reduce the likelihood of brain damage during seizures^{40,48}.

The dose of atropine required to counteract the effects of aldicarb toxicity is extremely high, more than 10 times the recommended pre-anaesthetic dose. The dose is between 0.2–0.5 mg/kg with a quarter of the dose given IV and the balance administered subcutaneously

(SC)¹⁸. This dose can be repeated every 15–30 minutes as needed, until the bronchospasm, excessive bronchial secretions and bradycardia are alleviated and mydriasis is seen^{31,66}. A dose of up to 2 mg/kg has also been cited to counteract carbamate toxicity⁵⁰, but clinical experience has indicated that a dose of up to 0.5 mg/kg appears to be adequate in most cases. If IV access is problematic, the atropine can be administered intramuscularly (IM) or SC.

Atropine is well absorbed from all routes of administration, reaching peak effects 3–4 min post IV administration. It is widely distributed and crosses the BBB. It is metabolised in the liver and excreted in the urine, with up to 50% being excreted in the unchanged form⁵⁰.

Atropine can cause a range of dose-related adverse effects⁵⁰. It crosses the BBB easily and central signs of atropine toxicity are common complications in humans treated with high doses³. The very high doses necessary to treat aldicarb poisoning effectively in dogs may result in neurological complications such as drowsiness, ataxia, seizures and respiratory depression. Gastro-intestinal side effects include xerostomia, dysphagia, constipation and vomiting. Ocular signs include blurred vision, mydriasis, cycloplegia and photophobia. Cardiovascular signs include tachycardia, hypertension, arrhythmias and cardiovascular failure⁵⁰.

Glycopyrrolate

Glycopyrrolate could be considered as an alternative drug to atropine for the treatment of aldicarb toxicity^{6,33}, or it could also be used in combination with atropine³. It is a quaternary ammonium anti-muscarinic agent³³ and is registered for use in dogs and cats as a pre-anaesthetic agent to treat sinus bradycardia, sino-atrial arrest and incomplete atrioventricular (AV) block⁵⁰. Glycopyrrolate is more effective in controlling excessive bronchial secretions and bradycardia in rats and rabbits than atropine⁶. However, similar references could not be found for dogs.

In contrast to atropine, glycopyrrolate is completely ionised after administration, and is therefore poorly lipid soluble. Glycopyrrolate does not enter the CNS in any appreciable amounts and as a result, does not cause the CNS adverse effects seen with atropine after high dose administration⁵⁰. This may be used to advantage in those patients showing signs of atropine toxicity. A combination of atropine and glycopyrrolate has been used in the treatment of human cases of organophosphate toxicity³.

The canine LD₅₀ of glycopyrrolate is 25 mg/kg after IV administration⁵⁰. A dose

of 0.5 mg/kg has been suggested for the treatment of organophosphate and carbamate poisoning cases⁴⁶. After IV administration the onset of action of glycopyrrolate is 1 min and 30–45 min following IM or SC administration respectively. It is rapidly eliminated with only minimal serum levels detectable 3 hours after IV administration⁵⁰.

Diphenhydramine

Although diphenhydramine is not used routinely for the treatment of organophosphate and carbamate poisonings in humans (not registered for this use in humans), it is often used 'extra label' by some veterinary clinicians to counteract the nicotinic signs¹⁰.

Diphenhydramine is a 1st generation antihistamine that is a competitive antagonist at the H₁ receptors⁵⁰. It is non-selective and therefore also an antagonist at muscarinic receptors with some sedative, anticholinergic, antitussive and antiemetic effects^{23,50}. Diphenhydramine is used as an adjunctive treatment in aldicarb poisoning in dogs to prevent over exertion of muscles by preventing excess stimulation of the nicotinic receptors at the neuromuscular junctions^{10,23,50}.

Diphenhydramine should be administered orally at presentation¹⁰. Dosing *via* a naso-oesophageal tube is essential to prevent aspiration if the patient is convulsing or has a weak swallowing reflex. A dose of between 1 and 4 mg/kg, *per os*, every 8 hours has been advised for dogs and can be administered for up to 3 weeks if necessary^{10,23}. It is well absorbed from the gastrointestinal tract, with a 1st pass effect of between 40–60%. It may cause severe sedation in dogs and further treatment should be reconsidered if unacceptable sedation is observed⁵⁰.

Oximes

The use of oximes in the treatment of organophosphate poisoning is commonly referred to in human medical literature^{31,39,61,65}. Oximes, such as pralidoxime and obidoxime, are phosphorylated AChE enzyme reactivators, indicated for the treatment of organophosphate toxicity before the process of 'aging' has occurred^{31,39,65}.

In contrast to organophosphate toxicity, the carbamate-induced inhibition of AChE is rapidly reversible with hydrolysis of the carbamylated complex often occurring within an hour³¹. The use of oximes in carbamate poisoning is controversial^{5,12,29,55} or even contraindicated^{27,50} and is therefore not recommended for the treatment of aldicarb poisoning in dogs. Many studies have indicated that the treatment of carbamate poisonings in

animals with oximes has resulted in a protective ratio of less than 1 (*i.e.* worse than no treatment at all)⁵⁵. Potential toxicity of oximes when used in the treatment of carbaryl (carbamate) poisoning has been reported⁵⁵. However, recent data suggest that this concern may be unwarranted^{27,55}.

If uncertainty exists as to whether the poisoning is due to an organophosphate or carbamate, the veterinarian may choose to include an oxime in the treatment protocol. In such a case, the dosage of pralidoxime in dogs is 20 mg/kg, 2–3 times a day, with slow IV administration of the initial dose and subsequent doses given IM or SC¹⁷. The dosage of obidoxime (10 % solution) is 40 mg/kg in dogs, by slow IV administration, followed by IM or SC administration, 2–3 times a day⁵⁰.

Benzodiazepines

Some patients may present in a state of seizure. Diazepam (benzodiazepine) is the drug of choice to control seizure activity^{33,54}, reduce anxiety and to induce muscle relaxation³¹. Benzodiazepines cause hyperpolarisation of neurons, reducing cholinergically induced depolarisation, resulting in cessation of propagation of convulsions³⁹. Benzodiazepines are gamma-aminobutyric acid (GABA) receptor agonists and do not activate the receptor directly, but alter GABA binding at the GABA_A receptors in an allosteric fashion³⁹.

It has also been reported that diazepam acts synergistically with atropine, potentiating the efficacy of a reduced dose of atropine, improving survival and preventing CNS complications^{14,31,54}. It has been shown that diazepam appears to decrease synaptic release of ACh in humans³¹. A dose of 0.5–1 mg/kg may be administered IV to dogs that are seizing⁴⁹.

Prevention of systemic absorption

Emesis

Stimulation of emesis shortly after intake would be beneficial³¹. The use of apomorphine is indicated and dogs may readily be induced to vomit by placing 0.25 mg/kg apomorphine, diluted in 3–5 ml water, on the conjunctival mucosa²⁸. It can also be administered IV at 0.04 mg/kg⁵³, or by the IM or SC routes at 0.08 mg/kg⁴⁴. The induction of emesis is contraindicated in dogs that are already vomiting, convulsing or losing consciousness, because of the high risk of ingesta aspiration in these cases⁵⁰.

Adsorption

The use of activated charcoal powder as an adsorbent is recommended in all cases

to bind the aldicarb within the gastrointestinal tract, thus limiting further systemic absorption^{31,50}. Activated charcoal powder is a highly porous form of carbon with a large surface area capable of adsorbing ingested toxins⁵⁰. At the OVAH, the powder formulation of activated charcoal is preferred, as it provides a much larger adsorptive surface area than the tablet formulation.

Administration of activated charcoal *per os* is contraindicated in a patient that is convulsing or has a weak swallowing reflex because of the high risk of aspiration and resultant severe pneumonia in these cases⁵⁰. A naso-oesophageal tube should be considered in these situations, particularly if the clinician plans to administer multiple doses of activated charcoal over time.

At the OVAH activated charcoal is administered for the initial adsorption of any aldicarb present in the gastrointestinal tract^{31,50}. Thereafter the administration of multiple doses of activated charcoal (chronic treatment) is primarily to adsorb any aldicarb that re-circulates back into the gastrointestinal tract *via* enterohepatic circulation⁵⁰.

Activated charcoal powder can initially be administered at a dose of 0.5–2.0 g/kg *per os* or *via* a naso-oesophageal tube. At the OVAH activated charcoal is mixed with water to form a slurry (1 g charcoal with 5 ml water) and lactulose is added to reduce the risk of constipation⁵⁰. Activated charcoal treatment can be administered every 3–6 hours. Once the dog is eating, the activated charcoal can be mixed with palatable food, as it has no taste or smell⁵⁰.

In contrast to veterinary practice, the use of activated charcoal in human aldicarb poisoning is not recommended, especially not repeated administrations, as it has been observed to be associated with constipation, impaction and obstruction by 1 of the authors (DJHV). In addition, the effectiveness of activated charcoal therapy in poisoned human patients is also not conclusive³¹.

Increase in the movement of ingesta

Lactulose is a disaccharide laxative and by drawing water into the colon, thus increasing the osmotic pressure, has a laxative effect. The chronic use of activated charcoal in patients can predispose to constipation, which is alleviated by the lactulose. In addition, the laxative effect of lactulose will increase the speed of gastrointestinal tract emptying, which will further assist in the rapid elimination of the ingested aldicarb. The dose of lactulose in dogs is 1 ml per 4.5 kg body mass 3 times daily⁵⁰.

POTENTIAL COMPLICATIONS OF ALDICARB TOXICITY

In view of the fact that the aldicarb case fatality rate is so high, complications are not often seen. However, in a case that survived the initial clinical crisis, complications may be diagnosed. Although the focus of this review is the treatment rationale, veterinarians need to be aware of potential complications.

Pancreatitis

A serious complication seen with organophosphate or carbamate poisonings is pancreatitis^{4,38,42}. Acute necrotic necrohaemorrhagic pancreatitis has been reported in about 12 % of human organophosphate and carbamate cases⁴. Pancreatitis was also experimentally reproduced in dogs that received diazinon (an organophosphate) IV³².

Observations from the OVAH confirmed that pancreatitis is a potential, significant complication in dogs. The clinical signs are typically seen within a few days after the intake of aldicarb, and they usually present with an acute abdomen. This condition is less likely in patients that received immediate and effective treatment⁴². Atropine prevents the overstimulation of muscarinic receptors causing smooth muscle contractions (also the sphincter of Odi) in all gastrointestinal organs⁴. In addition, pancreatic secretion (cholinergic effect) is stimulated by organophosphate and carbamate pesticides^{13,38}.

Acute necro-haemorrhagic interstitial pancreatitis (Fig. 2) was confirmed by the Pathology Section (Department of Paraclinical Sciences, Faculty of Veterinary Science, University of Pretoria) in dogs presented for necropsies after unsuccessful treatment. This is rarely seen in cases that died peracutely. A possible explanation for the development of pancreatitis after severe cholinergic stimulation is that the constrictive spasm of the sphincter of Odi and the increase in intraductal pressure increase the risk of activated pancreatic secretions escaping into the interstitial and peripancreatic tissue^{4,13,38}.

Intermediate syndrome

The intermediate syndrome (IMS) was 1st reported in the mid-1980s, describing clinical signs, mostly of muscle paralysis, after the successful treatment (and recovery) of organophosphate poisoning cases^{11,15,61}. It is called the IMS because it is observed after the acute cholinergic signs, but before organophosphate-induced delayed polyneuropathy (OPIDP), which is rarely seen¹¹. It was generally accepted that it is only associated with organophosphates, until Paul and Mannathuk-

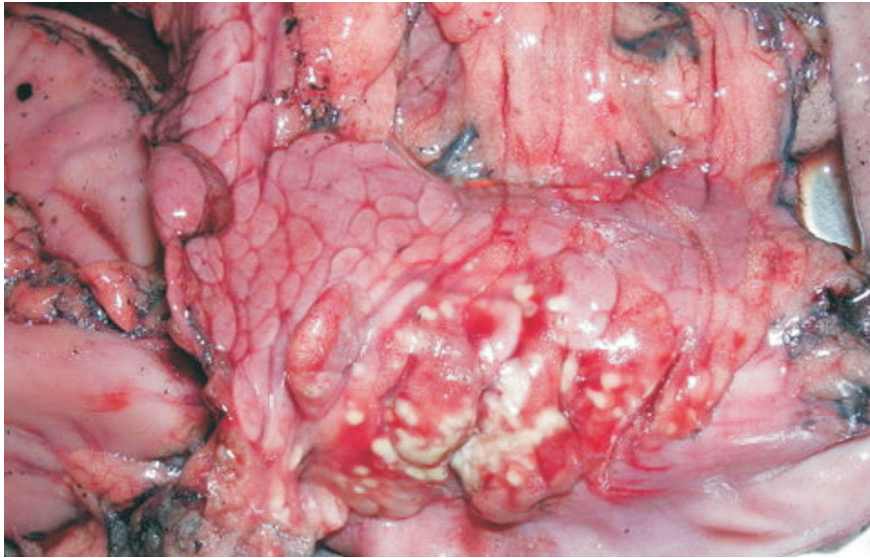


Fig. 2: Picture of acute necro-haemorrhagic interstitial pancreatitis in a dog that survived the initial poisoning.

karan⁴⁷ reported the development of IMS clinical signs in a human patient poisoned with carbofuran (carbamate).

Polyneuropathy

Organophosphate-induced delayed polyneuropathy (OPIDP) is classically associated with organophosphates^{36,58}. However, some carbamates (e.g. methylcarbamates) also inhibit neuropathy target esterase (NTE), the target enzyme in OPIDP development. Based on mechanistic considerations, carbamates were thought to be unable to cause polyneuropathy³⁷. Subsequently, 3 human polyneuropathy cases that occurred after poisoning by methylcarbamates were reported³⁷.

CONCLUSION

Aldicarb poisoning is the most common poisoning in dogs seen by veterinarians in South Africa. Owing to the toxic nature of aldicarb, immediate and effective treatment is essential to obtain a positive outcome. Atropine is the drug of choice to counteract the life threatening effects such as bronchospasm, increased bronchial secretions and bradycardia. Diphenhydramine may be considered to antagonise the nicotinic effects of aldicarb, thereby reducing muscle fasciculations and tremors. Diazepam may act synergistically with atropine, allowing for a reduction in atropine dosage. Diazepam also has muscle relaxant and sedative effects that may be beneficial in some patients. The use of oximes is not recommended in carbamate poisoning. The use of activated charcoal as an adsorbent to prevent further gastrointestinal absorption is essential. Pancreatitis should be considered in a dog that presents with signs of acute abdomen after aldicarb exposure.

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