ORIGINAL ARTICLE

Chocolate ingestion in dogs: 156 events (2015-2019)

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Objectives: To describe the clinical features and outcome of dogs after chocolate ingestion.

Material and Methods: Retrospective evaluation of clinical signs, clinical pathological findings, therapy and outcome of 156 dogs after chocolate ingestion. The concentration of methylxanthines (theobromine, caffeine) was calculated based on the type of chocolate and the amount ingested.

Results: One hundred and twelve dogs had no clinical signs. Forty-four dogs had clinical signs of chocolate intoxication. Twenty-eight of these 44 dogs ingested dark and bitter chocolate. Reasons for presentation were agitation (33), tremor (22), vomiting (21), panting (11), polyuria/polydipsia (seven) and diarrhea (two). Common clinical findings were sinus tachycardia (28), tachypnea/panting (14), hyperthermia (10) and dehydration (seven). Clinical pathological findings in 34 of 44 dogs consisted of hyperlactataemia (23), hypokalaemia (16), mild hyperglycaemia (16) and mild alanine aminotransferase (ALT) and aspartate aminotransferase (AST) elevation (14). After decontamination (apomorphine, activated carbon) and symptomatic treatment (fluid therapy, esmolol, forced diuresis, sedatives), 43 of the 44 dogs survived.

Clinical Significance: In dogs with potential chocolate intoxication, the type and amount of chocolate and the time of ingestion are important factors. Cardiovascular, neurological and gastrointestinal signs are the most common clinical signs. In this case series, the prognosis after decontamination and symptomatic therapy was good, with a mortality rate of less than 3%.

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INTRODUCTION

Suspected poisoning is a common reason for presentation in the veterinary practice. In an evaluation of questionnaires conducted among veterinary clinics in Germany, suspected poisoning was the reason for presentation to a veterinarian in one out of 200 dogs (Allkämper *et al.* 2018). The ingestion of raisins, grapes, macadamia nuts, onions, sugar additives (xylitol) and chocolate can lead to signs of intoxication in dogs (Hansen *et al.* 2000, Eubig *et al.* 2005, DuHadway *et al.* 2015, Cortinovis & Caloni 2016). The first report on chocolate intoxication in dogs was published in 1942 (Clough 1942). Chocolate contains the methylxanthines theobromine and caffeine. The amount of methylxanthines contained depends on the type of chocolate: Chocolate with a high cocoa content, such as baking chocolate and dark chocolate, contains a significantly higher concentration of methylxanthine than milk chocolate (Zoumas *et al.* 1980, Dolder 2013). The content of methylxanthines in white chocolate is considered too low for inducing intoxication.

Caffeine reaches maximum serum levels within 30 to 60 minutes after oral intake. Theobromine, on the other hand, is absorbed more slowly compared to caffeine (maximum plasma concentration after about 2 hours). Furthermore, caffeine is metabolised to theobromine (maximum plasma concentration after 6 to 8 hours) (Löffler *et al.* 2000a, 2000b). Both methylxanthines are metabolised in the liver, excreted via the bile ducts and undergo enterohepatic circulation (Dolder 2013). Methylxanthines have different mechanisms of action. Theobromine and caffeine inhibit cellular adenosine receptors, which leads to stimulation of the CNS, tachycardia and diuresis. Furthermore, methylxanthines increase intracellular calcium concentration by increasing intracellular calcium influx and decreasing intracellular sequestration of calcium into the sarcoplasmic reticulum of

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striated muscles. This results in increased contractility of the skeletal muscles. A further effect of methylxanthines is an inhibition of the phosphodiesterase and an increase in cAMP concentration (sympathomimetic effect). Methylxanthines also increase the concentration of epinephrine and norepinephrine in the blood. Theobromine concentration is higher in chocolate compared to caffeine, but the clinical effects of the two methylxanthines are very similar. Clinical signs can be expected at a theobromine dose of 20 mg/kg and consist of tachycardia, hyperthermia, hypertension, arrhythmias, muscle stiffness, ataxia, seizures and coma (Dolder 2013). Fatalities are also possible (Drolet *et al.* 1984, Dolder 2013). A high proportion of sugar and fat in the chocolate can lead to gastrointestinal signs. The fat content may cause pancreatitis.

Only few individual case reports describing chocolate intoxication in dogs have been published (Sutton 1981, Glauberg & Blumenthal 1983, Drolet *et al.* 1984, Stidworthy *et al.* 1997, Stosic *et al.* 2011, Agudelo *et al.* 2013). The objective of this retrospective study was to describe dogs after chocolate ingestion presented with and without clinical signs of chocolate intoxication.

MATERIAL AND METHODS

By means of a keyword search in the electronic patient files, dogs that were presented to one institution because of chocolate ingestion were included in this report. The institution treats both primary care and referral patients. Dogs were only included if chocolate ingestion was directly observed by the owner. The evaluation period ranged from January 2015 to January 2019. Medical records were reviewed for signalment, history, amount and type of chocolate ingested, presenting clinical signs, physical examination findings, results of laboratory examinations, treatment and outcome. The concentration of theobromine and caffeine was calculated as follows (CliniPharm 1996, vetpharm.uzh.ch):

Milk chocolate: theobromine 0.5 to 2 mg/g; caffeine 0.1 to 0.9 mg/g.

Dark chocolate (55% cocoa): theobromine 5 to 8.5 mg/g, caffeine 0.5 to 2.6 mg/g.

Bitter chocolate (>70% cocoa): theobromine 5.5 to 12.7 mg/g, caffeine 0.7 to 3 mg/g.

In each case, the theobromine and caffeine doses were calculated in relation to bodyweight. If the chocolate was composed of different chocolate types and the proportions were unknown, the chocolate with the highest methylxanthine content was used.

A clinical examination was performed on all dogs. Patients suspected of having ingested a critical theobromine concentration of 20 mg/kg or more were treated symptomatically.

In these cases, and in cases with suspected ingestion of package material, apomorphine [0.08 to 0.1 mg/kg subcutaneously (sc)] was administered if the chocolate had been ingested less than 6 to 8 hours before presentation and the if the dog did not show any signs of impaired consciousness. Symptomatic treatment included fluid therapy and, depending on clinical signs, esmolol [in euvolaemic dogs with tachycardia; 25 µg/kg/min intravenously (iv)], midazolam (in dogs with seizures, tremor, agitation; 0.2 to 0.5 mg/kg iv) and antiemetics (maropitant 1 mg/kg iv once a day or metoclopramide 0.3 mg/kg sc three times a day). Dogs without clinical signs but with predisposition for circulatory failure after emesis induction with apomorphine were also treated with fluid therapy. To inhibit further absorption, activated charcoal (1 g/kg twice a day) was administered orally over the following 72 hours. Gastric lavage was indicated in a dog with massive ingestion of chocolate 6 to 8 hours before presentation, unsuccessful vomiting and no obvious signs for an increased risk of anaesthesia. The decision for gastric lavage was made by the treating veterinarian.

Laboratory examination included haematological (XT-2000iV Sysmex Corporation, Norderstedt, Germany) and biochemical blood analyses (Konelab 60i, Thermo Fisher Scientific GmbH, Dreieich, Germany). The dogs with clinical signs were intensively monitored in the clinic (regular assessment of the rectal temperature, mucous membrane colour and dryness, capillary refill time, pulse rate and quality and heart rate). Depending on the clinical signs, ECG monitoring (Welch Allyn CP 50, County Meath, Ireland) was performed, and systolic blood pressure was measured (Doppler method, Doppler Flow Detector, Model 811-B, Parks Medical Electronics Inc, Aloha, Oregon, USA). To reduce reabsorption of the toxins via the bladder, a urinary catheter was placed in a few cases and the urine was directed into a closed system. In some cases, furosemide (1 to 2 mg/kg iv) was administered to promote the excretion of methylxanthines.

Descriptive statistics were performed, calculating the median, the range, maximum and minimum of the age and weight of the dogs, the time between chocolate ingestion and presentation, the theobromine and caffeine concentration, body temperature, heart rate, laboratory values and the duration of hospitalisation (Microsoft Excel, Munich, Germany).

RESULTS

Over a period of 48 months, 156 dogs were presented to the clinic because of chocolate ingestion. Two dogs had ingested chocolate twice. Most dogs (n=32, 20.2%) were presented in the month of December followed by April (n=18, 11.4%) and March (n=16, 10.1%) (Fig 1). The age ranged from 3 to 198 months (median 48). Seventy-seven dogs were male (27 of which were neutered) and 79 dogs were female (32 of which were spayed). A total of 51 different breeds were presented. The breeds Labrador (10), Chihuahua (seven), Australian Shepherd (five), beagle (five), boxer (four), Jack Russell Terrier (four) and Parson Russel Terrier (four) were represented with more than three dogs. The weight of the dogs ranged from 1.9 to 60 kg (median 13.7).

Dogs without clinical signs (n=112)

Dogs presented without clinical signs after observed chocolate ingestion were between 3 and 198 months (median 48) old. Two dogs were presented twice. Fifty-seven dogs were male (24 of them neutered), 53 were female (20 of them spayed). In two cases, the sex was not documented. The weight was 1.9 to 60 kg (median 14). In 104 cases, the chocolate had been ingested between 5 minutes

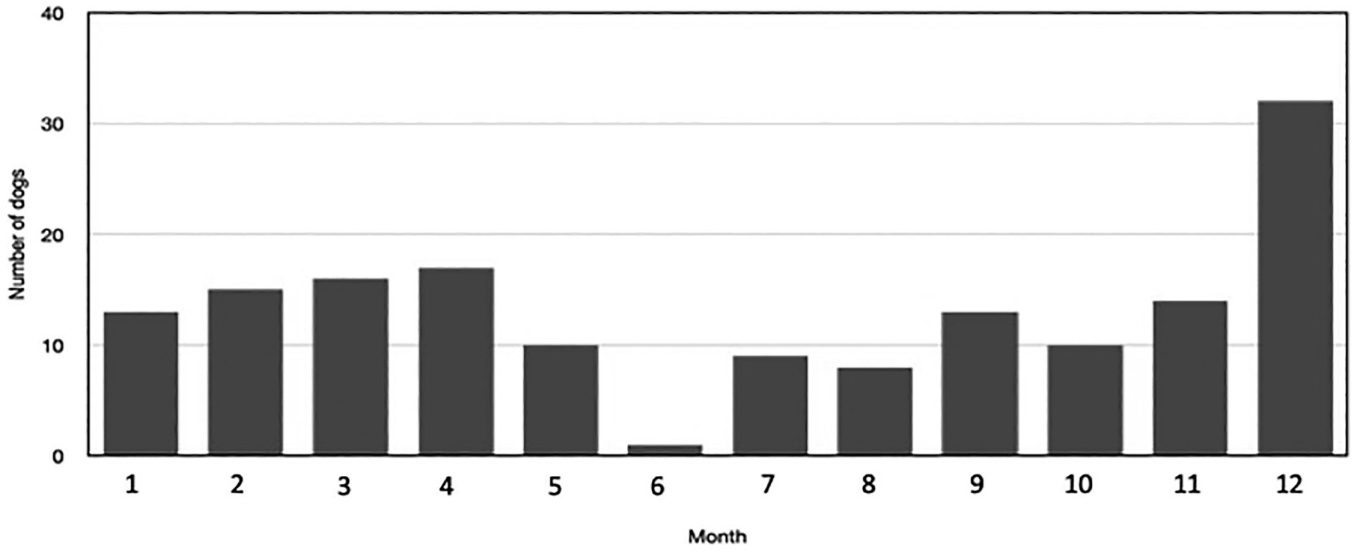

FIG 1. Monthly counts of dogs presented with ingestion of chocolate during the study period

and 14 hours (median 60 minutes) before presenting to the clinic. In 10 cases, the time of ingestion was not documented. Most dogs ingested milk chocolate (n=60). In the remaining dogs, dark chocolate (n=24), bitter chocolate (n=11) and a milk-dark chocolate mixture (n=3) were reported. In 16 cases, the owner could not give any information about the type of chocolate.

The calculated maximum theobromine dose was 0.8 to 303 mg/kg (median 22.4) and the calculated maximum caffeine concentration was 1.2 to 92.9 mg/kg (median 10.2). In 47 cases, the amount of chocolate ingested was not documented. In all dogs without clinical signs physical examination revealed no abnormal findings, laboratory examinations (n=13) also showed no abnormalities. In 96 cases, apomorphine was administered, which caused vomiting in all cases. In two cases, a gastric lavage was performed under general anaesthesia. Seventeen dogs were treated with fluid therapy and 48 with activated charcoal.

Dogs with signs of chocolate intoxication (n=44)

Forty-four dogs showed clinical signs of chocolate intoxication. The dogs were presented at an age of 5 to 180 months (median 60). Nineteen dogs were male (four of them neutered), 25 dogs were female (12 of them spayed). The dogs' bodyweight ranged from 3 to 35 kg (median 12.6). Three dogs were receiving medications (phenylbutazone, spironolactone, benazepril, thyroxine, omeprazole, sucralfate, metamizole [dipyrone]) due to different pre-existing medical conditions (osteoarthritis/hypothyroidism, food allergy, heart disease). The dogs were presented 45 to 1500 minutes (median 300) after the observed ingestion of chocolate. The dogs ingested milk chocolate (n=13), dark chocolate (22) and bitter chocolate (6). In three cases, the specific type of chocolate was unknown.

The calculated maximum amount of ingested theobromine was 19.5 to 332 mg/kg (median 70.8). The dog with a calculated ingested theobromine amount of 19.5 mg/kg had ingested a chocolate containing xylitol. This dog was presented with vomiting, polyuria /polydipsia and restlessness. The laboratory abnormalities (increased ALT, hypoglycemia) were suspicious for an intoxication with xylitol. The amount of ingested xylitol was unknown. The calculated maximum caffeine concentration was 7.9 to 78.6 mg/kg (median 21.7). In 11 cases, the owner could not provide information on the amount of chocolate ingested. Reasons for presentation were restlessness (n=33), tremor (22), vomiting (21), panting (11), polyuria /polydipsia (7), diarrhoea (2) and seizures (1). One dog each showed choking, swaying, seizures and salivation. At presentation, abnormal clinical findings included moderately moist to dry mucous membranes (seven), hyperthermia (10, 39.1 to 40°C, median 39.3), panting or tachypnea (14). Twenty-eight dogs exhibited tachycardia (140 to 280 bpm, median 180) without a pulse deficit. In all cases, sinus tachycardia was diagnosed with an ECG. The systolic blood pressure ranged from 100 to 185 mmHg (median 125). Two dogs exhibited hypertension (180 and 185 mmHg). The clinical pathologic findings of the dogs with clinical signs of chocolate intoxication are shown in Table 1 (n=34). Abnormal findings included hyperlactataemia (23/25; 92%), hypokalaemia (16/34; 47%), mild hyperglycaemia (16/34; 47%) and mild alanine aminotransferase (ALT) and aspartate aminotransferase (AST) elevation (14/34; 41%). Nineteen dogs were hospitalised for 1 to 4 days (median 2).

In 21 dogs, apomorphine was administered, the induction of emesis was successful in all cases. The dogs were treated with fluid therapy (44, crystalloids, continuous rate infusion, initially 2 to 3 mL/kg/hour), antiemetics (44), esmolol (10), forced diuresis (six) and sedatives (two, midazolam). Forty-three dogs with theobromine intoxication survived, one dog died. No dog showed progression of clinical signs during hospitalisation. The dog that died was a 72-month-old Kooikerhondje bitch who had ingested 100 g of dark chocolate 12 hours earlier (theobromine 64 mg/kg, caffeine 19.7 mg/kg). The dog presented with a pronounced sinus tachycardia (200 bpm), mild hyperthermia, vomiting and neurological signs (seizure). In addition, severe hypokalaemia (2.8 mmoL/L) and mild hyperglycaemia were detected. The dog received symptomatic treatment (fluid therapy, maropitant, diazepam, metamizole [dipyrone]), but died within 4 hours.

Table 1. Clinical pathological findings in 34 dogs with clinical signs of chocolate intoxication

Parameter	Dogs range (median)	Reference value	Increased number of dogs	Decreased number of dogs
Leukocytes ($x10^9$/L)	4.3 to 27 (10.2)	5.6 to 14	7	3
Haematocrit (L/L)	0.35 to 0.64	0.42 to 0.56	2	8
Platelets ($x10^9$/L)	230 to 680 (340)	165 to 400	10	0
Sodium (mmol/L)	136 to 155 (143)	140 to 150	1	6
Potassium (mmol/L)	2.6 to 4.6 (3.6)	3.6 to 4.8	0	16
Glucose (mmol/L)	3.2 to 9.4 (6.3)	4.5 to 6.2	16	2
Creatinine (µmol/L)	44 to 407 (71)	53 to 124	1	5
Urea (mmol/L)	1.7 to 44 (4.4)	3.5 to 10	3	5
ALT (U/L)	15 to 878 (108)	<76	14	0
AP (U/L)	10 to 1039 (83)	<97	9	0
AST (U/L)	9 to 435 (85)	<41	14	0
Bilirubin (µmol/L)	0.1 to 8.3 (1.9)	<5.1	1	0
Protein (g/L)	45 to 78 (66.2)	54 to 66	14	2
Albumin (g/L)	20 to 44 (31.5)	28 to 36	4	4
Lactate (mmol/L) n=25	1.7 to 9.6 (3.6)	<2.5	23	0

DISCUSSION

Many dog owners are aware of the fact that chocolate can be toxic for dogs and present their dogs after ingestion to a veterinarian. However, most of the dogs in this study did not show any clinical signs. Possible reasons might be the ingestion of milk chocolate and therefore a low methylxanthine concentration. Furthermore, some dogs were presented immediately after the chocolate ingestion and decontamination could be performed rapidly. Similar to a study evaluating data from 229 small animal practices in the UK, most cases of chocolate intoxication occurred around Christmas and Easter (Noble *et al.* 2017).

The methylxanthine caffeine is absorbed within 1 to 2 hours, so dogs can show signs within less than 60 minutes. The earliest time of presentation was 45 to 60 minutes after ingestion of the chocolate in 3 dogs showing clinical signs (tremor, agitation, vomiting). Theobromine is the more potent toxic component of the two methylxanthines. In addition, part of the caffeine is converted into theobromine (Löffler *et al.* 2000a). Besides the theobromine concentration, the theobromine:caffeine ratio is also considered crucial. A ratio of 5:1 has a high toxic potential (Johnston 2005). According to literature, mild clinical signs (agitation) occur at an intake of 20 mg/kg theobromine; cardiovascular signs are expected at ingested dosages above 40 mg/kg theobromine and seizures/tremor above 60 mg/kg theobromine (Gwaltney-Brant 2001). Fifty percent of dogs die after an intake of 100 to 200 mg/kg theobromine. Dogs with clinical signs in this study had eaten a median calculated theobromine concentration of 70.8 mg/kg. Calculating with the highest possible methylxanthine content in dogs that ingested an unknown proportion of different types of chocolate might have led to an overestimation in one case. The plasma half-life of theobromine is significantly longer in dogs compared to humans (17.5 hours *versus* 6 to 10 hours). Thus, dogs excrete theobromine at a considerably slower rate and are therefore predisposed to intoxication (Dolder 2013). There are no data in the literature on the minimal dose of caffeine inducing clinical signs. The lethal caffeine dose in dogs is 110 to 200 mg/kg (Tawde *et al.* 2012). The median caffeine dose was 21.7 mg/kg in dogs with clinical signs, the highest calculated dose was 78.6 mg/kg. Neurological signs such as restlessness and tremor were the most common reason for presentation in the patients described here. Gastrointestinal signs including vomiting and diarrhoea occurred in about 50% of the dogs in this study and might be explained by the high amount of ingested fat. Furthermore, caffeine leads to smooth muscle relaxation in the gastrointestinal tract and stimulation of the gastric secretion (Ooms *et al.* 2001). The most frequent finding of the clinical examination was tachycardia, which is caused by the sympathomimetic effect of methylxanthines. The clinical signs may vary if other toxic substances such as raisins or xylitol are ingested in combination with chocolate (Noble *et al.* 2017).

Forty-seven percent of dogs displayed hypokalaemia, which was severe in four cases (<3 mmoL/L). A possible explanation could be loss of potassium via the gastrointestinal tract, but only six of the dogs with hypokalaemia had vomiting or diarrhoea. Another cause for the development of hypokalaemia is respiratory alkalosis (panting) and epinephrine-related translocation of potassium into the cells (Moratinos & Reverte 1993). A high proportion of dogs showed an increase in the liver enzymes AST and ALT. The release of these enzymes is most likely caused by the increased muscle activity due to muscle tremors and spasms (Olby 2016). Creatine kinase concentrations were not measured in these dogs. Dogs with increased AST and ALT activity had a body temperature of 38.2 to 40.0°C (median 39.0). Another explanation for increases liver enzymes might be a malperfusion of the liver in cases of severe arrhythmias. The cause for polyuria might be renal resistance for ADH (secondary nephrogenic diabetes insipidus) due to hypokalemia in two dogs (plasma potassium concentration 2.6 and 2.8 mmoL/L). In human, medicine diuresis due to increased urinary sodium excretion after caffeine intake has been described (Yu *et al.* 2016).

Since an antidote against methylxanthines is not available, a symptomatic therapy is carried out in addition to decontamination. Vomiting was induced with apomorphine and was successful in all cases. The formation of a large chocolate mass in the stomach may be the reason for a lack of emitted chocolate through emesis in some cases described in the literature (Hooser & Beasley 1986). The use of apomorphine should be carefully evaluated in dogs with severe heart disease, seizure disorders or in dogs who have recently undergone abdominal surgery (Dolder 2013). Methylxanthines undergo enterohepatic circulation. Therefore, the administration of activated charcoal over a period of 72 hours is recommended (Luiz & Heseltine 2008). The

symptomatic therapy consists of fluid therapy with correction of the electrolyte deviations and, depending on the clinical signs, sedatives (midazolam, diazepam), antiepileptics (phenobarbital) and antiemetics (maropitant, metoclopramide) (Dolder 2013). Sinus tachycardia in euvolaemic dogs is treated with ß-blockers (esmolol, atenolol), in case of ventricular arrhythmias lidocaine is indicated.

The prognosis of a methylxanthine intoxication caused by chocolate ingestion is good, life-threatening complications of theobromine or caffeine intoxication may include the occurrence of arrhythmias with the development of pulmonary oedema and convulsions (Stosic *et al*. 2011, Agudelo *et al*. 2013). Fatalities are rare.

In cats, the toxic dose of caffeine and theobromine is lower compared to dogs. However, intoxication is very rare in cats due to their selective eating behaviour (Luiz & Heseltine 2008, Dolder 2013).

One limitation of the study is the lack of detection of methylxanthines in blood or urine.

The measurement of methylxanthine concentrations was not necessary for the care of the patients described here, since the diagnosis was confirmed on the basis of the observed chocolate ingestion and the typical clinical signs. In unclear cases or for forensic reasons, the methylxanthine concentration in blood, stomach contents, urine and liver parenchyma can be determined (Stosic *et al*. 2011, Dolder 2013). In the patients described here, clinical signs cannot be inferred from the amount of theobromine absorbed, since the treatment of the dogs reduced the amount absorbed. But the calculation of the theobromine amount is particularly useful for assessing the necessity of treatment. Further limitations are the retrospective nature of the data and the lack of treatment standardisation.

The type and the amount of chocolate ingested, and the time of ingestion are important criteria for planning the therapy and calculating the theobromine content. Patients with chocolate intoxication commonly show cardiovascular, neurological and gastrointestinal signs. After decontamination and symptomatic therapy, the prognosis in this case series was good, with only one fatality observed.

Conflict of interest

None of the authors of this article has a financial or personal relationship with other people or organisations that could inappropriately influence or bias the content of the paper.

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