Disseminated intravascular coagulation in dogs with gastric dilatation-volvulus syndrome

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ABSTRACT: Gastric dilatation and volvulus syndrome is associated with changes in haemostatic profiles. The aims of this study were to compare selected haemostatic and fibrinolytic parameters between healthy dogs and dogs with gastric dilatation and volvulus syndrome, estimate the incidence of disseminated intravascular coagulation (DIC), and determine the most sensitive test for detection of DIC in these patients. Blood was collected from 22 dogs with gastric dilatation and volvulus syndrome, and nine healthy control dogs. Platelet counts, prothrombin time, activated partial thromboplastin time, fibrinogen concentrations and fibrin/fibrinogen degradation products were measured in all control dogs and patients with gastric dilatation and volvulus syndrome, before and after surgery. Significant differences between control dogs and patients were seen in activated partial thromboplastin time and fibrin/fibrinogen degradation products before surgery and all measured parameters after surgery. The incidence of DIC was 59%. The most sensitive tests for detection of DIC before surgery were those for activated partial thromboplastin time and fibrin/fibrinogen degradation products.

Keywords: bleeding disorders; canine; coagulopathy; fibrin degradation products; haemostasis

List of abbreviations

aPTT = activated partial tromboplastin time, **AT** =antithrombin, **DIC** = disseminated intravascular coagulation, **FBG** = fibrinogen, **FDP** = fibrin degradation products, **GDV** = gastric dilatation and volvulus syndrome, **PT** = prothrombin time, **SIRS** = systemic inflammatory response syndrome

Gastric dilatation and volvulus syndrome (GDV) is a potentially life-threatening disease in dogs. Spatial changes in the stomach and proximal intestine lead to the hypoperfusion and mechanical compression of these and surrounding tissues (Monnet 2003). Alarmins and other mediators are released from cells, initiating systemic inflammatory response syndrome (SIRS) (Keel and Trentz 2005; Uhrikova et al. 2011). During SIRS, haemostasis is affected by various mechanisms, including decreased activity of plasma anticoagulants (protein C, protein S, antithrombin) or upregulation of tissue factor and plasminogen activator inhibitor 1. These changes may increase the activity of the coagulation and fibrinolytic system with subsequent initiation of thrombo-haemorrhagic disorder, disseminated intravascular coagulation (Wada 2004). Uncontrolled and excessive bleeding in GDV due to DIC can cause deterioration of shock state and lead to complications in surgical procedures; thus, its prompt recognition along with therapeutic intervention may be beneficial for the treatment and recovery from GDV.

The aims of this study were to compare selected haemostatic and fibrinolytic parameters between healthy dogs and dogs with GDV, estimate the incidence of DIC in dogs with GDV and determine the most sensitive test for detection of DIC in dogs with GDV.

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MATERIAL AND METHODS

Twenty-two dogs with gastric dilatation and volvulus admitted to the Small Animal Clinic at the University of Veterinary and Pharmaceutical Sciences, Brno, Czech Republic, were included in this retrospective study. Diagnosis was made on the basis of history, clinical signs and positive radiographic examination followed by surgical treatment. There were 13 males and nine females (none castrated or spayed) with an average age of seven years zero months (min. one year, max. 12 years four months) and average weight of 43.6 kg (min. 27 kg, max. 80 kg). The represented breeds were Rhodesian Ridgeback and Bernese Mountain Dog (n = 4), German Shepherd and Pyrenean Mountain Dog (n = 2), Basset Hound, Boxer, Central Asian Shepherd Dog, Dobermann, Fila Brasileiro, Great Dane, Labrador Retriever, Rottweiler, Saint Bernard and Weimaraner (n = 1).

The control group consisted of nine dogs, five males and four females with an average weight of 20.2 kg (min. 3.5 kg, max. 36 kg) and average age five years nine months (min. nine months, max. 11 years) and were of the following breeds: Bavarian Mountain Scenthound, Bohemian Shepherd, Border Collie, German Shepherd, Labrador Retriever, Small Musterlander (each n = 1). Three dogs were mongrels.

All dogs were sedated by intravenous application of midazolam 0.2 mg/kg (Dormicum, Roche Praha, s.r.o., Czech Republic), butorphanol 0.4 mg/kg (Butomidor, Richter Pharma, Austria) or buprenorphine 0.005 mg/kg (Vetergesic, Reckitt Beckiser Healthcare, UK), ketamine 2 mg/kg (Narkamon, 5% a.u.v. inj., Spofa a.s., Czech Republic) and general anaesthesia was induced by propofol (Norofol 1%, Norbrook Laboratories Limited, Germany). General anaesthesia was maintained by an inhalation mixture of oxygen, air and isoflurane (Isoflurane Nicholas Piramal India Ltd., UK) with artificial ventilation. Surgical treatment, with decompression and derotation of the stomach with gastropexy, was performed in all patients according to their individual needs. None of the patients received a transfusion. In cases of un-operable gastric necrosis, patients were euthanised.

Blood collection and analysis. Blood was collected before (sample A) and after surgery (sample B) from the jugular vein into test tubes containing citrate and EDTA (Dispolab, s.r.o., Czech Republic). The average time between sampling A and B was one and a half hour. In non-survivors, blood was collected directly before euthanasia. Haematological examination from EDTA blood was performed within 15 min using an automated haematology impedance analyser (Celtac alpha, Nihon Kohden, Japan). Citrated blood was immediately centrifuged (3000 rpm, 15 min) and stored at –20 °C until analysis (for a maximum of two weeks). Measurements of prothrombin time (PT; Tromboplastin-S, Dialab, s.r.o., Czech Republic), activated partial thromboplastin time (aPTT; APTT-S, Dialab, s.r.o., Czech Republic; 0.025M $CaCl_2$, Dr. Kulich Pharma, s.r.o., Czech Republic) and fibrinogen analyses (FBG, Bovinní trombin 100 NIH IU/ml, Dialab, s.r.o., Czech Republic) were performed on a two-channel analyser (Coatron M2, Teco, Germany) according to the manufacturer's instructions. Fibrin/fibrinogen degradation products (FDP) were measured using a latex-agglutination test (Diagnostica Stago, s.a.s., France).

Scoring system. Disseminated intravascular coagulation was diagnosed if four or more criteria were positive: low platelet count (< 200 × 10^9/l), increased prothrombin time (> 13 s), increased activated partial prothrombin time (> 19.5 s), decreased fibrinogen level (< 1.5 g/l) and increased fibrin/fibrinogen degradation products (> 10 mg/l). These criteria were adopted from Machida et al. (2010), but adjusted to our reference intervals and results from the control group. Tendency towards bleeding was scored as positive or negative based on subjective evaluation during surgery.

Statistical analysis. Data were evaluated using Statistica 6.0 (StatSoft, Inc., USA). Mann-Whitney U test were used for comparisons between the control group and patients. For comparisons between samplings A and B, Wilcoxon test were performed. The level of significance was set at $P < 0.05$, if not specified. Values are showed as medians.

RESULTS

Differences in laboratory profiles among control dogs and patients were noted at both samplings A and B. Before surgery, significant differences were present only in aPTT and FDP (Table 1). After surgery, differences were significant in all measured parameters. Between samplings A and B there were significant differences in all parameters except FDP. None of the dogs met the DIC criteria before surgery. After surgery, DIC was diagnosed

Table 1. Haemostatic parameters in control dogs and dogs with gastric dilatation–volvulus syndrome, before and after surgery

Sampling	Platelet count (×10^9/l)		PT (s)		aPTT (s)		FBG (g/l)		FDP (mg/l)	
	median	min–max	median	min–max	median	min–max	median	min–max	median	min–max
Before surgery	229	86–540	12.3	7.5–15.6	20.0*	16.1–45.9	2.7	0.6–6.3	12.5*	2.5–20.0
After surgery	150*†	4–318	14.6*†	9.9–31.4	24.6*†	17.0–110.9	1.3*†	0–3.4	12.5*	2.5–40.0
Controls	264	196–448	10.7	9.0–12.8	17.5	16.4–19.6	2.4	1.6–3.5	2.5	2.5–2.5

PT = prothrombin time; aPTT = activated partial thromboplastin time; FBG = fibrinogen concentration; FDP = fibrin/fibrinogen degradation products

*significant difference against control dogs ($P < 0.05$)

†significant difference against sampling before surgery ($P < 0.05$)

in 13 dogs (59%). In the non-DIC group there was one non-survivor (11%) and three dogs underwent splenectomy (33%). In the DIC group, there were four non-survivors (31%), three survivors with gastric necrosis who underwent gastrectomy and splenectomy (23%) and two dogs that underwent splenectomy (15%). Tendency towards bleeding was observed in 22% of dogs in the non-DIC group and 54% of participants in the DIC group. Between the DIC and non-DIC group there were significant differences in aPTT (26.6 vs. 19.7 s, $P < 0.01$) and fibrinogen concentration (1.0 vs. 2.1 g/l, $P < 0.05$) before surgery (Table 2). After surgery, these two groups differed significantly in all parameters ($P < 0.05$) except platelet count and FDP.

Before surgery, the highest sensitivity and specificity for development of DIC was observed in aPTT with values of 77% and 88%, respectively. The same sensitivity was reached with measurements of FDP (Table 2). After surgery, the parameters with the highest sensitivity were aPTT and PT, both with 92%, whilst fibrinogen concentration had the highest specificity with 88%.

DISCUSSION

One of the major complications in GDV is an increased risk of development of disseminated intravascular coagulation, which may cause further direct or indirect organ damage. Abnormal haemostatic profiles in dogs with GDV were described previously (Millis et al. 1993) and our study confirmed significant differences in both haemostatic and fibrinolytic parameters between control dogs and dogs with GDV.

Millis et al. (1993) defined DIC as positive, if three or more of the following criteria were met: prolonged aPTT, prolonged PT, thrombocytopenia, hypofibrinogenemia, elevated FDP, and decreased antithrombin (AT). In their study, 40% of dogs were considered positive for DIC. If we use these crite-

Table 2. Comparison of haemostatic parameters between patients with and without disseminated intravascular coagulation before and after surgery

Group	Platelet count (×10^9/l)		PT (s)		aPTT (s)		FBG (g/l)		FDP (mg/l)	
	before	after	before	after	before	after	before	after	before	after
DIC-negative	230	164	10.6	11.6	17.2	19.7	4.2	2.1	12.5	13
DIC-positive	227	130	12.3	14.8*	20.7*	26.6*	2.2*	1.0*	12.5	13
Sensitivity (%)	46	85	30	92	77	92	38	77	77	70
Specificity (%)	78	33	75	75	88	63	88	88	33	33

Values are shown as medians; before/after = sampling before/after surgery; PT = prothrombin time, aPTT = activated partial thromboplastin time; FBG = fibrinogen concentration; FDP = fibrin/fibrinogen degradation products; sensitivity/specificity = sensitivity/specificity for development of disseminated intravascular coagulation (DIC) if parameter is above reference range (platelet count below reference range)

*significant difference between DIC-negative and DIC-positive dogs ($P < 0.05$)

ria, DIC was present before surgery in 36% of dogs in our study. Therefore, we can conclude that the incidence was similar.

With respect to diagnostic tests, the highest sensitivity and specificity for prediction of DIC were achieved with measurements of aPTT with 77% and 88%, respectively. After surgery, the highest sensitivities were for aPTT and PT, both at 92%. It is well known that the most reliable laboratory tests for detection of DIC are FDP and AT. We did not measure AT, but increased FDP together with prolonged aPTT were the only significant differences in laboratory profiles between patients and control dogs before surgery. Since other causes of increased bleeding besides DIC are unlikely in dogs with GDV, aPTT seems to be a good laboratory indicator of increased risk for DIC.

Millis et al. (1993) concluded that FDP, aPTT and AT were the most useful parameters in predicting gastric necrosis. In our study, however, a significant difference between dogs with (n = 7) and without gastric necrosis (n = 15) was observed only in platelet count (data not shown). A decreased platelet count had a specificity of 86% for detection of gastric necrosis in this study, whilst specificities for FDP and aPTT were 29% and 61%, respectively. Nonetheless, increased aPTT and FDP and decreased platelet count had the highest sensitivities for detection of gastric necrosis (aPTT 86%, FDP and platelet count 71%).

Relationships between the haemostatic parameters and final outcome were not studied due to the low number of non-survivors (n = 5). In a study on DIC by Vlasin et al. (2004), the most reliable predictors of prognosis were the AT and thrombin clotting time; platelet count and fibrinogen concentration were slightly less sensitive. FDP levels were not helpful in determining prognosis. Since the majority of the non-survivors belonged to the group of patients with gastric necrosis (four out of seven dogs), we concur that a decreased platelet count may be useful in predicting final outcome.

In summary, we have found significant differences in haemostatic parameters between control dogs and dogs with gastric dilatation and volvulus and determined that the most sensitive test for early detection of DIC, before and after surgery, was aPTT.

REFERENCES

Keel M, Trentz O (2005): Patophysiology of polytrauma. Injury 36, 691–709.

Machida T, Kokubu H, Matsuda K, Miyoshi K, Uchida E (2010): Clinical use of D-dimer measurement for the diagnosis of disseminated intravascular coagulation in dogs. Journal of Veterinary Medical Science 72, 1301–1306.

Millis DL, Hauptman JG, Fulton RB (1993): Abnormal hemostatic profiles and gastric necrosis in canine gastric-dilatation volvulus. Veterinary Surgery 22, 93–97.

Monnet E (2003): Gastric dilatation-volvulus syndrome in dogs. Veterinary Clinics of North America: Small Animal Practice 33, 987–1005.

Uhrikova I, Rehakova K, Rauserova-Lexuamlova L, Doubek J (2011): Initial HMGB1 values in dogs with gastric dilatation and volvulus – a pilot study. Veterinary Clinical Pathology 40, 587.

Vlasin M, Rauser P, Fichtel T, Novotny J (2004): Disseminated intravascular coagulopathy of the dog. Acta Veterinaria Brno 73, 497–505.

Wada H (2004): Disseminated intravascular coagulation. Clinical Chemistry Acta 344, 13–21.

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