Effect of tranexamic acid on intra- and postoperative haemorrhage in dogs with surgically treated hemoperitoneum

N.E. Sigrist, L. Olgiati, R. Jud Schefer

Department for Small Animals, Vetsuisse Faculty, University of Zurich, Switzerland

https://doi.org/10.17236/sat00160

Received: 08.12.2017
Accepted: 29.01.2018

Summary

Tranexamic acid (TXA) is an antifibrinolytic drug that is used for uncontrolled bleeding of various origin. This retrospective study investigated the effect of tranexamic acid administration on bleeding tendency in dogs with surgically managed hemoperitoneum. Thirty dogs were treated with (TXA group) and 25 dogs without (CTR group) tranexamic acid prior to surgery. Various parameters (decrease in haematocrit, number of transfusions, shock index and changes in abdominal fluid accumulation) were used for characterization of bleeding tendency and compared between groups. Groups were similar at presentation and prior to surgery. None of the dogs undergoing rotational thromboelastography analysis showed hyperfibrinolysis prior to surgery. Overall transfusion and erythrocyte transfusion requirements as well as bleeding tendency, hospitalisation time and hospital discharge rate were similar between groups. Dogs of the TXA group received significantly more intraoperative plasma transfusions (P=0.013) and showed a higher systolic and mean arterial blood pressure (P=0.002 and 0.050) and lower shock index (P=0.028) with less dogs being in shock (P=0.012) at 24h. In summary, in this study population of dogs with surgically managed spontaneous hemoperitoneum dogs treated with tranexamic acid received more plasma transfusions intraoperatively and showed a lower shock index 24h after presentation. In dogs with surgically treated hemoabdomen tranexamic acid administration prior to surgery does not reduce red blood cell transfusion requirements or postoperative bleeding tendency.

Keywords: canine, hyperfibrinolysis, antifibrinolytic, hemoabdomen

Effekt von Tranexamsäure auf intra- und postoperative Blutungen in Hunden mit einem chirurgisch stabilisierten Hämoperitoneum

Tranexamsäure ist ein Fibrinolysehemmer, welcher bei unkontrollierten Blutungen verschiedener Ursachen eingesetzt wird. In dieser retrospektiven Studie wurde die Wirkung von Tranexamsäure auf die Blutungstendenz von Hunden mit chirurgisch stabilisiertem Hämoperitoneum untersucht. Dreissig Hunde wurden mit (Gruppe TXA) und 25 ohne Tranexamsäure (Kontrolle) behandelt. Verschiedene Parameter (Hämatokritabfall, Anzahl Transfusionen, Schockindex, Verlauf von abdominaler Flüssigkeit) wurden als Parameter für die Blutungstendenz zwischen den Gruppen verglichen. Bei Präsentation sowie präoperativ waren die Hunde beider Gruppen in allen untersuchten Parametern vergleichbar. Keiner der untersuchten Hunde zeigte Hyperfibrinolyse vor der Operation. Hämatokritabfall, Anzahl Erythrozytentransfusionen, Menge an abdominaler Flüssigkeit postoperativ, Hospitalisationzeit und Entlassungsrate zeigten keinen Unterschied zwischen den zwei Gruppen. Die Hunde der Gruppe TXA benötigten intraoperativ mehr Plasma-Transfusionen (P-Wert 0.013) und zeigten nach der Operation einen signifikant höheren systolischen und mittleren Blutdruck (P-Wert 0.002 und 0.050), einen tieferen Schockindex (P-Wert 0.028) und weniger Hunde waren im Schock (P=0.012). Zusammengefasst konnte in dieser Population von Hunden mit chirurgisch behandeltem spontanen Hämoabdomen kein reduzierter Transfusionsbedarf und keine Verminderung der postoperativen Blutungstendenz nach Therapie mit Tranexamsäure nachgewiesen werden. Tranexamsäure therapierte Hunde zeigten einen niedrigeren Schockindex 24h nach Präsentation und bekamen intraoperativ signifikant mehr Plasmatransfu-

Effect of tranexamic acid on intra- and postoperative haemorrhage in dogs with surgically treated hemoperitoneum

N. E. Sigrist, L. Olgiati, R. Jud Schefer

sionen verabreicht was die Interpretation der Resultate schwierig macht und keine eindeutige Aussage über den Nutzen von Tranexamsäure zulässt.

Schlüsselwörter: Hund, Hyperfibrinolyse, antifibrinolytisch, Hämoabdomen

Introduction

Causes for hemoperitoneum include trauma, coagulopathies and rupture of abdominal masses (Clarke et al., 2002; Nelson and Couto, 2010). Regardless of the cause, haemostasis aims at production of a clot to temporarily close the endothelial layer. After repair of the vascular endothelium, the clot is fibrinolysed (Chapin and Hajjar, 2015). With severe haemorrhage, as seen with hemoperitoneum, inhibition of fibrinolysis may occur. However, hypoperfusion and hypotension can inhibit physiological inhibition of fibrinolysis during clot production, leading to hyperfibrinolysis (Brohi et al., 2003 and 2008). While surgically treated abdominal haemorrhage should theoretically stop after surgical ligation of the bleeding vessel, ongoing fibrinolysis may lead to postoperative bleeding tendency (Marin et al., 2012). Hyperfibrinolysis can be treated with an antifibrinolytic such as tranexamic acid (McCormack, 2012). Tranexamic acid is a synthetic analogue of lysine. By binding to the lysine binding site on plasminogen, binding of plasmin to fibrinogen and fibrin followed by fibrinolysis is prevented (Astedt, 1987). While tranexamic acid is routinely administered to human patients including children with severe bleeding (Zufferey et al., 2006; Schouten et al., 2009; Crash-2 collaborators, 2010; Ker et al., 2012; Roberts et al., 2014), only a few studies have looked at the effects of antifibrinolytics in dogs and have reported conflictive results (Marin et al., 2012; Kelmer et al., 2013 and 2015). To the author's knowledge, no studies investigating the benefit of tranexamic acid administration to dogs with surgically controlled bleeding exists.

The goal of this retrospective study was to compare transfusion requirements and presence of postoperative bleeding tendency in dogs treated with and without tranexamic acid prior to surgical management of abdominal haemorrhage. The null hypothesis was that tranexamic acid administered prior to surgery to dogs with hemoabdomen would show no effect on transfusion requirement and signs of postoperative bleeding.

Animals, Material and Methods

The hospital's databank was searched for dogs that were diagnosed with hemoperitoneum between 2010 and 2016 and undergoing surgical treatment of abdominal bleeding. Exclusion criteria included missing data regarding bleeding, administration of tranexamic acid after induction of anaesthesia and death or euthanasia prior to or during surgery. Breed, age, sex and weight, clinical signs and laboratory parameters at presentation, prior to induction of anaesthesia and 24/48h post operatively, amount and duration of fluid administration, diagnosis, transfusion requirements, administration of tranexamic acid, duration of hospital stay and hospital discharge were extracted from patient records.

Clinical signs

Recording of clinical signs included heart rate (HR), respiratory rate (RR), mucous membrane colour, capillary refill time (CRT) and level of consciousness. Shock at presentation was defined as identification of >2 of the following: HR > 120/min, pale/white mucous membranes, CRT≥2s and decreased level of consciousness. Prior to surgery and at 24h and 48h the shock index (SI) was determined by calculating HR/systolic arterial blood pressure (Olaussen et al., 2014). A SI > 1.00 was considered as haemorrhagic shock (McGowan et al., 2017). The amount of abdominal fluid was graded as none, mild, medium, and severe. Changes in fluid accumulation over time were defined as "increase" or "same/decrease".

Laboratory parameters

Laboratory parameters from the first 24h were extracted as needed for determination of the SPI2 score (King et al., 2001) and determination of hypocoagulability. Hypocoagulability was defined as ≥2 coagulation parameters (PT or ExTEM coagulation time (CT), aPTT, fibrinogen Clauss concentration or FibTEM maximal clot firmness (MCF), and ExTEM MCF or thrombocyte count and maximal ExTEM lysis > 15%) indicating decreased coagulation. All haematocrit (Hct) measurements over hospitalization time were extracted and the lowest and last measured Hct were used for analysis of changes over time. Dogs that received red blood cell transfusions were excluded from analysis of follow-up parameters or changes over time once they received a transfusion. For each dog, the number of whole blood, packed red blood cells (pRBC) and plasma transfusions where recorded for the preoperative, intraoperative and postoperative period. For analysis, 450 ml of autotransfusion, 450 ml of fresh whole blood and 1 Unit pf pRBC

were defined as "300 ml erythrocyte transfusion". One unit of plasma was defined as 300 ml of plasma for determination of ml/kg transfusion doses. Postoperative haemorrhage ("continuous bleeding") was defined as ≥1 of the following: shock index >1.0 at 48h, decrease in haematocrit between 24 and 48h, need for erythrocyte transfusion post operatively, and increase in abdominal fluid accumulation between 24 and 48h. For comparison, dogs were assigned to one of the following groups: Group TXA received tranexamic acid at least 30 minutes prior to surgery while the group CTR was not treated with TXA.

Table 1: Parameters prior to surgery of 30 dogs with surgically treated hemoperitoneum treated with (group TXA) and 25 dogs without (group CTR) tranexamic acid.

	Group CTR (n=25)				Group TXA (n=30)				
Parameter	n/N	Min	Max	Mean +/– SD median	n/N	Min	Max	Mean +/– SD Median	P-value
Age (years)	25/25	3.0	14.7	9.4 ± 3	30/30	4.2	15.3	9.6 ± 3	0.764
Weight (kg)	25/25	10.8	39.5	28 ± 9	30/30	8.4	46.5	26.6 ± 10	0.570
Parameters at presentation									
Heart rate (beats/min)	25/25	60	200	132 ± 34	30/30	80	200	137 ± 32	0.552
Respiratory rate (breath/min)	22/25	20	100	38	30/30	16	100	33	0.436
Temperature (°C)	23/25	35.1	39.9	37.9 ± 1	26/30	35.7	39.6	37.9 ± 1	0.940
Hematocrit (%))	25/25	19	49	33 ± 8 33	30/30	24	51	31	0.665
Thrombocytes (10*9 /L)	16/25	40	294	107	25/30	16	472	124	0.702
Parameters prior to induction of anaesthesia									
Heart rate (beats/min)	25/25	56	200	127 ± 38	30/30	70	200	129 ± 33	0.912
Respiratory rate (breaths/min)	24/25	10	160	24	26/30	6	100	24	0.350
Temperature (°C)	24/25	35.7	39.1	27.6 ± 0.8	26/30	36.1	39.7	37.6 ± 0.9	0.875
Systolic blood pressure (mmHg)	24/25	60	150	106 ± 26	30/30	65	169	108 ± 24	0.692
MAP (mmHg)	24/25	40	113	71 ± 17	30/30	40	115	75 ± 18	0.418
Lactate (mmol/L)	14/25	1	8	1.89	19/30	1	8	2.5	0.226
Shock index	24/25	0.5	2.8	1.12	30/30	0.68	3.08	1.2	0.964
SPI2 Score	22/25	0.62	0.75	0.73	26/30	0.67	0.75	0.73	0.649

MAP: mean arterial blood pressure, SPI: survival prediction index

Table 2: Categorical parameters at presentation and prior to induction of anaesthesia in 30 dogs treated with and 25 dogs treated without tranexamic acid for surgically managed hemoperitoneum.

		Group CTR (n=25)		Group TXA (n=30)		
Parameter		n/N	%	n/N	%	P-value
Diagnosis	Malignant neoplasia	13/25	52	23/30	77	0.120
	Hemangiosarcoma	11/25	44	18/30	60	
	Benigne mass	11/25	44	7/30	23	
	trauma	1/25	4	0/30	0	
Amount of abdominal fluid at presentation	None	0	0	0	0	0.399
	Mild	10/25	40	8/30	27	
	Medium	9/25	36	10/30	33	
	Severe	6/25	24	12 /30	40	
Hypocoagulability at presentation	Yes	2/5	40	7/17	41	0.684
Hyperfibrinolysis at presentation	ML>15%	0/5	0	0/17	0	NA
Presence of shock at presentation	yes	16/25	64	20/30	67	0.530
Shock index at induction of anaesthesia	>1.00	17/24	71	19/29	66	0.455

Statistical analysis

Data were entered into a spreadsheet and analyses were performed using the statistical software program SPSS. The dataset was split into groups TXA and CTR. Distribution of data was assessed by Shapiro-Wilk and continuous variables are recorded as mean +/-SD if normally distributed and median if not normally distributed. The frequency distributions of the categorical or ordinal (score) variables were derived. Non-normally distributed continuous variables were compared with Mann-Whitney-U tests and normally distributed continuous variables were analysed with t-tests. Associations between categorical variables were evaluated using the Chi-Square test. When both variables were binary and expected cell frequencies were < 5, Fisher's test was used. Significance was set at $P \leq 0.05$.

Results

A total of 55 dogs were analysed and included 30 dogs (55%) treated with (group TXA) and 25 dogs (45%, group CTR) treated without tranexamic acid. Various breeds were represented with mixed breeds being the most common (17/50, 31%) followed by Retrievers (10/55, 18%). Signalement and evaluated parameters at presentation and at the time of anaesthesia induction were not significantly different between groups (Tab. 1 and 2). Dogs of the TXA group received a median dose of 20 mg/kg (range, 10-25 mg/kg) tranexamic acid at least 30 minutes prior to surgery and over a median number of 1 day (range, 0.5-2 days) and 1 treatment (range, 1-8).

Neither the amount of crystalloid and colloidal fluids ($P=0.702$ and 0.907), administration of erythrocytes ($P=0.221$), postoperative continuous bleeding ($P=0.597$), hospitalization time ($P=0.716$) nor survival ($P=0.412$) were significantly different between groups (Tab. 3 and 4). However, dogs of the TXA group showed a significantly higher systolic and mean arterial blood pressure ($P=0.002$ and 0.050) and a lower median shock index ($P=0.028$) with less dogs in shock ($P=0.012$) 24h after surgery (Tab. 3). Furthermore, significantly more dogs of the TXA group received plasma transfusions during surgery ($P=0.013$) and less dogs in the TXA group underwent splenectomy ($P= 0.043$) (Tab. 3 and 4).

Discussion

Our study investigating dogs presenting with surgically controlled abdominal haemorrhage did not identify a significant difference in intra- or postoperative overall transfusion requirements, erythrocyte transfusion requirements or signs of continuous bleeding after surgery. Tranexamic acid is used to both prevent bleeding in patients undergoing surgeries with high-risk of blood loss as well as to decrease bleeding in patients with existent haemorrhage (Zufferey et al., 2006; Ker et al., 2012; Napolitano et al., 2013; Lundin et al., 2014; Roberts et al., 2014). The rationale of tranexamic acid administration is the occurrence of hypoperfusion-associated hyperfibrinolysis that may continue after ligation of the bleeding vessel. Hypoperfusion and hypotension can diminish physiological inhibition of fibrinolysis by an increased release of protein C (Brohi et al., 2003 and 2008). Protein C causes disinhibition of tissue plasminogen activator (tPA) leading to hyperfibrinolysis (Brohi et al., 2008). Hyperfibrinolysis has been described in dogs with hemoperitoneum (Fletcher et al., 2016; Zoja et al., 2017) and has been associated with shock (Fletcher et al., 2016). However, the effect of treatment with tranexamic acid has not been investigated in dogs with hemoperitoneum. Kelmer et al. investigated dogs with both primary and secondary haemostasis abnormalities and did not find a significant difference in overall transfusion requirement (including plasma) and pRBC transfusion in dogs treated with tranexamic acid if only dogs requiring transfusion therapy were included (Kelmer et al., 2013). Another study investigating prophylactic administration of Epsilon aminocaproic acid, a similar antifibrinolytic, to greyhounds undergoing gonadectomy showed a significant decrease in the prevalence of postoperative bleeding (Marin et al., 2010). None of the dogs undergoing rotational thromboelastometry (ROTEM) analysis showed hyperfibrinolysis prior to surgery, however only 22/50 dogs were analyzed. Ongoing hyperfibrinolysis was not assessed but as the dogs in our study population treated with tranexamic acid did not need less erythrocyte transfusions and did not show decreased incidence of continuous bleeding after surgery, hyperfibrinolysis-associated postoperative haemorrhage does not seem to dominate in this study population. Of note, while the overall transfusion rate was not significantly different in our study population, analysis of specific blood components showed that dogs treated with tranexamic acid received significantly more plasma transfusions intraoperatively. Plasma is commonly administered for fibrinogen or coagulation factor deficiency at our institution. While the detailed reason for plasma administration could not be retrospectively determined, the assumption that dogs of the TXA group had additional coagulation deficiencies and/or plasma administration was subject to bias, stands to reason.

Other causes for continuous bleeding after surgical ligation of the bleeding vessel besides hyperfibrinolysis may be caused by dilution and loss of coagulation factors, fibrinogen and thrombocytes (Ledgerwood et al., 2003). Tranexamic acid has no effect on primary or secondary haemostasis (McCormack, 2012). Dogs in

Table 3: Continuous postoperative parameters of 30 dogs treated with (group TXA) and 25 dogs without (group CTR) tranexamic acid and surgically managed hemoperitoneum.

	Group CTR (n=25)				Group TXA (n=30)				
Parameter	n/N	Min	Max	Mean +/– SD median	n/N	Min	Max	Mean +/– SD Median	P-value
Hematocrit 24h (%)	19/25	17	34	24 ± 5	26/30	12	43	25	0.381
Hematocrit lowest (%)	22/25	10	34	20 ± 7	29/30	12	28	20 ± 5	0.811
Hematocrit last (%)*	13/19	17	40	27 ±7	14/30	21	43	26	0.756
Hematocrit change 24-48h	6/25	–8	8	0.5	6/30	–3	13	2.5	0.553
Hematocrit change from presentation to lowest (%)	25/25	–44	3	–15 ± 11	30/30	–33	–3	–14 ± 8	0.793
Hematocrit change from presentation to last (%)*	13/25	–21	7	–13 ± 9	14/30	–23	10	–8 ± 8	0.792
Tc day 1 (10*9/L)	8/25	29	238	121 ± 70	13/30	31	230	70	0.374
Tc last (10*9/L)	11/25	72	661	189	20/30	52	1270	156	0.359
HR 24h	24/25	60	180	119	30/30	60	185	95	0.223
Systolic BP 24h	17/25	84	134	110 ± 12	25/30	94	197	133 ±27	0.002
MAP 24h	17/25	67	101	76 ± 10	26/30	53	136	93 ± 22	0.050
Shock index 24h	17/25	0.51	1.67	1.04 ± 0.4	25/30	0.39	1.83	0.73	0.028
HR 48h	23/25	50	150	100	29/30	53	194	84	0.580
Systolic BP 48h	11/25	95	157	122 ± 18	21/30	96	163	125 ± 19	0.584
MAP 48h	11/25	72	100	89 ± 8	22/30	64	111	88 ± 14	0.919
Shock index 48h	11/25	0.42	1.37	0.84 ± 0.3	21/30	0.36	1.88	0.78 ± 0.4	0.618
Erythrocytes intra/post operatively (ml/kg)	25/25	0	28	0	30/30	0	29	3.2	0.296
Plasma intra/post operatively (ml/kg)	25/25	0	23.6	2.1 ± 6 0	30/30	0	35	8.4 ± 11 0	0.019
Hospitalisation (days)	25/25	1	10	4	30/30	0	9	4	0.716

Table 4: Categorical postoperative parameters of 30 dogs treated with (group TXA) and 25 dogs without (group CTR) tranexamic acid and surgically managed hemoperitoneum.

		Group CTR (n=25)		Group TXA (n=30)		
Parameter		n/N	%	n/N	%	P-value
Splenectomy	yes	23/25	92	21/30	70	0.043
SI at 24h	>1.00	10/17	59	5/25	20	0.012
SI at 48h	>1.00	4/11	36	5/21	24	0.362
Fluid increase presentation - 24h	Yes	1/17	6	1/24	4	0.663
Fluid increase between 24-48h	Yes	0/14	0	0/23	0	NA
Continuous bleeding	Yes	8/20	40	11/28	39	0.597
Transfusion (pRBC, whole blood or plasma)	Yes	9/25	36	17/30	57	0.104
Number of dogs that received Erythrocyte transfusions	Yes	9/25	36	15/30	50	0.221
	Intraoperatively	6/25	24	11/30	37	0.237
	Postop	3/25	12	7/30	23	0.233
Number of dogs that received plasma	Intraoperatively	1/25	4	9/30	30	0.013
	Post op	2/25	8	3/30	10	0.588
Hyperfibrinolysis post op	ML>15%	1/2	50	0/6	0	0.250
Hospital discharge	Yes	22/25	88	28/30	93	0.412

our study were thrombocytopenic both at admission and 24h after presentation and the degree of thrombocytopenia was similar in both groups. Furthermore, as discussed above, dogs in both groups were similar prior to surgery in terms of hypocoagulability based on plasmatic coagulation times and ROTEM parameters but dogs in the TXA group received more intraoperative plasma transfusions which does not allow a clear conclusion. The increased administration of plasma during surgery may also be the reason of the significantly lower shock index 24h after presentation in the TXA group.

The time frame of ongoing haemorrhage may also be important and is unknown in spontaneous hemoperitoneum. The CRASH-2 trial identified the best benefit of tranexamic acid if administered within 3 hours of trauma/start of bleeding (Crash-2 investigators, 2010). This may be unique to trauma patients as hyperfibrinolysis in trauma is seen early after trauma in both humans (Brohi et al., 2008; Roberts, 2015) and dogs (Muri et al., accepted 2017). Additionally, it is recommended to repeat administration of tranexamic acid every 6-8h if hyperfibrinolysis is evident (McCormack, 2012). With less evident hyperfibrinolysis, some studies in humans showed an effect on postoperative bleeding despite only intraoperative administration of tranexamic acid (Tanaka et al., 2001; Madershaian et al., 2015). All dogs received tranexamic acid 30 minutes to 3 hours prior to surgery and an antifibrinolytic effect is expected for the intraoperative and early postoperative period (McCormack, 2012; Kakiuchi et al., 2014). As only a few dogs received repeated doses of tranexamic acid we can only conclude that a single dose of tranexamic acid prior to surgery was not associated with a decrease of transfusion requirement and signs of "continuous bleeding". Hospitalization time and survival further was not different between groups, indicating that tranexamic acid administration has no effect on these parameters in this patient population.

Main limitations of the study are the small study population and the lack of randomization of tranexamic acid administration. However, dogs in both groups were comparable at presentation and prior to surgery and showed similar SPI2 scores, indicating that despite the lack of randomization of tranexamic acid administration, the TXA group did not receive tranexamic acid because of severity of abdominal haemorrhage or clinical presentation. The lack of a clear indication for the increased plasma administration intraoperatively precludes a clear conclusion and the study should therefore be interpreted with regards to this finding. Another reason for the lack of benefit of tranexamic acid administration may be the power of the study to detect a significant difference. The need for intra- and postoperative red blood cell transfusion was low in both groups. It may be possible that haemorrhage was not severe enough to cause hyperfibrinolysis, hence no benefit of treatment with an antifibrinolytic in this study population. The amount of abdominal fluid present at the time of surgery could not be retrospectively determined, therefore transfusion requirements have been used as an outcome as previously described (Ker et al., 2011 and 2013; Lundin et al., 2014; Madershahian et al., 2015).
In summary, in this study population of dogs with surgically managed hemoperitoneum, tranexamic acid administration prior to surgery did not result in a significant decrease in erythrocyte transfusions. Dogs treated with tranexamic acid received more plasma transfusions intraoperatively and showed a lower shock index 24h after presentation. None of the 55 dogs showed hyperfibrinolysis at presentation, further questioning the rationale for tranexamic acid administration in dogs with surgically treated hemoabdomen.

Effet de l'acide tranexamique sur les hémorragies intra- et postopératoires chez des chiens traités chirurgicalement pour un hémopéritoine

L'acide tranexamique (TXA) est un médicament antifibrinolytique utilisé lors d'hémorragies incontrôlées d'origines diverses. Cette étude rétrospective analyse les effets de l'administration d'acide tranexamique sur la tendance aux hémorragies sur des chiens souffrant d'un hémopéritoine traité chirurgicalement. Trente chiens ont été traités avec de l'acide tranexamique avant chirurgie (groupe TXA) et vingt- cinq ne l'ont pas été (groupe CTR). Divers paramètres (baisse de l'hématocrite,

Effetto dell'acido tranexamico sulle emorragie intra- e post-operatorie nei cani con emoperitoneo trattato chirurgicamente

L'acido tranexamico (TXA) è un farmaco antifibrinolitico usato nei casi di sanguinamento incontrollato di varia origine. Questo studio retrospettivo ha esaminato l'effetto della somministrazione di acido tranexamico sulla tendenza al sanguinamento nei cani con emoperitoneo trattato chirurgicamente. Prima dell'intervento chirurgico, trenta cani sono stati trattati con l'acido tranexamico (gruppo TXA) e 25 senza di esso (gruppo CTR). Vari parametri sono stati usati per caratterizzare

nombre de transfusions, index de choc et modification de l'accumulation de fluide intrapéritonéal) ont été utilisés pour caractériser la tendance à l'hémorragie et effectuer une comparaison entre les deux groups. Les deux groupes étaient semblables lors de l'admission et avant la chirurgie. Aucun des chiens soumis à une analyse par thromboélastométrie rotationnelle ne montrait une hyper fibrinolyse avant la chirurgie. Les besoins en matière de transfusions en général ou de transfusions d'érythrocytes de même que la tendance aux hémorragies, la durée d'hospitalisation et le taux de sortie d'hospitalisation étaient semblables entre les deux groupes. Les chiens du groupe TXA ont reçu significativement plus de transfusions de plasma intra opératives (P=0.013) et présentaient des pressions systoliques et moyennes plus élevées (P=0.002 and 0.050) de même qu'un index de choc plus bas (P=0.028) avec moins de chiens souffrant de choc à 24 heures (P=0.012). En résumé, dans cette étude, la population de chiens présentant un hémopéritoine spontané traité chirurgicalement et ayant reçu de l'acide tranexamique a reçu plus de transfusions de plasma intra opératives et présentait un indexe de choc plus bas 24 heures après l'admission. Chez les chiens traités chirurgicalement pour un hémoabdomen, l'administration d'acide tranexamique avant l'opération n'a pas réduit les besoins en matière de transfusions d'érythrocytes ou la tendance aux hémorragies post-opératoires.

la tendenza al sanguinamento e sono stati confrontati tra i gruppi (diminuzione dell'ematocrito, numero di trasfusioni, indice di shock e modifiche nell'accumulo di liquidi nell'addome). I gruppi erano simili alla presentazione e prima dell'intervento chirurgico. Nessun cane sottoposto a tromboelastografia rotazionale ha mostrato iperfibrinolisi prima dell'intervento. I requisiti generali di trasfusione e di trasfusione di eritrociti, così come la tendenza al sanguinamento, la durata dell'ospedalizzazione e la percentuale di dimissione ospedaliera erano simili tra i gruppi. I cani del gruppo TXA hanno ricevuto trasfusioni di plasma intraoperatorie significativamente più elevate (P = 0.013), hanno mostrato una pressione arteriosa sistolica e media più alta (P = 0.002 e 0.050) e un indice di shock inferiore (P = 0.028) con meno cani in stato di shock su 24 ore (P = 0.012). In sintesi, nella popolazione di questo studio, i cani affetti da emoperitoneo spontaneo gestito chirurgicamente e trattati con acido tranexamico hanno ricevuto più trasfusioni di plasma intraoperatorie e hanno mostrato un indice di shock inferiore 24 ore dopo la presentazione. Nei cani con emoaddome trattato chirurgicamente la somministrazione di acido tranexamico prima dell'intervento chirurgico non ha ridotto la quantità di trasfusione di eritrociti o la tendenza al sanguinamento postoperatorio.

References

Astedt B.: Clinical Pharmacology of tranexamic acid. Scand. J. Gastroent. 1987, 22: S137.

Brohi K., Cohen M. J., Ganter M. T., Schultz M. J., Levi M., Mackersie R. C., Pittet J.: Acute Coagulopathy of trauma: Hypoperfusion induces systemic anticoagulation and hyperfibrinolysis. J. Traum. Inj. Inf. Crit. Care 2008, 64: 1211-1217.

Brohi K., Singh J., Heron M., Coats T.: Acute traumatic coagulopathy. J. Trauma. Inj. Inf. Crit. Care 2003, 54: 1127-1131.

Chapin J.C., Hajjar K.A.: Fibrinolysis and the control of blood coagulation. Blood. Rev. 2015, 29: 17-24.

Clarke J.R., Trooskin S.Z., Doshi P.J., Greenwald L., Mode C.J.: Time to laparotomy for intra-abdominal bleeding from trauma does affect survival for delays up to 90 minutes. J. Trauma 2002, 52: 420–425.

CRASH-2 trial collaborators: Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2): a randomised, placebo-controlled trial. Lancet 2010, 376: 23-32.

Edwards P., Shakur H., Barnetson L., Prieto D., Evans S., Robers I.: Central and statistical data monitoring in the Clinical Randomisation of an Antifibrinolytic in significant Haemorrhage (CRASH-2) Trial. Clin. Trials 2014, 11: 336–343.

Fletcher D.J., Rozanski E.A., Brainard B.M., De Laforcade A.M., Brooks M.B.: Assessment of the relationships among coagulopathy, hyperfibrinolysis, plasma lactate, and protein C in dogs with spontaneous hemoperitoneum. J. Vet. Emerg. Crit. Care 2016, 26: 41-51.

Kakiuchi H., Kawarai-Shimamura A., Fukuu Y., Aoki T., Yoshiike M., Arai H., Nakamura A., Orito K.: Efficacy and safety of tranexamic acid as an emetic in dogs. Am. J. Vet. Res. 2014, 75: 1099-1103.

Kelmer E., Marer K., Bruchim Y., Klainbart S., Aroch I., Segev G.: Retrospective Evaluation of the Safety and Efficacy of Tranexamic Acid (Hexakapron®) for the Treatment of Bleeding Disorder in Dog. Isr. J. Vet. Med. 2013, 68: 94-100.

Kelmer E., Segev F., Segev G., Papashvilli V., Rahimi-Levene N., Bruchim Y., Aroch I., Klainbart S.: Effects of intravenous administration of tranexamic acids on hematological, hemostatic and thromboelastographic analyses in healthy adult dogs. J. Vet. Emerg. Crit. Care 2015, 25: 495 – 501.

Ker K., Edwards P., Perel P., Shakur H., Roberts I.: Effect of tranexamic acid on surgical bleeding: systematic review and cumulative meta-analyse. Brit. Med. J. 2012, 344: e3054.

Ker K., Prieto-Merino D., Roberts I.: Systematic review, meta-analysis and meta-regression of the effect of tranexamic acid on surgical blood loss. Brit. J. Surg. 2013, 100: 127-129.

King L.G., Wohl J.S., Manning A.M., Hackner S.G., Raffe M.R., Maislin G.: Evaluation of the survival prediction index as a model of risk stratification for clinical research in dogs admitted to intensive care units at 4 locations. Am. J. Vet. Res. 2001, 62: 948–954.

Ledgerwood A.M., Lucas C.E.: Review of Studies on the Effects of Haemorrhagic Shock and Resuscitation on the Coagulation Profile. J. Trauma 2003, 54: 68 –74.

Lundin E.S., Johansson T., Zachrisson H., Leandersson U., Backman F., Falknea L., Kjolhede P.: Single-dose tranexamic acid in advanced ovarian cancer surgery reduces blood loss and transfusions: double-blind placebo-controlled randomized multicentre study. Obstetr. Gyn. Scand. 2014, 93: 335-344.

Madershahian N., Scherner M., Pfiste R., Rudolph T., Deppe A. C., Slottosch I., Kuhn E., Choi Y. H., Wahlers T.: Prophylactic intraoperativ tranexamic acid administration and postoperative blood loss after transapical aortic valve implantation. J. Cardiothor. Surg. 2015, 10:45.

Marin L.M., Lazbik M.C., Zaldivar-Lopez S., Guillaumin J., McLoughlin M.A., Couto C.G.: Epsilon aminocaproic acid for the prevention of delayed postoperative bleeding in retired racing Greyhounds undergoing gonadectomy. Vet. Surg. 2012, 41: 594–603.

McCormack P.L.: Tranexamic Acid, A Review of is Use in the Treatment of Hyperfibinolysis. Drugs 2012, 72: 585-617.

McGowan E.E., Marryott K., Drobatz K.J., Reineke E.L.: Evaluation of the use of shock index in identifying acute blood loss in healthy blood donor dogs. J. Vet. Emerg. Crit. Care 2017, 27: 524-531.

Muri B., Schmierer P., Schwarz A., Sigrist N.E.: Hyperfibrinolysis diagnosed with rotational thromboelastometry and treated with tranexamic acid in a dog with acute traumatic coagulopathy. Schweiz. Arch. Tierheilk. 2017, (accepted).

Napolitano L.M., Cohen M.J., Cotton B.A., Schreiber M.A., Moore E.E.: Tranexamic acid in trauma. J. Trauma Acut. Care Surg. 2013, 74: 1575–86.

Nelson R.W., Couto C.G.: Small animal internal medicine, 5th Ed. St. Louis, Mosby, 2013.

Olaussen A., Blackburn T., Mitra B., Fitzgerald M.: Review article: shock index for prediction of critical bleeding post-trauma: A systematic review. Emerg. Med. Austral. 2014, 26: 223-228.

Roberts I.: Tranexamic acid in trauma: how should we use it? J. Thromb Haem. 2015; 13: 195–199.

Roberts I., Prieto-Merino D., Manno D.: Mechanism of action of tranexamic acid in bleeding trauma patients: an exploratory analysis of data from the CRASH-2 trial. Crit. Care 2014, 18: 685.

Schouten E.S., van de Pol A.C., Schouten A.N., Turner N.M., Jansen N.J., Bollen C.W.: The effect of aprotinin, tranexamic acid, and aminocaproic acid on blood loss and use of blood products in major pediatric surgery: a meta-analysis. Pediatr. Crit. Care. Med. 2009, 10: 182-190.

Spiel A.O., Mayr F.B., Firbas C., Quehenberger P., Jilma B.: Validation of rotation thrombelastography in a model of systemic activation of fibrinolysis and coagulation in humans. J. Thromb. Haemost. 2006, 4: 411–416.

Tanaka N., Sakahashi H., Sato E., Hirose K., Ishima T., Ishii S.: Timing of the administration of tranexamic, acid for maximum reduction in blood loss in arthroplasty of the knee. J. Bone. Joint. Surg. Br. 2001, 83 : 702-705.

Zoia A., Drigo M., Simioni P., Caldin M., Piek C.J.: Association between ascites and primary hyperfibrinolysis: a cohort study in 210 dogs. Vet. J. 2017, 223: 12-20.

Zufferey P., Merquiol F., Laporte S., Decousus H., Mismeti P., Aboyer C., Samama C.M., Molliex S.: Do antifibrinolytics reduce allogeneic blood transfusion in orthopaedic surgery? Anaesth. 2006, 105: 1034-46.

Corresponding author

Nadja Sigrist
Department for Small Animals
Vetsuisse Faculty
University of Zurich
Winterthurerstrasse 258c
8057 Zurich
Switzerland
E-Mail: nsigrist@vetclinics.uzh.ch