

Effect of 50 mg/kg intravenous tranexamic acid on coagulation assessed by rotational thromboelastometry (ROTEM) in healthy Beagle dogs

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Summary

In people, the antifibrinolytic drug tranexamic acid reduces bleeding and the need for blood products with both normal and exaggerated fibrinolysis without increasing the number of thromboembolic events. In dogs, in addition to prevention and treatment of bleeding, higher doses of tranexamic acid can be used to induce vomiting. The objective of this study was to evaluate the effect of a high dose of tranexamic acid on the coagulation of healthy Beagle dogs.

A prospective trial was conducted in eight healthy Beagles receiving tranexamic acid for a concurrent trial evaluating different antiemetics. Rotational thromboelastometry (ROTEM) analysis (EXTEM, APTEM, FIBTEM, INTEM) was performed before and 30 minutes after intravenous administration of 50 mg/kg tranexamic acid. ROTEM parameters before and after tranexamic acid administration and between EXTEM and APTEM were compared with Wilcoxon matched-pairs signed rank test and data is presented as median (range).

After tranexamic acid administration, FIBTEM clotting time became significantly shorter ($p=0.03$) from 37 s (28-124 s) to 33 s (27-40 s) and INTEM clot formation time significantly decreased ($p=0.02$) from 82 s (47-132 s) to 60 s (43-107 s). After tranexamic acid APTEM MCF was significantly weaker ($p=0.01$) with 45 mm (30-63 mm) than EXTEM MCF with 55 mm (43-69 mm) and than APTEM MCF before tranexamic acid with 55 mm (43-69 mm) ($p=0.02$). All other analysed parameters including maximum lysis did not change after administration of tranexamic acid.

The administration of 50 mg/kg intravenous tranexamic acid resulted in small changes in ROTEM profiles without inducing a hypercoagulable clot. In conclusion,

Wirkung von 50 mg/kg intravenös verabreichter Tranexamsäure auf die Blutgerinnung, beurteilt durch Rotations-Thromboelastometrie (ROTEM) bei gesunden Beagle-Hunden

Der antifibrinolytische Wirkstoff Tranexamsäure reduziert beim Menschen Blutungen und den Bedarf an Blutprodukten, dies sowohl bei normaler als auch bei übertriebener Fibrinolyse und ohne die Anzahl der thromboembolischen Ereignisse zu erhöhen. Bei Hunden können höhere Dosen von Tranexamsäure neben der Vorbeugung und Behandlung von Blutungen auch zur Induktion von Erbrechen verwendet werden. Ziel dieser Studie war es, die Wirkung einer hohen Dosis Tranexamsäure auf die Koagulation von gesunden Beagle-Hunden zu bewerten.

Die prospektive Studie wurde bei acht gesunden Beagles durchgeführt, die Tranexamsäure während einer Studie zur Bewertung verschiedener Antiemetika erhielten. Rotations-Thromboelastometrie (ROTEM) Analyse (EXTEM, APTEM, FIBTEM, INTEM) wurde vor und 30 Minuten nach intravenöser Verabreichung von 50 mg/kg Tranexamsäure durchgeführt. Die ROTEM-Parameter vor und nach der Verabreichung von Tranexamsäure und zwischen EXTEM und APTEM wurden mit dem Wilcoxon-Matched-Pair-Test verglichen und der Medianwert (Range) angegeben.

Nach der Verabreichung von Tranexamsäure wurde die Gerinnungszeit von FIBTEM von 37 s (28-124 s) auf 33 s (27-40 s) signifikant verkürzt ($p=0,03$) und die Bildung der INTEM-Gerinnsel reduzierte sich signifikant ($p=0,02$) von 82 s (47-132 s) auf 60 s (43-107 s). Nach Tranexamsäure war APTEM MCF mit 45 mm (30-63 mm) signifikant schwächer ($p=0,01$) als EXTEM MCF mit

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tranexamic acid can safely be administered to healthy dogs with normal coagulation profiles. As an additional finding, APTEM parameters measured in the current study do not support the use of this test in dogs.

Keywords: Antifibrinolytic, canine, emetic, tranexamic acid, viscoelastic coagulation test, vomiting

55 mm (43-69 mm) und als APTEM MCF vor Tranexamsäure mit 55 mm (43-69 mm) ($p = 0,02$). Alle anderen analysierten Parameter einschließlich der maximalen Lyse änderten sich nach Verabreichung von Tranexamsäure nicht.

Die Verabreichung von 50 mg/kg intravenöser Tranexamsäure führte zu kleinen Änderungen der ROTEM-Profile, ohne ein hyperkoagulierbares Gerinnsel zu induzieren. Zusammenfassend kann Tranexamsäure gesunden Hunden mit normalen Gerinnungsprofilen sicher verabreicht werden. Als zusätzliches Ergebnis der aktuellen Studie konnten die gemessenen APTEM-Parameter die Verwendung dieses Tests bei Hunden nicht bestätigen.

Schlüsselwörter: Antifibrinolytikum, Hund, Emetika, Tranexamsäure, viskoelastischer Gerinnungstest, Erbrechen

Introduction

Fibrinolysis is a physiologic mechanism leading to the breakdown of a blood clot once the endothelium has healed. Plasminogen is converted by tissue plasminogen activator (tPA) or urokinase to plasmin. Plasmin adheres to the lysine binding site on fibrin and enzymatically breaks down the fibrin strands of the clot, which generates fibrin degradation products¹.

Too early and/or exaggerated fibrinolysis (defined as hyperfibrinolysis) is pathologic and can cause bleeding¹². Hyperfibrinolysis has been reported in dogs with haemoabdomen^{6,25}, ascites with or without right sided heart failure^{28,29}, *A. vasorum* infection²⁴, trauma²⁰, liver disease^{7,25} and neoplasia²⁵.

Tranexamic acid (TXA) is a synthetic lysine analogue that blocks fibrinolysis by preventing the binding of plasmin to fibrin¹¹. In dogs infected with *A. vasorum*²⁴ and after trauma²⁰, TXA was able to inhibit hyperfibrinolysis. A recent study in dogs²² showed that 20 mg/kg intravenous (IV) TXA resulted during 6 hours in plasma levels that were formerly reported to be effective to inhibit *in vitro* hyperfibrinolysis⁵. In addition to inhibition of hyperfibrinolysis, administration of TXA in people with or without a diagnosis of hyperfibrinolysis reduced the need for blood products¹⁰ and decreased mortality^{2,23}. In dogs, only one retrospective study evaluating the effect of TXA at a dose of 5.9–16.5 mg/kg IV is available¹⁵. Both mortality and the total number of blood products administered were lower when bleeding dogs receiving TXA with ($n = 38$) and without ($n = 30$) blood product administration were compared to bleeding dogs receiving blood products without TXA ($n = 62$). However, when only the dogs receiving blood with

TXA were compared to the dogs receiving blood without TXA no difference could be found. Tranexamic acid induces vomiting if administered fast and/or in high dosages and has therefore been recommended as an emetic agent in dogs¹³. A starting dose of 50 mg/kg of TXA IV is currently recommended to induce vomiting in dogs²¹.

Potentially, TXA administration could lead to thromboembolism. In people, the use of TXA has not increased the occurrence of thromboembolic events²³.

The objective of this study was to evaluate the effect of 50 mg/kg IV TXA on ROTEM parameters of healthy dogs.

The hypothesis was that a high dose of TXA does not induce clinically relevant procoagulatory effects in healthy dogs. Because viscoelastic coagulation testing allows for fast visual inspection of clot formation, stability and lysis¹⁸, rotational thromboelastometry (ROTEM) was chosen to assess the effects of TXA on coagulation.

Materials and Methods

The project was approved by the Committee for Animal Experimentation of the Canton Zurich, Switzerland (191/2016). Eight healthy Beagle dogs (4 intact females, 4 intact males), aged 6.5 (6-6.5) years old (median (range)), and weighing 13.1 kg (10.7-16.6 kg) were included in the study. The dogs were judged to be healthy based on history, physical examination and blood analysis (packed cell volume, total plasma protein and ve-

nous blood gas analysis (RAPIDPoint 500 Blood Gas System, Siemens Healthcare AG, Freilagerstrasse 40, 8047 Zürich, Switzerland). The dogs lived in groups of 4 dogs in a research facility and were under regular supervision by two trained animal keepers.

The current work was performed during a blinded randomized crossover trial evaluating the efficacy of maropitant and ondansetron versus placebo against TXA-induced nausea and vomiting¹⁴. The dogs were given all three treatments with a wash-out period of 3 weeks between trials. On the days where the animals were scheduled to receive the placebo treatment, the effect of TXA on viscoelastic coagulation tests was assessed with the following protocol. A baseline blood sample ("before TXA") was collected from the *V. jugularis* with a 20 G needle and a 5 ml syringe and was transferred into two 1.3 ml tubes containing 3.2% sodium citrate (Sarstedt AG, Bahnhof Süd 36, 9475 Sevelen, Switzerland).

Immediately thereafter the dogs received 3 ml 0.9% NaCl solution IV through a 22 G cephalic vein catheter (Surflo IV catheter, Terumo, Bodenackerstrasse 3, 8957 Spreitenbach, Switzerland) followed 10 minutes later by 50 mg/kg TXA IV (Tranexam OrPha®; OrPha Swiss-GmbH, Untere Heslibachstrasse 41A, 8700 Küsnacht, Switzerland) administered over 2 minutes. Nausea and vomiting was monitored as described by Kantyka et al.¹⁴. Thirty minutes after the end of administration of TXA a second whole blood sample ("after TXA") was collected as described above. The blinded observer assessing nausea and vomiting (MK) left the room during the possible blood sampling times during all trials.

ROTEM analysis

The ROTEM profiles were analysed with a ROTEM delta® (Axon Lab AG, Täferstrasse 15, 5405 Baden, Switzerland) before and 30 minutes after administration of TXA. The citrated samples were kept in the dedicated warming pit of the ROTEM device until analysis was performed. Pipetting was performed with the automated pipet of the device adding 300 µL of citrated blood to the reagent. Analysis was performed at 37°C for 60 minutes.

Lyophilized single reagents were used to evaluate different parts of the coagulation cascade at the same time in the four measurement channels. The extrinsic pathway was evaluated with the EXTEM test, which contains recombinant human tissue factor, phospholipids and calcium chloride. The fibrin clot was assessed with FIBTEM, a test that contains the EXTEM reagents with the addition of cytochalasin D to inactivate the platelets

present in the whole blood sample. The APTEM test was developed to assess hyperfibrinolysis *in vitro*. The APTEM test combines EXTEM and the antifibrinolytic drug aprotinin leading to faster/stronger APTEM parameters compared to EXTEM parameters, if hyperfibrinolysis is present. The intrinsic pathway was assessed with the INTEM test. It contains ellagic acid, partial thromboplastin, phospholipid and calcium chloride.

The following parameters were evaluated in the current study: Clotting time (CT) is the time in seconds from activation of the sample until a first clot with the defined amplitude of 2 mm is built. It is dependent on the activity of the clotting factors. EXTEM CT and INTEM CT correlate to PT and aPTT, respectively⁴.

Clot formation time (CFT) is the time in seconds measured from the end of CT (2 mm) until an amplitude of 20 mm is reached.

Maximum clot firmness (MCF) is the maximum amplitude displayed in mm that is reached during the 60 minutes of measurement time. The MCF in the platelet-containing test (all but FIBTEM) is dependent on both fibrin and platelet concentration and function.

Maximum lysis (ML) is the relative amount of lysis measured in percent during the measurement time of 60 minutes.

Statistical analysis

The sample size was calculated for the project evaluating antiemetics¹⁴ and eight dogs entered the study. A commercially available software (Graphpad Prism, GraphPad Software, 2365 Northside Drive, San Diego, CA 92108, USA) was used for analysis. After normality testing with the Shapiro-Wilk test, a Wilcoxon matched-pairs signed rank test was performed to compare ROTEM parameters before and after TXA treatment, between EXTEM and APTEM at each time point and to compare the time lag between blood collection and beginning of ROTEM analysis. The significance level was set at $p < 0.05$.

Results

All eight dogs completed the study. ROTEM parameters before and after administration of TXA are summarized in Table 1. FIBTEM CT (Figure 1) and INTEM CFT were significantly shorter ($p = 0.03$ and $p = 0.02$, respectively) and APTEM MCF was significantly smaller ($p = 0.02$) after TXA administration. While EXTEM and APTEM MCF were similar at baseline, APTEM MCF

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Table 1: Clotting time (CT), clot formation time (CFT), maximum clot firmness (MCF) and maximum lysis (ML) measured with rotational thromboelastometry (ROTEM) using different activators for the evaluation of the extrinsic pathway (EXTEM), the fibrinogen clot (FIBTEM), hyperfibrinolysis with the addition of aprotinin (APTEM) and the intrinsic pathway (INTEM) before and after tranexamic acid (TXA).

| | Before TXA | | In - House Reference Range | After TXA | |
|---------------|------------|----------------|----------------------------|------------------|---------------|
| | Median | Range | | Median | Range |
| EXTEM | | | | | |
| CT (s) | 42 | 30-83 | 23-87 | 36 | 27-73 |
| CFT (s) | 119 | 62-203 | 85-357 | 145 | 65-260 |
| MCF (mm) | 58 | 46- 69 | 32-65 | 55 [§] | 43- 69 |
| ML (%) | 0 | 0-10 | 0-12 | 2 | 0- 15 |
| FIBTEM | | | | | |
| CT (s) | 37 | 28- 124 | 21-112 | 33* | 27-40 |
| MCF (mm) | 6.5 | 3- 12 | 2-9 | 5.5 | 5- 10 |
| ML (%) | 17 | 0- 78 | 1-99 | 30 | 0-99 |
| APTEM | | | | | |
| CT (s) | 36 | 28-78 | 21-75 | 36 | 28- 93 |
| CFT (s) | 141 | 76-241 | 99-485 | 184 | 65-411 |
| MCF (mm) | 55 | 43- 69 | 32-63 | 45* [§] | 30-63 |
| ML (%) | 2 | 0-7 | 0-10 | 2.5 | 0-10 |
| INTEM | | | | | |
| CT (s) | 118 | 86-151 | 133-210 | 129 | 97-136 |
| CFT (s) | 82 | 47-132 | 59-201 | 60* | 43-107 |
| MCF (mm) | 62 | 55- 73 | 52-71 | 65 | 54-71 |
| ML (%) | 0.5 | 0-3 | 0-3 | 0 | 0-5 |

* marks statistical significant changes before and after TXA, [§] marks statistical significant differences between MCF EXTEM and APTEM. Values out of reference range are marked in bold.

was smaller than EXTEM MCF ($p = 0.01$) after TXA administration. All other analysed parameters including maximum lysis did not change after administration of TXA.

Baseline samples were analysed within 9 (6 to 56) minutes (median (range)), which was a significantly shorter time period ($p = 0.01$) in comparison to the one of the samples after TXA administration that were analysed within 48 (27 to 110) minutes.

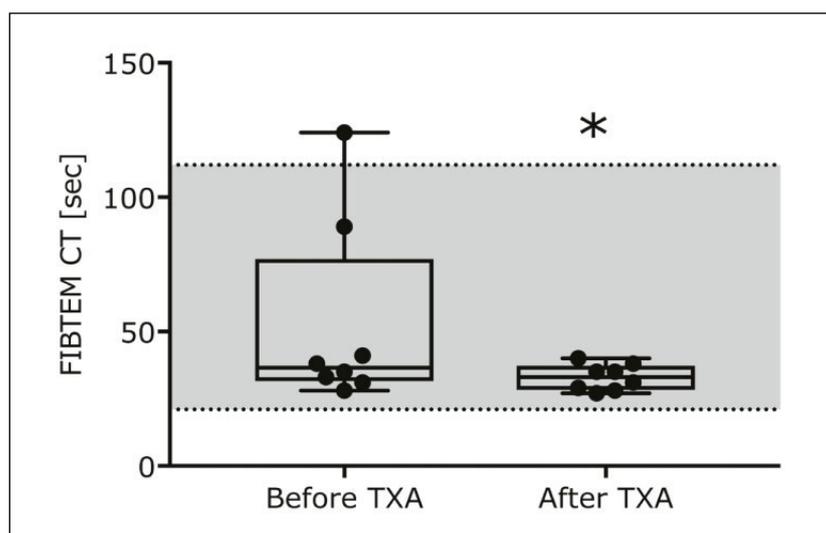


Figure 1: Box and whiskers plot showing fibrinogen specific thromboelastometry (FIBTEM) clotting time (CT) results in seconds of all individual dogs before and after tranexamic acid (TXA). The asterisk shows a statistically significant change and the in-house reference range is shaded in grey.

Discussion

The intravenous administration of 50 mg/kg TXA resulted in small statistically significant changes in early ROTEM parameters, but no changes in clot firmness and no hypercoagulable ROTEM tracings were found in this study in healthy dogs.

Doses currently used in dogs to treat bleeding diathesis with or without hyperfibrinolysis range from 10 - 80 mg/kg IV^{16,24}. A starting dose of 50 mg/kg IV has been recommended to induce vomiting in dogs^{13,21}. Dogs that are given drugs to induce vomiting are typically not expected to suffer from hyperfibrinolysis or hypocoagulability. The administration of a high dose of an anti-fibrinolytic drug as an emetic may therefore potentially lead to hypercoagulability and thrombotic events. In the current study, the use of 50 mg/kg TXA IV did not lead to increased clot firmness (a measure of hyperco-

agulability). This is supported by the fact that, compared to people, dogs lyse clots earlier than people^{5,19}. In a research study that used dogs as a model for pulmonary thromboembolism, a very high dose of TXA (110 mg/kg per os twice daily) was necessary to stabilise thrombin-induced clots and to prevent their complete lysis within hours¹⁹. Another study directly compared thromboelastography (TEG) parameters in people and dogs and found that 10 times higher TXA plasma levels were necessary to inhibit *in vitro* induced hyperfibrinolysis in dogs⁵. Based on these studies, dogs seem to be able to very effectively induce fibrinolysis.

The administration of 50 mg/kg TXA IV shortened the CT only in FIBTEM but not in EXTEM. Earlier work with 10 mg/kg IV TXA followed by a infusion of 10 mg/kg infusion over three hours showed that the R time in tissue factor activated TEG (similar to CT EXTEM) was reduced from 3.3 (\pm 0.6) (mean (SD)) to 2.7 (\pm 0.8) minutes ($p = 0.05$)¹⁶. However, in a more recent study, tissue factor activated R time was not changed after 20 mg/kg IV TXA²².

In the current study CFT was only significantly shortened in the INTEM profile after the administration of TXA. Comparison with the earlier mentioned studies evaluating the effect of 10 and 20 mg/kg TXA, respectively, is not possible as they did not test the intrinsic activation. The concentration and activity of clotting factors and/or platelets influencing CT and CFT should theoretically not be influenced by the administration of TXA. In the population of healthy dogs used in this study, two dogs showed an abnormally high FIBTEM CT that normalized after TXA (Figure 1), which may be a sign of subtle early fibrinolysis in these dogs. In the FIBTEM test the platelets are inactivated and the weak fibrin clot is less resistant to fibrinolysis⁹. The fact that EXTEM CT, which should theoretically be identical to FIBTEM CT, was not prolonged supports this explanation. In earlier studies in clinical patients, we suspected that a non-forming FIBTEM clot (MCF of 2 mm) might also be a sign for activated fibrinolysis and not only for hypofibrinogenemia^{24,25}. However, why the CFT results of the intrinsically activated test were shortened cannot be answered with the current study.

In the current study in dogs, the APTEM MCF in ROTEM was weaker after the administration of TXA compared to both APTEM baseline and to EXTEM after TXA. This is an unexpected finding questioning the use of APTEM in dogs. A weaker APTEM than EXTEM clot has been observed before in bleeding dogs²⁵ and during the collection of reference values in 48 healthy dogs analysed within 20-30 minutes after blood collection with samples stored at 37°C prior to analysis. (Jud Schefer R, personal communication). Similar to

this, we reported previously that APTEM results in cats were not stronger but more prone to an artefact called clot retraction compared to EXTEM results¹⁷. In people, the APTEM test was developed to detect hyperfibrinolysis *in vitro* by adding aprotinin to the probe. Aprotinin also inhibits fibrinolysis and should lead to a stronger APTEM profile compared to the EXTEM profile. However, in people, APTEM was not able to detect hyperfibrinolysis earlier than with EXTEM clot firmness alone³. Based on these results, APTEM results should be interpreted with caution in dogs and additional studies investigating the usefulness and reliability of APTEM profiles to detect hyperfibrinolysis are required.

Limitations

The present study has several limitations.

Firstly, the blood samples collected before administration of TXA were analysed within shorter time than those after TXA. The second time point was planned only 30 minutes after drug administration in order to have a maximal effect of TXA on ROTEM parameters. Blood kept at room temperature became more hypercoagulable if stored between 30 and 120 minutes in a study performed with citrated canine blood and tissue factor (extrinsic) activated thromboelastography²⁷. In this study R and K time (similar to CT and CFT) were shorter and maximum amplitude (similar to MCF) was stronger after longer storage times. Although the decrease in FIBTEM CT and/or INTEM CFT may have been caused by the administered TXA as described above, an influence of the longer preanalytical time cannot be excluded with the current study and in future studies the baseline sample should be taken well before administration of TXA. In people, ROTEM values were stable for 120 minutes after collection²⁶. However, the weakening of the APTEM maximum clot firmness can neither be explained by the effect of TXA nor by the observed preanalytical differences.

As a second limitation not all results of the eight dogs before TXA were within the in house reference ranges (Table 1). The reference values were assessed on a different ROTEM machine and slight differences between devices have been reported⁸. The dogs that had results outside of the reference range were rather hyper- than hypocoagulable. It is therefore unlikely that the abnormal baseline values masked a prothrombotic effect of 50 mg/kg TXA IV.

As a third limitation, neither fibrinogen (Clauss), thrombocyte count nor thrombocyte function testing were performed. However, TXA should theoretically only inhibit fibrinolysis by blocking the action of plasminogen and all procoagulant effect should be caused by decreased fibrinolysis. Furthermore fibrinolysis can-

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not be diagnosed with fibrinogen (Clauss) analysis and fibrinogen (Clauss) values correlate closely to MCF FIBTEM in dogs⁴.

As a forth limitation only the *in vitro* effects of TXA on coagulation were assessed by ROTEM. However, although the study did not concentrate on the assessment of thromboembolic side effects *in vivo*, none of the dogs showed an obvious sign of thromboembolic complications such as tachypnoea or lameness after the administration of 50 mg/kg IV TXA.

In future, it needs to be analysed if the administration of a high dose of TXA to non-bleeding dogs i.e. as an emetic is safe in patients in dogs with diseases commonly associated with hypercoagulability.

Conclusions

The administration of 50 mg/kg TXA IV resulted in small changes in ROTEM profiles without inducing a hypercoagulable clot. In conclusion, TXA can safely be administered to healthy dogs with normal coagulation profiles. As an additional finding, APTEM parameters measured in the current study do not support the use of this test in dogs.

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Effet de 50 mg/kg d'acide tranexamique par voie intraveineuse sur la coagulation évaluée par thromboélastométrie rotationnelle (ROTEM) chez des chiens Beagle en bonne santé

Chez l'homme présentant une fibrinolyse normale et exagérée, l'acide tranexamique, un agent antifibrinolytique, réduit les saignements et le besoin de produits sanguins sans augmenter le nombre d'événements thromboemboliques. Chez les chiens, en plus de la prévention et du traitement des saignements, des doses plus élevées d'acide tranexamique peuvent être utilisées pour provoquer des vomissements. L'objectif de cette étude était d'évaluer l'effet d'une dose élevée d'acide tranexamique sur la coagulation de chiens Beagle en bonne santé.

Un essai prospectif a été mené chez huit Beagles en bonne santé recevant de l'acide tranexamique dans le cadre d'un essai simultané évaluant différents antiémétiques. Une analyse de la thromboélastométrie rotationnelle (ROTEM) (EXTEM, APTEM, FIBTEM, INTEM) a été réalisée avant et 30 minutes après l'administration intraveineuse de 50 mg/kg d'acide tranexamique. Les paramètres ROTEM avant et après l'administration d'acide tranexamique et entre EXTEM et APTEM ont été comparés au test de rang de Wilcoxon à paires appariées et les données sont présentées sous forme de médiane.

Après administration de l'acide tranexamique, le temps de coagulation de FIBTEM est devenu significativement plus court ($p = 0,03$) de 37 s (28-124 s) à 33 s (27-40 s) et le temps de formation du caillot INTEM a été significativement réduit ($p = 0,02$) de 82 s (47-132 s) à 60 s (43-107 s). Après l'acide tranexamique, APTEM MCF était significativement plus faible ($p = 0,01$) avec 45 mm

Effetto di 50 mg/kg di acido tranexamico per via endovenosa sulla coagulazione determinato mediante tromboelastografia rotazionale (ROTEM) nei cani di razza Beagle sani.

Nelle persone, il farmaco antifibrinolitico acido tranexamico riduce l'emorragia e la necessità di prodotti ematici con fibrinolisi normale ed esagerata senza aumentare il numero di eventi tromboembolici. Nei cani, oltre alla prevenzione e al trattamento dell'emorragia, dosi più elevate di acido tranexamico possono essere utilizzate per indurre il vomito. L'obiettivo di questo studio è stato quello di valutare l'effetto di un'alta dose di acido tranexamico sulla coagulazione dei cani Beagle sani. È stato condotto uno studio prospettico in otto Beagle sani a cui veniva somministrato acido tranexamico per uno studio concomitante che valutava diversi antiemetici. L'analisi tromboelastografica rotazionale (ROTEM) (EXTEM, APTEM, FIBTEM, INTEM) è stata eseguita prima e 30 minuti dopo la somministrazione endovenosa di 50 mg/kg di acido tranexamico. I parametri ROTEM prima e dopo la somministrazione di acido tranexamico e tra EXTEM e APTEM sono stati confrontati con il test di Wilcoxon dei ranghi con segno con misure accoppiate e i dati sono stati presentati come mediana (rango). Dopo la somministrazione di acido tranexamico, il tempo di coagulazione FIBTEM è diventato significativamente più breve ($p=0.03$) da 37 s (28-124 s) a 33 s (27-40 s) e il tempo di formazione del coagulo INTEM è diminuito significativamente ($p=0.02$) da 82 s (47-132 s) a 60 s (43-107 s). Dopo la somministrazione dell'acido tranexamico APTEM MCF era significativamente più debole ($p=0.01$) con 45 mm (30-63 mm) di EXTEM MCF con 55 mm (43-69 mm) e di APTEM MCF prima dell'acido tranexami-

(30-63 mm) que EXTEM MCF avec 55 mm (43-69 mm) et qu'APTEM MCF avant l'acide tranexamique avec 55 mm (43-69 mm) ($p=0,02$). Tous les autres paramètres analysés, y compris la lyse maximale, n'ont pas changé après l'administration d'acide tranexamique.

L'administration de 50 mg/kg d'acide tranexamique par voie intraveineuse a entraîné de légers changements dans les profils ROTEM sans induire de caillot hypercoagulable. En conclusion, l'acide tranexamique peut être administré en toute sécurité à des chiens en bonne santé présentant des profils de coagulation normaux. Autre constatation supplémentaire, les paramètres APTEM mesurés dans la présente étude n'appuient pas l'utilisation de ce test chez le chien.

Mots-clés: antifibrinolytique, chien, émétique, acide tranexamique, test de coagulation viscoélastique, vomissements

co con 55 mm (43-69mm) ($p=0.02$). Tutti gli altri parametri analizzati, compresa la lisi massima, non sono cambiati dopo la somministrazione di acido tranexamico. La somministrazione di 50 mg/kg di acido tranexamico per via endovenosa ha portato a piccole modifiche nei profili ROTEM senza indurre un coagulo trombofilo. In conclusione, l'acido tranexamico può essere somministrato con sicurezza nei cani sani con profili di coagulazione normali. Come ulteriore risultato, i parametri APTEM misurati nello studio attuale non supportano l'uso di questo test nei cani.

Parole chiave: Antifibrinolitico, canino, emetico, acido tranexamico, test di coagulazione viscoelastica, vomito

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