ACTIVITY OF PLASMA-PROTEIN C IN DAIRY COWS WITH LEFT-SIDED DISPLACEMENT OF THE ABOMASUM AND FATTY LIVER SYNDROME

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I) INTRODUCTION

Fatty infiltration of the liver, occurring within 1 to 5 weeks post partum, and due to excessive lipomobilisation, is the most common liver disease in dairy cows[1]. Case studies showed that 91% of cases with left-sided displacement of the abomasum (LDA), accompanied by suppression of appetite and enhanced lipomobilisation, occurred during this period[2]. Our experience indicates that nearly 4% of cows with LDA, admitted for surgical treatment, develop hepatic failure in the postoperative period and die in hepatic coma or are slaughterd for that reason[3].

It has been shown in humans that the plasma activity of Protein C, synthesized in the liver as a Vitamin K-dependant anticoagulant factor, decreases in severe liver disease[4]. Therefore, dairy cows suffering from LDA were studied in order to gain information about the correlation between plasma-protein C-activity and hepatic lipidosis.

II) MATERIALS AND METHODS:

Thirty-six dairy cows (German Black Pied, average age: 5,4 +/- 1,4 years) with LDA referred to the Hannover Clinic for Diseases of Cattle for surgical treatment were studied: Clinical investigations were carried out and blood samples for biochemistry were taken the day before (D-1), one (D1) and three days (D3) post-op. On D-1, liver biopsy samples were obtained for semi-quantitiv histological estimation of their fat- (6 degrees according to amount and distribution; here summed up to A:no/low lipidosis; B: moderate; C: severe [panlobular]) and glycogen content (5 degrees)[5].
On D-1, D1, and D3 protein-C-activity[#], prothrombin time (PT)[+], and partial thromboplastin time (PTT)[+] were measured functionally by commercial clotting testkits on a Fibrintimer[R(+)] (#: Boehringer Mannheim GmbH, Mannheim, FRG; +:Behring AG, Marburg, FRG). Pooled plasma from 34 healthy dairy (German Black Pied, age: 5,3 +/-1,5 years) cows was used as reference. The normal range of the investigated coagulation parameters was estimated in further 51 healthy lactating dairy cows (German Black Pied, age: 5,2 +/- 1,2)[3].
As statistical method analysis of variance was used.

III) RESULTS:

For protein C plasma activity a preliminary reference was assessed in 51 healthy dairy cows ranging from 78 % to 118 % to a bovine plasma pool.

In the studied period cows suffering from left sided displacement of the abomasum with no fatty infiltration of the liver showed plasma protein C levels within the normal range (Fig.1). On D-1 and D1 even in cows with moderate liver fat content a significant decrease in

protein C levels were measured (p<o,o1). In cows with severe hepatic lipidosis a further decrease of protein C levels compared to cows with moderate liver fat content were found (p<o,o5). Three animals showed protein C activities of less than 40 % to normal. In tendency changes in PT (p<o,o5) were comparable to results in protein C but of less extent (Tab.1).
All studied patients were discharged 4 days after surgical treatment with good appetite and general condition.

IV) DISCUSSION:

In cows suffering from LDA routine biochemistry gives insufficient information about the risk of hepatic failure[3]. Here too, the first clinical symptoms of hepatic failure (loss of appetite, general depression) are difficult to distinguish from the symtoms of the primary disease. For that reason it seems necessary to look for parameters which give information about the metabolic capability of the liver.

The liver plays a central role in synthesis and clearance of coagulation factors[6]. Although there is a substantial overlap in hemostatic abnormalities in patients suffering from severe liver disease (decreased synthesis and clearance of clotting factors, thrombocytopenia, abnormalities of platelet function, disseminated intravascular coagulation) coagulation profiles in humans are recommended as one method of estimating the degree of liver damage[6].

Our results indicate that disturbances in hemostasis due to hepatic lipidosis occur even in cows with no clinical symptoms of hepatic failure. However, further investigations are necessary to obtain subtly differentiated information about the diagnostical and prognostical value of coagulation profiles in cows.

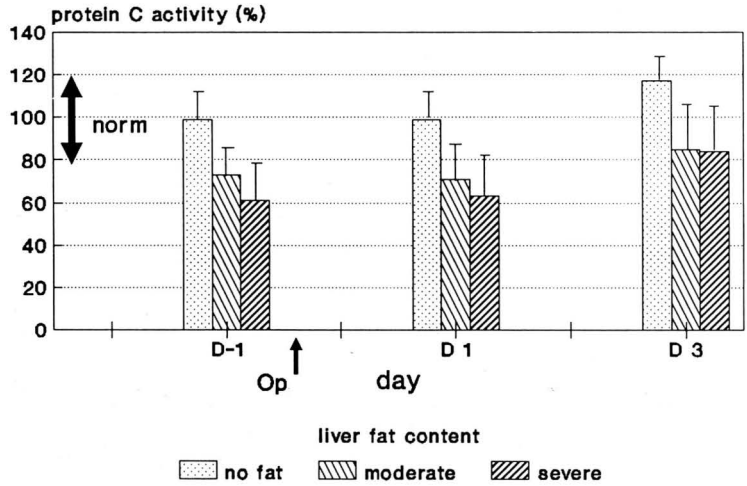

Fig.1: Plasma activity of Protein C in dairy cows suffering from left sided displacement of the abomasum related to liver fat content.

Tab.1: Plasma activity of prothrombin time and partial thromboplastintime in dairy cows suffering from left-sided displacement of the abomasum related to liver fat content (mean +/- SD).

liver fat content	n	prothrombin-time (sec) D-1	D1	D3	thromboplastin-time (PTT; sec) D-1	D1	D3
no/low fat	10	26,1 2,7	29,8 4,1	24,4 3,2	31,9 3,9	32,0 2,4	31,1 2,4
moderate	15	24,7 2,4	27,7 3,0	24,7 1,8	32,0 3,1	33,3 2,6	32,4 2,9
severe (pan-lobular)	11	23,9 2,1	26,9 3,6	23,7 3,1	29,8 4,6	31,7 3,3	30,5 5,5
preliminary reference values		20 - 28			29 - 41		

REFERENCES:

1.) STÖBER, M., & G. DIRKSEN (1982): Prakt. Tierarzt 63, Colleg. Vet., 79 - 88
2.) DIRKSEN, G. (1967). Dtsch.Tierärztl.Wschr. 74, 625 - 633
3.) MERTENS, M. (1992): Hannover, Tierärztl. Hochschule, Diss.
4.) MANNUCCI, P.M., & VIGANO, S. (1982): Lancet II, 463 - 466
5.) KRAMER, J. (1992): Hannover, Tierärztl. Hochschule, Diss.
6.) JOIST, J.H. (1987): in COLMAN, R.W., J. HIRSH, V.J. MARDER & E.W. SALZMANN: Hemostasis and Thrombosis - Basic Principles and Clinical Practice; Lipincott Company, Philadelphia; 861 - 872

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Summary:

Hepatic failure related to fatty liver is a common complication in dairy cows suffering from left-sided displacement of the abomasum (LDA). Protein C is assumed to be synthesized by the liver. In humans it has been shown that protein C levels are decreased in patients with severe liver disease. Therefore, dairy cows suffering from LDA were studied in order to gain information about the correlation between plasma-protein C-activity and hepatic lipidosis. Our investigations showed that protein C levels in cows with moderate fatty liver are considerable decreased (n=15; average prot.C-activity: 72 +/- 20 % of reference [mean: 100%; 76% - 120%]) compared to healthy control cows

(n=10; 99 +/- 15 %). In cows with severe hepatic lipidosis (n=11; average: 61 +/- 20 %) protein C levels of even less than 40% of reference were measured. Comparable changes in prothrombin time were found but of less extent.

Zusammenfassung:

Kühe mit linksseitiger Labmagenverlagerung (LDA) leiden häufig zusätzlich an schwerer Leberverfettung, die nicht selten zum Tode des Tieres infolge Leberinsuffizienz führt. Die Plasma-Protein-C Aktivität gilt in der Humanmedizin als empfindlicher Indikator für eine sich anbahnende oder bereits manifeste Leberinsuffizienz. Aus diesem Grunde wurde geprüft, ob bei Kühen mit linksseitiger Labmagenverlagerung in Abhängigkeit vom Leberfettgehalt Veränderungen in der Plasma-Protein-C-Aktivität vorliegen und damit Hinweise auf eine gestörte hepatogene Proteinsythese geben können. Nach unseren Untersuchungen weisen bereits Kühe mit LDA sowie histologisch bestimmter mittelgradiger Leberverfettung (n=15; Prot.-C-Aktivitat: 72 +/- 20 %), verglichen mit lebergesunden Kontrolltieren (n=10; 99 +/- 15 %) und Referenzwerten (78% - 120%) erhebliche Verluste in der Plasmaaktivität des Prot.-C auf. Ein weiterer Abfall in der Prot.C-Aktivität, teilweise bis auf 35% der Norm, wurde bei Kühen mit hochgradiger Leberverfettung (n=11; 61 +/- 20 %) beobachtet. In den Globaltesten sowie in der ATT-III-Aktivität wurden Veränderungen vergleichbaren Ausmaßes nicht gemessen. Ähnliche Veränderungen, allerdings in geringerem Ausmaß, wies die Plasma-Prothrombinzeit auf.

RESUMEN:

Bovinos que presentaron dislocación de abomaso a la izquierda, sufren con mucha frecuencia de adiposidad hepática que incluso muchas veces conduce a la muerte por insuficiencia hepática. En medicina humana, la prueba de actividad de proteína-C plasmática es considerada como indicadora de insuficiencia hepátiva leve o evidente. Con este antecedente se controló si existe en bovinos con dislocación de abomaso a la izquierda una relación entre las modificaciones del contenido graso hepático y la actividad proteína-C plasmática. Ésto indicaría un transtorno de la síntesis proteínica plasmática. Se demuestra que vacas con dislocación de abomaso a la izquierda que por controles histológicos evidenciaron adiposidad hepática mediana(n=15; 72 % +/- 20) comparadas con controles sin daño hepático (n=10; 99 % +/- 15) y valores referenciales (68% - 120%) evidenciaron significativas perdidas en la actidad proteína-C plasmática. En vacas con adiposidad hepátiva severa (n=11; 61% +/- 20) se constató niveles proteínicos-C plasmáticos infe-riores al 40% de los valores referenciales.