Liver Function in Dairy Cows in Late Pregnancy and Early Lactation

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Introduction

During early lactation, the dairy cow has to contend with a variety of factors which can lead to impairment of hepatic function. Studies have shown that since the overall energy requirement is greatly increased, rates of metabolic processes within the liver have to be increased in proportion.[1] Priority appears to be given to the nutrient requirements of the foetus during gestation and to the lactating mammary gland in early lactation. The cow may be in a state of negative energy balance as peak milk yields are reached 3 to 7 weeks after calving whereas peak voluntary food intake is not reached until 8 to 10 weeks after calving. Hormone production is such as to encourage lipid mobilization. As a result of this energy deficit, cows mobilize their tissue reserves for milk production and may lose appreciable amounts of body weight and muscle. Similar factors may also pertain in late pregnancy.[12]

One of the possible consequences of mobilization of body reserves is the development of a fatty liver.[4,10] It was estimated that up to a third of high yielding dairy cows in the U.K. were affected by consequence of fatty liver.[12,15] Substantial mortality may occur as a consequence of fatty liver in dairy cows and complications such as chronic ketosis, parturient paresis, displaced abomasum, retained placenta, endometritis, an impaired immune response and an adverse effect on fertility[10] have been reported.

The purpose of this investigation was to establish any changes that may occur in liver function in periparturient dairy cows, when compared with non-lactating cows, in order to aid identification of the cows which are likely to develop fatty liver.

Materials and Methods

Twenty-four adult, non-pregnant, non-lactating dairy cattle aged 3 to 14 years were studied on one occasion. Most were Friesian or Friesian cross cattle apart from one Jersey and three Guernsey cows. They were housed indoors tied in stanchions and were used to handling. Hay and water were always freely available. Eight Friesian and one Guernsey cow were studied two weeks before the predicted calving date and two weeks after calving. The cows were aged between 6 and 14 years and had completed between three and ten lactations. The milk yields of the Friesian in the previous lactations had been at least 5500kg and the Guernsey had given 5000kg. The cows calved during October and November and were fed a diet of self feed silage, hay and concentrates containing 16% crude protein. The amount fed was adequate to meet their requirements for pregnancy and lactation. The cows were weighed and condition scored at the time of sampling.

Bromosulphthalein (BSP) clearance tests were carried out at the same time as clinical chemistry estimations. Analysis of plasma samples for BSP concentration was as described previously[17] with modifications[3] and calculations from the plasma clearance graph were as described.[19] Plasma total bilirubin, glucose, total ketone bodies, urea and non-esterified fatty acid (NEFA) concentrations and activities of plasma aspartate amino-transferase (AST), glutamate dehydrogenase (GD), iditol dehydrogenase (ID), γglutamyl-transferase (γGT) and creatine kinase (CK) were measured by standard methods.[19]

Liver biopsy was performed in the right eleventh intercostal space[8] at the time of blood sampling.[19] The percentage volume of visible fat in parenchymal cells was estimated by a stereological point-counting method[13] on oil Red O stained sections.

Results

The periparturient cows lost between 30 and 56 kg bodyweight during the time of study. The condition score before calving varied from 3 to 4 and after calving from 2 to 3.5. The actual calving dates were very close to the predicted times so sampling was carried out 8 to 22 days before the actual calving date.

The liver biopsies from non-pregnant, non-lactating cows were normal. In periparturient cows the distribution of fat on liver biopsy sections was mainly centrilobular and midzonal.

BSP was cleared in two phases by the liver of cattle following a single dose of 4mg/kg intravenously.[19] In late pregnancy, the BSP clearance graph was less rapid with

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TABLE 1. Comparison of results of bromosulphthalein excretion in periparturient cows with those from non-pregnant non-lactating cows.

	Transfer constants 'a'	'h'	'b'	Plasma Volume, V ml.kg-1	Half time, T1/2 (mins)	K (mins-1)	15 min retention %	30 min retention %
Before calving	0.197 ± 0.0227	0.116 ± 0.0318	0.0403 ± 0.0162	46.9 ± 3.59	4.5 ± 0.11	0.154 ± 0.004	18.6 ± 2.4	3.8 ± 0.9
After calving	0.288 ± 0.0462	0.126 ± 0.0256	0.0540 ± 0.0199	42.2 ± 3.96	4.1 ± 0.17	0.172 ± 0.007	9.1 ± 1.9	1.8 ± 0.5
Adult non-preg. cows	0.262 ± 0.0113	0.099 ± 0.0070	0.0169 ± 0.0025	43.7 ± 1.9	3.4 ± 0.13	0.213 ± 0.010	5.9 ± 0.7	1.3 ± 0.2

TABLE 2. Comparison of clinical chemistry results in periparturient and non-pregnant non-lactating cows.

	Bilirubin umol/l	AST iu/l	GD iu/l	ID iu/l	γGT iu/l	CK iu/l	Glucose mmol/l	Ketone bodies umol/l	Urea mmol/l
Before calving	7.8 ± 0.90	22 ± 3.2	3.9 ± 0.42	5.7 ± 0.68	16.9 ± 0.75	32 ± 10.1	2.6 ± 0.23	567 ± 55	5.1 ± 0.47
After calving	6.0 ± 0.64	37 ± 9.8	5.2 ± 1.34	6.3 ± 0.56	20.6 ± 4.62	38 ± 19.4	3.1 ± 0.18	833 ± 109	3.4 ± 0.36
Non-pregnant cows	4.1 ± 0.21	22 ± 1.6	3.6 ± 0.66	5.9 ± 1.07	16.9 ± 1.09	13 ± 2.3	3.8 ± 0.15	262 ± 13	4.7 ± 0.29

less well-defined second exponential components than in early lactation. BSP clearance was more rapid in non-pregnant non-lactating cows and the change in slope between the two exponential components more easily discernible.

The BSP clearance and clinical chemistry results from cows before and after calving were analyzed by paired "t" tests and compared with those obtained in non-pregnant non-lactating cows by one way analysis of variance.

There was no significant alteration in the transfer constants or plasma volume when results from cows before and after calving were compared. The value of 'a' fell significantly before calving ($P<0.01$) when compared with non-pregnant non-lactating cows. The value of 'b' was significantly higher when results from cows before calving ($P<0.05$) and after calving ($P<0.01$) were compared with those in non-pregnant non-lactating cows.

The BSP half-time and 15 and 30 minute retention were significantly higher and the fractional clearance (K) significantly lower in cows before calving compared with two weeks after calving (P<0.05) and with non-pregnant cows (P<0.001) (Table 1).

The total plasma bilirubin concentrations in periparturient cows were higher than in non-pregnant, non-lactating healthy cows (P<0.001) although there was quite wide individual variation.

There were no significant alterations in plasma GD, ID, and γGT activities around calving. The plasma AST activities in cows after calving were significantly higher when compared with non-pregnant, non-lactating cows (P<0.05) (Table 2).

A degree of hypoglycemia was apparent in periparturient cows which was more marked before than after calving. There was a significant increase in plasma total ketone body concentration in cows after calving compared to late pregnancy (P<0.05) and when both values were compared with those in non-pregnant, non-lactating cows (P<0.001).

The plasma urea concentration was significantly reduced after calving when compared with cows before calving (P<0.01) and non-pregnant, non-lactating cows (P<0.05).

NEFA, glucose and bilirubin but not AST all correlated with the percentage hepatic fat infiltration both before and after calving. The percentage fatty infiltration of the liver was correlated with the value 'h', BSP halftime and 15 minute retention before and after calving and with 'a', 'b' and 30 minute retention in addition after calving.

Discussion

The marked infiltration of fat before as well as after calving was in contact to previous results[14] although the appearance of stainable fat in the hepatic cell in the last week of pregnancy has been shown.[5] The severity of fatty livers in cows has been related to the loss of condition score after calving[12] and the problem seems to be more severe in older high yielding cows. There is evidence that fat mobilization may commence in late pregnancy.[5,14]

It was possible in all cases to fit two exponential components to the BSP experimental data graph because reading at two wavelengths removed potential errors due to turbidity, color and haemolysis[17] and a sufficiently high dose of BSP was used with sampling for 60 minutes. A higher dosage (5mg/kg) of BSP and sampling only for 30 minutes in periparturient cattle previously caused difficulty in defining the second exponential phase precisely.[18] A single phase BSP excretion pattern has been described in cattle using a lower dosage of BSP.[9] The individual variation in the transfer constants was consistent with the differences in shape of the plasma disappearance graph. As in the present study, little change in 'a' and 'h' in periparturient cattle has previously been described.[18] The increase in 'b' and the alteration in the transfer constants, half-time and retention of BSP before calving suggested that functional changes were occurring in the liver at this time.

The lack of alteration in plasma ID and GD and γGT activities is indicative of an absence of hepatic necrosis and cholestasis.[6] It is possible that the rise in AST activity in plasma around parturition was attributable to muscle damage as evidenced by the increase in CK activities at this time.

The more severe hypoglycemia in cows before than after calving contrasts with previous observations.[4,10] There was appreciable variation between individuals. The increase in plasma total ketone body concentrations after calving compared to late pregnancy agreed with previous findings.[4] However, opinions vary as to whether this measurement is helpful in the diagnosis of fatty liver or in reflecting the nutritional status of the cow accurately.[7] The low urea concentration in cows after calving could be a reflection of the reduced anabolism of proteins due to fatty infiltration.[12]

The alterations in the clinical chemistry are evidence for subclinical liver damage occurring before parturition. The use of changes in serum enzyme activity to diagnose liver dysfunction has been further complicated by the suggestion[2] that the hepatic content of these enzymes may alter during energy deficiency. The correlation of hepatic fatty content with NEFA, glucose and bilirubin concentration was expected.[10,12,16] However, the lack of correlation of hepatic fat with AST activity was at variance with previous reports[16] and it is likely that this enzyme was released into plasma from the liver some time before calving. The correlation of hepatic fat content with the transfer constants, BSP half-time and retention although not reported previously, was expected and it is of interest that these changes became more marked with the duration of the fatty infiltration.

The ultrastructural changes in postparturient cows,[11] particularly the decrease in the volume of rough endoplasmic reticulum and mitochondrial damage, have functional consequences and could account for alterations in the pattern of BSP excretion and in clinical chemistry in periparturient cows observed in this study. These were functional and reversible rather than pathological. Further studies are necessary to correlate the ultrastructural changes with alterations in hepatic function tests around calving. This investigation suggests that sub-clinical liver damage occurs well before calving.

Summary

The possibility that alterations in liver function may occur during late pregnancy as well as after calving has been investigated in healthy dairy cows and the results compared with those from non-pregnant, non-lactating cows.

There were significant alterations in plasma concentration of total bilirubin, glucose, total ketone bodies and urea, in bromosulphthalein kinase activities in peripar

turient cows compared to non-pregnant, non-lactating cows. Of these, only the alterations in glucose, total ketone bodies and urea concentrations and BSP half-time, fractional clearance and retention were significantly different prior to calving. The extent of fatty infiltration of the liver was as marked 2 weeks before as after calving, which differed from previous reports.

It seems likely that the changes in the liver in dairy cows are functional and reversible and related to the metabolic demands of late pregnancy and early lactation. The results suggest that such changes in the liver occur well before calving.

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Abstract:

Development of a microcomputer system for recording veterinary visits, preparing accounts, and as an aid to herd fertility and herd health schemes

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A computerized method of recording clinical information from farm animal practice visits and using it for herd fertility visits, herd health schemes, the investigation of disease outbreaks and as a source of data for epidemiological studies was developed in the University of Liverpool farm animal practice. The system stores clinical and reproductive information in a data base from which data can be readily extracted and analyzed, and monthly bills produced.