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Article

Use of a glycogenic precursor during the prepartum period and its effects upon metabolic indicators and reproductive parameters in dairy cows

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Abstract:

The aim was to evaluate if 1-2 propanodiol plus calcium propionate (glycogenic precursor) supplementation during the transition period in high yielding dairy cows reduces metabolic and reproductive dysfunctions during early lactation. Cows (n= 202) were divided into two homogeneous groups regarding number of lactations and body condition score. 1) Treated group (GG; n= 112) received 60 g/cow/d for15 d of a glycogenic precursor during the transition period. 2) Control group (GC; n= 90) received no treatment. Postpartum levels of beta hydroxybutyrate (BHB) (GG= 0.9 ± 0.2 mmol/L *vs* GC =1.3 ± 0.2 mmol/L; $P<0.05$), and non-esterified fatty acids (NEFA) (GG= 0.6 ± 0.1 mEq/L *vs* GC = 0.8 ± 0.1 mEq/L; $P<0.05$) were higher in the GC-group. Similarly, GC-cows had a higher percentage of retained placenta (23 % *vs* 13 %; $P\leq0.06$) subclinical ketosis (GG= 10 %, GC= 56 %; $P<0.05$), and mastitis (GG= 8 %, GC= 16 %; $P<0.05$). Metritis, dystocia, abortions, clinical ketosis, hypocalcemia and ruminal acidosis showed no differences between groups. Administration of a glycogenic precursor during the transition period demonstrated a positive effect upon BHB and NEFA blood levels during early lactation, with parallel decreases of subclinical ketosis and retained placenta; this could be an alternative to enhance the dairy herd reproductive efficiency.

Key words: Beta hydroxybutyrate, NEFA, Subclinical ketosis, Postpartum.

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Introduction

During the first weeks of lactation, cows with a high milk production face a negative energy balance (NEB), because of the high energy usage promoted by an inadequate adaptation during the transition period and the low intake of dry matter during the beginning of the lactation[1,2]. This situation promotes the mobilization of hepatic lipids, increasing the plasmatic levels of non-esterified fatty acids (NEFA) and beta hydroxybutyrate (BHB), which are considered as sensitive markers of NEB[3,4]. Such physiologic and metabolic scenario may cause hepatic lesions leading to a high probability of suffering other disorders related to metabolic dysfunction such as ketosis, mastitis, metritis, hypocalcemia, abomasal

displacement and retained placenta[2]. In fact, at the onset of lactation, BHB concentrations higher than 1.2 mmol/L are related with the presence of subclinical ketosis[5], and that levels of NEFA from 0.7 to 1.0 mEg/L are able to predict postpartum health problems[6]. Considering all the processes that take place during the transition period and with the aim of maintaining normoglycemia, several metabolic alternatives have been used in order to maintain glycaemia to fulfill the requirements of the peripheral tissues[7]. The last throughout the process of glycogenesis, which allows the production of glucose starting from the glucose precursors as propionate or propylene glycol[8-11]. Based on the previous findings, the aim of this study was to evaluate the use of a glycogenic precursor during the transition period upon the blood levels of NEB (NEFA and BHB) and the incidence of metabolic and reproductive diseases at the beginning of lactation in high yielding dairy cows.

Material and methods

Study site, animals and management

The research took place from August to September 2015, in the Comarca Lagunera (25° 44 36 N, 103° 10 15 W; 1,111 m asl). This northern region of Mexico is characterized by an extremely hot-dry climate, with temperatures ranging from 23 ºC to 43 ºC in summer and 2 ºC to 9 ºC in winter, annual mean rainfall of 240 mm and relative humidity of 29 to 83 %. The study was conducted in a commercial dairy herd with a stock of 1,600 Holstein cows, managed under an intensive production system in open pens. The cows were fed with a completely mixed diet (50 % forage and 50 % concentrate, DM basis 1.62 Mcal/Kg NEL, 18 % CP), formulated in order to fulfill the nutritional requirements of cows in lactation with a milk production > 33 kg milk/d[12]. The cows were fed *ad libitum* with a daily fed leftover of 10 % of the feed offered in four times (06:0, 1000, 12:0 & 16:0 h).

Health and reproductive management

All cows received four intramammary infusions of 375 mg of cephalexin (Rilexine®, Virbac, Mexico), during the dry period. Also, cows received a prolonged released cake consisting in micro minerals and vitamins A, D and E (Megabric®, Neolite, Laboratory, France). Routine

control of mastitis included disinfection of nipples before and after milking, the California mastitis test and a regular somatic cell count.

Cows included in this study were subjected to a reproductive management of fresh cows from d 0 to 10; in order to achieve an adequate uterine involution, a 25 mg PGF2α injection was administered on d 35 and 47 postpartum. Besides, every cow was vaccinated according to the vaccine preventive program of the herd, mainly focused against diseases like bovine viral diarrhea, infectious bovine rhinotracheitis, bovine respiratory syncytial virus, parainfluenza type 3 and leptospirosis (5 varieties).

Experimental design and response variables

Cows (n= 202) with no reproductive issues were selected and divided into two homogenous groups regarding the number of previous lactations (3.2 ± 1.17) and body condition score (3.3 ± 0.5; 1-5 scale). While the average milk production at 305 d was 12,200 ± 147 kg the average number of inseminations was 3.7 ± 2.4 (1-10 inseminations range). A first group of cows (n= 112; GG; 41.1 ± 0.7 L per day) received a daily administration of 60 g/cow of a glycogenic precursor (1-2 propanediol and calcium propionate, Lipofeed®, Mexico) during the first 15 d of the transition period, which was added to the diet, while the second group (n= 90; GC; 40.1 ± 0.7 L per day) received no treatment.

Fatty acids and beta hydroxybutyric acid

Concentrations (mean ± SE) of non-esterified fatty acids (NEFA) in serum was determined by taking a coccygeal blood sample with vacuum tubes (BD Vacutainer®) at 7, 14 and 21 d postpartum; the obtained samples were identified and refrigerated until they arrived at the laboratory where they were centrifuged (450 gx 20 min), afterwards, they were frozen and stored at -20 ºC until analyzed. *In vitro* quantitative determination of serum NEFA was performed with an automatic analyzer (Randox RX Monza®, USA), while the determination of concentrations (mean ± SE) of beta-hydrybutyric acid (BHB) at 7, 14 and 21 d postpartum was done with a portable BHB-meter (Precision Xtra system tests®), which consists of the use of reagent strips to quantify the ketone bodies in blood[3,13].

Metabolic diseases

The percentage of cows with clinical ketosis was calculated, it was diagnosed based on a low milk yield and decreased appetite and the percentage of subclinical ketosis was determined with reagent strips during the first 21 d in milk. In addition, their relationship with other clinical diseases during the first 35 d postpartum were also evaluated[14]. The occurrence of clinical mastitis was detected at milking by determining heat and inflammation by touching the udder and by evaluating consistency changes of the milk (watery-bloody, secretions and blood clots); this was daily performed during the first 3 wk postpartum[15].

Reproductive diseases

Percentage of cows with retained placenta (RP) was quantified in both groups, and was defined as the failure to expel fetal membranes within the first 24 h after parturition[16] and diagnosed by observing the presence of fetal membranes protruding from the vulva for more than 24 h after parturition. Metritis was defined as the inflammation that involved all the uterine wall[17]. This was confirmed by evaluating, by rectal palpation, the size of the uterus in relation to the moment of parturition, the uterine wall thickness and the presence of liquid in one or both uterine horns. Abortion was defined as fetal death and expulsion between 50 and 260 d of pregnancy.

Statistical analyses

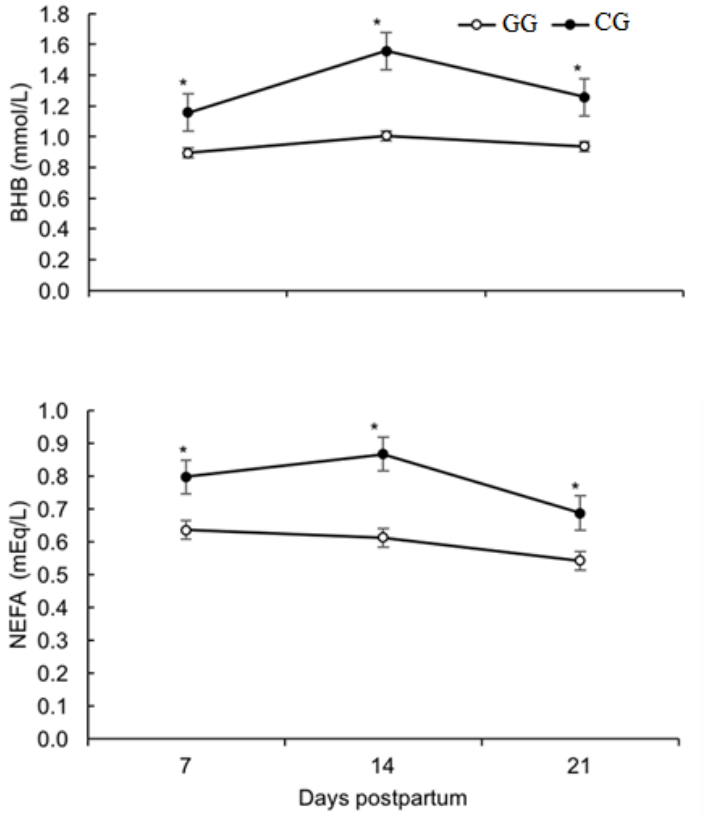
Blood concentrations of BHB and NEFA were analyzed with the GLM procedure and mean comparison was performed by a Student-T. Percentage of cows showing reproductive (retained placenta, metritis, abortion and dystocia) and metabolic (clinical and subclinical ketosis, hypocalcemia, mastitis and ruminal acidosis) diseases, was calculated and compared by a X^2 test. All analyses were performed with the SAS program, considering a significance level of $P<0.05$ and of $P>0.05$ and $P\leq0.10$ for statistical tendency.

Results

BHB and NEFA concentrations

The results for concentrations of BHB and NEFA for both groups at 7, 14 and 21 d postpartum are shown in Figure 1. Levels of BHB during the first 3 wk of lactation were higher in the GC-cows (1.3 ± 0.2 *vs* 0.9 ± 0.2 mmol/L; $P<0.05$). No differences were found neither in time nor treatment at d 7 postpartum. Nonetheless, a difference was found between time and treatment at 14 and 21 d postpartum ($P<0.05$). Moreover, NEFA levels were higher for GC cows (0.8 ± 0.1 *vs* 0.6 ± 0.1 mEq/L; $P<0.05$). A treatment *x* time interaction effect occurred at 7, 14 and 21 d postpartum ($P<0.05$).

Figure 1: Postpartum blood levels of non-esterified fatty acids (NEFA) and BHB (mean ± SE) in high yielding dairy cows treated (GG) or non-treated (GC) with a glucose precursor for 15 d during the transition period



*Significant difference ($P<0.05$).

Reproductive and metabolic dysfunction incidence

Table 1 concentrates the percentage for reproductive and metabolic diseases in both experimental groups. The percentage of retained placenta for GG cows was 13 % (15/112) *vs* 23 % (21/90) for the GC-cows, ($P \geq 0.06$). No differences between experimental groups ($P > 0.05$) occurred for percentages of metritis, dystocia or abortion. In relation to metabolic diseases, a higher percentage ($P < 0.05$) of subclinical ketosis was observed in the GC-cows (56 %; 50/90 *vs* 10 %; 12/112) as well as for mastitis (18 %; 16/90 *vs* 8 %; 9/112, respectively). No differences were observed for the remaining metabolic diseases between experimental groups ($P > 0.05$).

Table 1: Percentage of postpartum reproductive and metabolic diseases of dairy cows treated (GG) or no treated (GC) with a glucose precursor for 15 d during the transition period (%)

Variables	**Groups**		***P* value**
	GG (n= 112)	**GC (n =90)**	
Reproductive diseases:			
Retained placenta	13 (15/112)	23 (21/90)	0.067
Metritis	5 (6/112)	11 (10/90)	0.132
Dystocia	7 (8/112)	11 (10/90)	0.325
Abortion	1 (1/112)	2 (2/90)	0.438
Metabolic diseases:			
Clinical ketosis	1 (1/112)	3 (3/90)	0.216
Subclinical ketosis	10 (12/112	56 (50/90)	0.000
Hypocalcemia	1 (1/112)	1 (1/90)	0.864
Mastitis	8 (9/112)	18 (16/90)	0.037
Ruminal acidosis	6 (10/112)	10 (9/90)	0.467

Discussion

The results demonstrate that cows treated with a glycogenic precursor during the transition period depicted a lower NEB regarding the non-treated cows. In fact, females facing NEB have higher BHB levels[18]; high yielding dairy cows during the beginning of lactation increase their glucose requirements for lactose production and, with the lack of this, the animal mobilizes the glycogenic substrates that originate ketone bodies[19]. The last could probably be due because such glycogenic precursor is an important substrate for gluconeogenesis, which may have stimulated the hepatic glycogen dynamic that is necessary to satisfy the requirements of hepatic glucose during the transition period[19]. In fact, some studies have demonstrated that the use of propionate[10,11], or propylene glycol[8,9], stimulate glucose synthesis in dairy cows at the beginning of lactation[20]. The above probably helped to reduce the blood BHB levels in the GG-cows; it has been stated that glycogenic precursors decrease ketonic bodies concentration[20]. On the other hand, the administration of a glycogenic precursor decreased the blood NEFA concentrations in the GG-cows (0.6 ± 0.1 mEq/L) compared to GC-cows (0.8 ± 0.01 mEq/L), suggesting that the GG-cows were probably on a less intense NEB regarding the control-cows[6]. Certainly, at the beginning of lactation cows face a NEB, due to the high milk yield which parallels a decrease in feed consumption, causing an increased lipid mobilization from body fat to the liver in order to make available the required glucose levels essential to compensate the observed energy deficit during the NEB[1,6,21].

Therefore, those cows treated with the glycogenic precursor during the transition period decreased the incidence of females facing metabolic disturbances. In fact, the GG-cows had less subclinical ketosis than the control cows (10 % *vs* 56 %). McArt *et al*[18] indicate that the mean level of BHB in blood to assume the presence of a subclinical ketosis is > 1.2 mmol/L, which was near the average for the non-treated group (1.3 mmol/L). Indeed, more than 50 % of the cows in the GC showed subclinical ketosis, which is a risk factor for the health of the animals, and increases the incidence of reproductive diseases during the cool period. In addition, subclinical ketosis also increases the return-to-estrus interval, as well as, rises the rate of waste of the herd while it decreases milk production, causing economic losses[3,4,14]. This was probably due because of the administration of the glycogenic precursor which reduced, in turn, the circulating BHB concentrations (0.9 mmol/L in the GG-cows), suggesting failures in the adaptation ability during the transition period[22]. Certainly, a high milk yielding cow has a high glucose demand for lactose production. Yet, since there is a lack of blood glucose, cows try to compensate such metabolic challenge by mobilizing lipids from liver. Such physiological and metabolic scenario probably provoked that the control

cows generated an increased serum BHB level which, in turn, provoked a high percentage of subclinical ketosis[6,19,20]. The last, may also promoted an increased risk of diseases like fat liver and ketosis([6,10,20].

On the other hand, the GG-cows had 50 % less clinical mastitis than the control-cows. The last probably was due to the fact that control-cows had blood BHB concentrations ≥ 0.6 mmol/L from the pre-partum to the beginning of lactation, which has been reported as a factor that increases the probability of cows presenting pre-partum diseases and a consequent decrease in milk production[6,23]. This scenario probably occurred because ketosis has been associated as a factor that increases the risk of clinical mastitis[14,24]. Moreover, NEFA increases (≥ 0.8 mEq/L) is another risk factor associated to other diseases like metritis, mastitis and clinical ketosis[4,6]. Certainly, any unbalance of both energy status and health status, decreases the immune compensatory response of cows and make them susceptible to poorly counteract any health compromising insult[25]. Studies have demonstrated that high concentrations of NEFA are related with metabolic and inflammatory diseases that induce inflammation and affect the immune system[26,27]. On the other hand, the reduced percentage of cows with retained placenta, in comparison with the control cows, could be explained because of the treated cows had a better energetic metabolism which improved the functionality of their immune system and, in consequence, promoted less incidence of inflammation processes[28]. The low NEFA concentrations of the GG-cows, it is known to increase the blood lipid content while a higher serum NEFA concentration, and it is associated with a higher incidence of peri-parturient diseases (i.e. retained placenta, abomasal displacement) as well as the predisposition to inflammatory diseases (i.e mastitis, metritis)[29,30] the last may have increased the percentage of retained placenta incidence[22,31]. Furthermore, a higher concentration of blood BHB, generates a higher risk of cows presenting reproductive diseases[3,4].

Conclusions and implications

Cows treated with a glycogenic precursor during the transition period reduced the impact of the negative energy balance and, in consequence, diminished some health problems such as retained placentas, subclinical ketosis and mastitis at the beginning of lactation. The results indicate also that such supplementation strategy could be an interesting alternative to positively influence the energetic balance during the transition period of dairy cows while improving their health status. All of these metabolic and health responses should contribute to improve the reproductive efficiency of high yielding dairy cows.

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