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Original Article
Özgün Araştırma

Effects of propylene glycol in different doses on metabolic parameters in dairy cows

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Abstract: The study evaluated the effects of propylene glycol (PG) drenched in different doses in dairy cows with a positive energy balance on serum metabolic parameters. Twenty-four Simmental dairy cows in 60-190 days of lactation period with positive energy balance were included in this study. PG was drenched three hours after morning feeding, at a dose of 300 mL (8 dairy cows, Group I) and 500 mL (8 dairy cows, Group II) once a day for 3 days. Eight dairy cows were included in the control group (Group III). Blood samples were collected once before PG drenching, daily after drenching of PG, and finally on day 4. Serum biochemical parameters were determined.

With regard to energy metabolism, glucose concentrations from serum biochemical parameters significantly increased on day 3 in the 500 mL PG group compared to the control group, and there were no significant changes in BHBA and NEFA concentrations. Decreased urea and increased chloride concentrations were determined within reference limits. In dairy cows with positive energy balance, 500 mL PG oral drenching had a positive effect on energy balance as determined by serum glucose measurements, might not have adverse effects on hepatic and renal function, and may cause serum electrolyte changes within reference limits.

Keywords: Dairy cows, propylene glycol, serum metabolic parameters

Süt ineklerinde farklı dozlarda propilen glikolün metabolik parametreler üzerine etkileri

Özet: Çalışma pozitif enerji dengesine sahip süt ineklerinde farklı dozlarda propilen glikol (PG) uygulamasının serum metabolik parametreleri üzerine etkilerini değerlendirdi. Çalışmaya 60-190 günlük laktasyon döneminde pozitif enerji dengesine sahip 24 adet Simental ırkı süt ineği dahil edildi. PG, sabah yemlemesinden 3 saat sonra, günde bir kez 300 mL (8 süt sığırı, Grup I) ve 500 mL (8 süt sığırı, Grup II) dozlarında 3 gün boyunca uygulandı. Kontrol grubu (Grup III) için sekiz süt sığırı dahil edildi. Kan örnekleri PG uygulamasından önce bir kez, PG uygulamasından sonra günlük olarak ve son olarak 4. günde toplandı. Serum biyokimyasal parametreleri belirlendi. Enerji metabolizması ile ilgili olarak, serum biyokimyasal parametrelerinden glikoz konsantrasyonları kontrol grubuna kıyasla 500 mL PG grubunda 3. günde önemli ölçüde arttı, BHBA ve NEFA konsantrasyonlarında ise önemli bir değişiklik olmadı. Üre konsantrasyonlarında azalma, klorür konsantrasyonlarında artma ise referans sınırlar içerisinde tespit edildi. Pozitif enerji dengesine sahip süt ineklerinde, 500 mL PG'nin oral uygulanması serum glikoz ölçümleri ile belirlendiği gibi enerji dengesi üzerinde olumlu etkiye sahipti, hepatik ve renal fonksiyonlar üzerinde olumsuz etkileri olmayabilir ve referans sınırlar içinde serum elektrolit değişikliklerine neden olabilir.

Anahtar kelimeler: Propilen glikol, serum metabolik parametreleri, süt ineği

Introduction

Propylene glycol (PG) is a gluconeogenic substrate that has beneficial effects on carbohydrate and lipid metabolism in the early lactation period in dairy cattle (Gordon et al. 2013; Piantoni and Allen 2015; Gordon et al. 2017; Jeong et al. 2018). In a recent study, a long time PG drenching to dairy cattle in the transition period has been reported to decrease subclinical ketosis incidence and increase milk production (El-Kasrawy et al. 2020). Also, PG can reduce the incidence of fatty liver (Kristensen and Raun 2007). Some farmers and veterinarians have expressed that clinical signs such as ataxia, salivation, depression, and shallow breathing develop in some cattle (Nielsen and Ingvartsen, 2004). High-dose PG treatment for ketosis treatment (800-1800 g/day) has been determined to cause clinical signs such as salivation and ataxia, but 200-500 g PG treatment once a day in cows with ketosis has been reported not to cause toxicity signs (Johnson 1954). A study

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has reported that PG toxicity develops in one of three cattle-drenched PGs (Bertram et al. 2009). PG drenching dose in the treatment of ketosis related to dairy cattle is reported as 300 mL/day for three days (Mann et al. 2017) and 500 mL (Maurer et al. 2017). In dairy cattle, the maximum dose of PG is limited to 500 mL (Nielsen and Ingvartsen 2004; Zhang et al. 2020). During PG treatment, taking care of the development of toxicity signs is required (Zhang et al. 2020). A high dose of PG treatment increases the toxicity risk in the case of renal and liver function disorders (Zar et al. 2007). According to the authors' knowledge, there is no study in which the effects of PG at 300 and 500 mL doses are evaluated on serum biochemical parameters in dairy cattle with positive energy balance. Thus, this study evaluated the effects of PG at 300 and 500 mL doses once a day for three days orally on serum biochemical parameters of dairy cattle in positive energy balance.

Material and Method

Animal material

This study was approved by Atatürk University Ethics Committee (13.01.2020/5) and was funded by Atatürk University Scientific Research Unit (TDK-2021-9002).

Feeds of dairy cows comprised dry roughage (29.14%), corn silage (37.47%), and forage (33.38%) were prepared by a veterinary specialist (Sunar Feed Company, Osmaniye, Turkey, Kardelen 21 Dairy Cattle Feed). 24 Simmental breed dairy cattle in positive energy balance, 3-4 years old, with normal physical examination findings, 60-190 days of lactation, were used. The study animals comprised 300 mL PG (Group I), 500 mL PG (Group II) and control (Group III) groups. PG was drenched at a dose of 300 mL (Mann et al. 2017) and 500 mL (Maurer et al. 2017) once a day for three days after morning feeding.

Blood sampling

The venous blood samples were collected into vacutainer tubes 3 hours after PG drenching, centrifuged after 30 minutes at 4 C° (Heraeous sepatec, Labofuge 200, Germany). Sera samples were stored until analyses at -20 °C.

Serum biochemical analyses

Serum triglyceride, total cholesterol, total protein, total bilirubin, urea, creatinine, aspartate aminotransferase (AST), sodium, potassium and chloride concentrations were measured using the device for serum biochemical analyses (Siemens Atellica Solution, Germany).

Blood beta-hydroxybutyric acid (BHBA) and glucose concentrations were measured using the blood ketone (CentriVet™ ACON Laboratories, ABD) and blood glucose (On-call plus, USA) measurement devices.

Serum nonesterified fatty acid (NEFA) (Cat. No: E0021Bo Bioassay Technology Laboratory, China) and glutamate dehydrogenase (GLDH) (Cat. No: E2262Bo Bioassay Technology Laboratory, China) concentrations were measured using ELISA kits as specified by producing company.

Statistical analysis

All data were statistically analyzed using SPSS 20.00 (Windows, IBM, USD). Parametric and nonparametric data were presented as mean±standard error of means (SE) and median (minimum-maximum), respectively. Parametric and nonparametric data were analyzed using repeated measurements ANOVA and repeated measurements using the Kruskal-Wallis test, respectively. Triglyceride was analyzed with chi square test. Statistical significance for all data was considered as $P<0.05$.

Results

Serum metabolic parameters of dairy cows with positive energy balance were presented in Table 1.

BHBA concentrations were not significantly different at all the time points among groups and within groups ($P>0.05$). Glucose concentrations were significantly increased at the third time point in the 500 mL PG group compared to the control group ($P<0.05$), but there was no significant difference within the group. NEFA concentrations were not significantly different at all the time points among groups and within groups ($P>0.05$).

Urea concentrations were significantly decreased at the third time point in the 500 mL PG group compared to the control group and were significantly decreased at the first and third time points than the zeroth time point within the 500 mL PG group ($P<0.05$). Creatinine concentrations were not significantly different at the first, second and third time points among groups, and there was no significant difference at the fourth time point in 300 mL PG and 500 mL PG than the control group ($P>0.05$). Within the 500 mL PG group, creatinine concentrations were significantly increased at the first and third time points than the zeroth time point ($P<0.05$). AST concentrations were not significantly

different at all the time points in 300 and 500 mL PG groups than in the control group and within the groups (P>0.05). GLDH concentrations were not significantly different among the three groups and within groups (P>0.05).

Total protein concentrations were not significantly different at the first, second, third and fourth time points among groups (P>0.05). Total bilirubin concentrations were not significantly different at the first, second, third and fourth time points among groups and within groups (P>0.05). Total cholesterol concentrations were not significantly different at all the time points among groups and within groups (P>0.05). Triglyceride concentrations were not significantly different among groups (P>0.05). Sodium concentrations were not significantly different at all the time points among groups and within groups (P>0.05).

Potassium concentrations were not significantly different at all the time points among groups (P>0.05). In addition, the increase in potassium concentrations was more significant at the first and second time points than the zeroth time point within the 300 mL PG group (P<0.05). Within the 500 mL PG group, a tendency for non-significant increase and decrease was observed in potassium concentrations.

Chloride concentrations were significantly increased at the first, second, and fourth time points than the zeroth time point within the 300 mL PG group, and at the second time point in the 300 mL PG group than the control group (P<0.05), and at the first time point than the zeroth time point within 500 mL PG group (P<0.05).

Table 1. Serum metabolic parameters in dairy cows with positive energy balance in the PG groups and the control group.

Parameters	Time (Day)	300 mL PG Group	500 mL PG Group	Control Group
BHBA (mmol/L)	0	0,60 (0,50-0,90)	0,65 (0,50-0,80)	0,55 (0,40-0,90)
	1	0,50 (0,40-0,70)	0,65 (0,50-0,90)	0,60 (0,50-0,80)
	2	0,70 (0,50-0,80)	0,70 (0,40-0,70)	0,65 (0,00-0,80)
	3	0,60 (0,50-0,70)	0,60 (0,50-0,80)	0,60 (0,50-0,80)
	4	0,70 (0,50-0,90)	0,70 (0,60-0,90)	0,65 (0,60-0,90)
Glucose (mg/dl)	0	41 (32-56)	43,50 (35-78)	42 (33-56)
	1	48 (35-62)	54,50 (40-75)	44,50 (32-63)
	2	47 (40-54)	51,50 (44-62)	45 (36-63)
	3	47 (37-56)^{ab}	52 (48-58)^{a}	43 (36-52)^{b}
	4	39,50 (31-55)	41,50 (36-68)	41,50 (33-56)
NEFA (µmol/L)	0	77,82 (60,48-199,85)	147,98 (53,54-226,95)	94,81 (72,30-160,66)
	1	97,57 (40,00-219,43)	83,07 (46,49-297,40)	71,22 (52,90-203,09)
	2	129,84 (62,31-933,13)	124,12 (47,49-724,61)	88,54 (57,44-337,02)
	3	76,78 (53,86-134,90)	87,59 (54,84-775,00)	103,06 (76,51-125,58)
	4	94,32 (62,29-196,06)	105,50 (71,00-194,00)	92,50 (75,00-139,00)
Urea (mg/dl)	0	18,62±0,80 18,00 (16-23)^{AB}	18,25±0,55^{B} 18,00 (16-20)	18,87±0,98^{AB} 18,50 (15-24)
	1	17,00±0,56 17,00 (15-19)^{B}	16,25±0,49^{C} 16,00 (14-18)	17,50±0,90^{B} 17,00 (14-22)
	2	18,00±0,77 17,50 (15-21)^{AB}	16,50±0,42^{BC} 16,50 (15-18)	18,87±0,63^{AB} 19,00 (16-21)
	3	16,62±1,11 17,00 (10-21)^{Bab}	16,25±0,49^{C} 16,00 (14-18)^{a}	19,12±0,63^{AB} 19,50 (16-22)^{b}
	4	20,00±0,70 19,50 (18-24)^{A}	19,25±0,45^{A} 19,00 (18-21)	21,00±0,73^{A} 21,00 (18-24)

Parameters	Time (Day)	300 mL PG Group	500 mL PG Group	Control Group
Creatinine (mg/dl)	0	0,98±0,03 1,01 (0,82-1,08)	0,92±0,03^{BC} 0,93 (0,76-1,02)	0,96±0,04 0,94 (0,82-1,18)
	1	1,03±0,04 1,07 (0,81-1,14)	1,07±0,01 ^{A} 1,07 (1,01-1,12)	0,98±0,03 0,94 (0,88-1,15
	2	1,05±0,02 1,08 (0,91-1,14)	1,01±0,02^{ABC} 1,01 (0,92-1,11)	0,98±0,04 0,94 (0,86-1,21)
	3	1,05±0,03 1,08 (0,91-1,16)	1,07±0,02^{A} 1,08 (0,99-1,15)	1,04±0,04 0,99 (0,91-1,25)
	4	1,14±0,11 1,05 (0,92-1,91)^{a}	0,93±0,02^{C} 0,94 (0,82-1,03)^{b}	0,98±0,04 0,92 (0,90-1,20)^{ab}
AST (U/L)	0	109,50 (89-122)^{a}	83,50 (72-102)^{b}	101 (72-125)^{ab}
	1	109 (87-120)^{a}	87 (80-102)^{b}	101,50 (79-130)^{ab}
	2	109,50 (84-121)^{a}	86,50 (77-107)^{b}	99 (75-123)^{ab}
	3	110 (86-119)^{a}	90 (78-104)^{b}	102 (78-114)^{ab}
	4	109 (76-118)^{a}	88 (76-98)^{b}	100,50 (70-120)^{ab}
GLDH (ng/mL)	0	13,21 (9,30-19,52)	12,87 (8,77-22,00)	13,71 (10,36-17,95)
	1	13,09 (8,61-18,41)	11,12 (8,53-21)	14,49 (9,77-20,00)
	2	15,75 (11,32-19)	12,88 (8,17-17,46)	12,09 (8,78-24)
	3	11,79 (9,28-15,64)	10,77 (7,93-18,94)	12,59 (10,51-21)
	4	12,80 (11,48-15,79)	12,17 (9,67-16,28)	12,91 (11,01-16,42)
Total Protein (g/L)	0	70,00 (59-76)^{a}	62,50 (55-66)^{Bb}	69,00 (60-71)^{a}
	1	71,50 (60-88)	67,00 (62-80)^{ABCD}	73,00 (61-88)
	2	76 (58-89)	65,50 (60-78)^{BCD}	70,00 (63-87)
	3	73,50 (63-88)	70,00 (60-82)^{AC}	70,00 (63-85)
	4	69,50 (55-91)	77,50 (72-85)^{A}	83,50 (61-86)
Total Bilirubine (mg/dl)	0	0,04 (0,02-0,09)^{a}	0,03 (0,01-0,05)^{ab}	0,01 (0,01-0,05)^{b}
	1	0,04 (0,01-0,09)	0,01 (0,01-0,04)	0,03 (0,00-0,06)
	2	0,05 (0,01-0,07)	0,02 (0,01-0,04)	0,03 (0,01-0,08)
	3	0,01 (0,01-0,04)	0,02 (0,01-0,15)	0,01 (0,01-0,06)
	4	0,04 (0,01-0,06)	0,02 (0,01-0,06)	0,02 (0,01-0,06)
Total Cholesterol (mg/dl)	0	135 (94-166)	136,50 (126-149)	132,50 (79-188)
	1	133,50 (93-163)	143 (125-159)	136 (82-200)
	2	131,50 (91-166)	140,50 (120-156)	130,50 (79-192)
	3	128 (96-161)	139 (122-163)	137,50 (80-188)
	4	136 (90-161)	143 (133-160)	130 (87-188)

Parameters	Time (Day)	300 mL PG Group	500 mL PG Group	Control Group
Sodium (mmol/L)	0	139 (137-140)	138 (134-142)	138 (137-139)
	1	138 (136-144)	140 (137-144)	138 (136-142)
	2	139 (139-144)	139 (136-142)	138 (136-144)
	3	139 (137-141)	140 (137-143)	139 (137-142)
	4	141 (138-146)	140,50 (137-147)	140 (135-144)
Potassium (mmol/L)	0	3,89±0,09 3,84 (3,54-4,36)^{B}	3,94±0,05 4 (3,69-4,09)	3,94±0,07^{AB} 4 (3,67-4,19)
	1	4,28±0,07 4,22 (4,01-4,65)^{A}	4,12±0,09 4,15 (3,78-4,56)	4,25±0,10^{A} 4,21 (3,92-4,65)
	2	4,23±0,07 4,19 (3,99-4,49)^{A}	4,07±0,05 4,05 (3,88-4,41)	4,05±0,09^{AB} 3,99 (3,69-4,53)
	3	4,06±0,06 4,04 (3,79-4,40)^{ABC}	3,91±0,11 3,88 (3,29-4,28)	3,99±0,09^{AB} 3,94 (3,72-4,55)
	4	3,80±0,08 3,86 (3,35-4,02)^{BC}	3,93±0,11 3,93 (3,37-4,44)	3,85±0,10^{B} 3,86 (3,42-4,45)
Chloride (mmol/L)	0	102,02±0,63 102 (99,20-105)^{B}	101,42±0,72^{B} 102 (98,20-104)	100,45±0,80 101 (97,70-103)
	1	104,25±0,45 104 (103-106)^{A}	104,12±0,58^{A} 104 (102-107)	102,60±0,66 102,50 (99,80-106)
	2	104,87±0,39 105 (103-106)^{Aa}	103,50±0,56^{AB} 103,50 (101-106)^{ab}	101,55±0,84 101,50 (98,20-106)^{b}
	3	103,50±0,59 103 (101-106)^{AB}	102,31±0,66^{AB} 102,50 (99,50-105)	101,77±0,70 101,50 (98,20-105)
	4	104,12±0,47 104,50 (102-106)^{Aa}	102,87±0,51^{AB} 102,50 (101-105)^{ab}	101,51±0,76 101,50 (98,50-104)^{b}

^{a,b}: Lower letters in the same row indicate statistical significance (P<0.05).

^{A,B,C}: Capital letters in the same column indicate statistical significance (P<0.05).

Discussion and Conclusion

Propylene glycol (PG) is a gluconeogenic substrate that has beneficial effects on carbohydrate and lipid metabolism in the early lactation period in dairy cattle (Gordon et al. 2013; Piantoni and Allen 2015; Gordon et al. 2017; Jeong et al. 2018). Mikula et al. (2008) have reported that 4 hours after top dressing PG in the morning, blood glucose and NEFA concentrations are not significantly affected in dairy cows after parturition. Cozzi et al. (1996) have reported that 200 and 400 mL PG mixed with TMR have an increased effect on the blood glucose increase during 0-6 hours in mid-lactating dairy cattle. Mikula et al. (2020) have revealed a non-significant effect on the blood glucose in the PG delivery methods, a significant decrease of the blood BHBA concentration 1.5 and 2.5 h after oral PG drenching, a decreasing trend of the blood NEFA concentration 1.5 h after oral PG drenching in dairy cattle with positive energy balance. Maurer et al. (2017) have stated that oral PG drenching at 100, 300 and 500 mL doses has dose-dependent effects on serum glucose and insulin, and 500 mL PG administration provides a long-lasting decrease of blood NEFA concentrations in lactating dairy cows. In this study, 500 mL PG had a significant effect on the blood glucose concentration at the third time point compared to the control group, but the blood glucose concentration had no significant increase at different time points within the 500 mL PG group. Thus, a 500 mL PG dose rather than a 300 mL PG dose could contribute to an increase in blood glucose concentrations. In addition, in the present study, the blood BHBA and serum NEFA concentrations were not significantly affected at different doses of PG administration. Similarly, the blood BHBA concentrations have been reported not to be affected by PG administration in dry and close-up periods of dairy cows (Maurer et al. 2017). Thus, in the present study, the ineffective PG on the blood BHBA concentrations could be related to positive energy balance in dairy cows during the lactation period.

Different results have been obtained from various studies on the gluconeogenic effects of PG in dairy cows. This could be attributed to the PG delivery method, blood sampling times after PG ad-

ministration, and the lactation period of dairy cows (Maurer et al. 2017).

In ruminants, GLDH is an important marker of hepatic disorders (Smith, 2014). Skeletal and liver tissues have large amounts of AST enzyme. In hepatic disorders, increased serum AST activity is evaluated with specific liver enzymes (Constable et al. 2017). Hoedemaker et al. (2004) have reported that in dairy cows before parturition, PD administration has no effects on the increase of AST and GLDH activities, and AST and GLDH activities should be assessed as metabolic profile tests in monitoring liver health. Maurer et al. (2017) have found that oral PG administration has no effect on cholesterol concentration and AST and GLDH activities, but a decrease of bilirubin concentrations is carried out with 500 mL PG in early lactating periods of dairy cows. In the present study, oral PG administration did not have a significant effect on GLDH activities and total cholesterol, total bilirubin and triglyceride concentrations among groups and within groups, as well as on AST activities and total protein concentrations between PG groups and control group. Thus, the present study revealed that 300 mL and 500 mL PG doses could not have adverse effects on liver function as indicated by serum GLDH and AST activities and total protein, total cholesterol, total bilirubin, and triglyceride concentrations.

An increase in serum urea nitrogen concentration can be a marker for kidney failure. However, if serum creatinine is not increased, kidney disorder may not be present. Serum creatinine and urea increase appear in kidney disorders and dehydration (Constable et al., 2017). In addition, Xu et al. (2020) have revealed that in dairy cows with negative energy balance, energy balance is related to the mobilization of muscle proteins.

In the present study, serum urea concentrations significantly decreased at the third time point in the 500 mL PG group compared to the control group. They were significantly decreased at the first and third time points than the zeroth time point within the 500 mL PG group. Serum creatinine concentrations were not significantly different among groups. Within the 500 mL PG group, serum creatinine concentrations were significantly increased at the first and third time points than at the zeroth time point. However, Mikula et al. (2020) found increased serum urea concentration 30 min after oral PG drenching at 400 mL dose and then decreased after 2.5 hours and reached the concentrations of the control group. Miyoshi et al. (2001) have reported a tendency to increase blood urea nitrogen concentration after oesophagal PG administration. Conversely, Chibisa et al. (2008) have not found the effect of PG on BUN concentration. Conversely, in the present study, 500 mL PG dose had an effect on serum urea decreases and creatinine increases. Thus, because serum creatinine concentrations were not significantly different in the PG groups compared to the control group, serum urea increases were not found, and urea and creatinine concentrations were not significantly different at the fourth time point in the PG groups compared to the control group, it was concluded that kidney functions could not have been negatively affected.

Mann et al. (2017) have found that in dairy cows during the early lactation period, 300 mL PG administration once a day for three days did not significantly affect serum sodium, potassium, and chloride concentrations. In the present study, serum sodium and potassium concentrations did not differ significantly among groups. Potassium concentrations in the PG groups and the control group showed a tendency to increase and decrease according to the time points. Chloride concentrations significantly increased at the second point in the 300 mL PG group compared to the control group. In addition, increases in serum chloride concentrations were within acceptable limits (95-110 mEq/L) (Constable et al. 2017).

In dairy cows with positive energy balance, 500 mL PG oral drenching has a positive effect on energy balance as determined by serum glucose measurements, might not have adverse effects on hepatic and renal function, and might cause serum electrolyte changes within reference limits.

Ethics Committee Approval: This study was approved by Atatürk University Animal Experiments Local Ethics Committee (13.01.2020/5).

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