Heat stress, intestinal barrier disruption and calves: multidisciplinary perspective field study

Research Article

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ABSTRACT

Intestinal barrier might be deteriorated by heat stress (HS) that is important disruption factor affected animal productivity, as resulted leaky gut in cattle. Therefore, the aim of this study is to demonstrate that the intestinal barrier is disrupted by HS detected by the zonulin, as an intestinal permeability biomarker. The study was conducted in local farm in the Aydın Province of Turkey in August that had the average highest temperature [41.1^{0}C (36-44^{0}C)] with %36 humidity recorded by the meteorological data. Further, serum zonulin levels were assessed by ELISA. Serum zonulin (ng/ml) levels increased (60,07 ± 21,20) at mid night 00.00 am in contrast to mid-day values at 12.00 pm (34,60 ± 10,90) (p=0,018). Regarding increased zonulin levels indicated that disrupted intestinal barrier with increasing intestinal permeability and it might be affected to reduced productivity of lactation cattle with HS during hotter summer montHS in Aegean Region in Turkey. Therefore, preventive measures should be taken reflected to HS.

Keywords: Cattle; heat stress; leaky gut; zonulin

INTRODUCTION

Considering global warming (Schär et al., 2004) and demanding of production animals with intensive breeding (Renaudeau et al., 2012), dairy industry is facing HS to being significant environmental challenge. Unsurprisingly, geographic areas where long hot summer climates having with higher humidity as like Turkey is more exposed to these challenges (Schüller et al., 2014; Duru, 2018; Demirhan and Şahinler, 2019). High milk production cattle have more vulnerable to HS related to increasing heat production by yield and small surface: volume ratio that limited to heat dissipation (Chebel et al., 2004). This resulted as accommodation of the heat toward the periphery but reducing the blood flow in especially splanchnic area that inducing gut permeability (Hall et al., 2001; Lambert, 2009; Gupta et al., 2017). On the other hand, apart from the hypoxia, one of the factors that created intestinal permeability is direct effect of HS on intestinal barrier integrity with triggering the shift of the inflammatory cells for maintaining the homeostasis to the region against penetration of the toxin and bacteria (Koch et al., 2019). Heat stress is an important factor on cattle production that to be abating welfare, health and reproduction and the most well-known among these is reducing milk yield and the economic losses associated with all impacts (Gernand et al., 2019; Fabris et al., 2020; Tao et al., 2020).

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Weather of the Aegean Region in Turkey is subtropical and heat weather increasing steadily in year to year and it has been recorded the highest temperatures in recent years due to global warming (Demirtaş, 2017; Ertugrul et al., 2021). HS has a negative impact on dairy lactation cattle in Turkey as in World. Considering this, we aimed to effect of HS on zonulin levels which is intestinal permeability biomarker and to generated preliminary data for implicating intestinal impairment related to HS.

MATERIAL and METHOD

Demographic Data

The study was performed in a commercial unit rearing calves located in Aegean Region of Turkey. Aydin city, is very well known by Mediterranean climatic conditions (i.e. summers are extremely hot and dry). The most elevated temperature in the city is recorded in July with an annual average temperature of 31.0 °C between 1991-2020.

The farm composed of 47 apparently healthy calves, to those of which 40-70 days old ones were involved at the present study. Solely 7 healthy calves (5 female, 2 male) were enrolled, due to limited ELISA options (Figure 1).

Figure 1. Heat stress may be tolerated in a self-manner, although apparently healthy calves were evident. In the present study 2 of 7 calves were enrolled, showed varying degree of respond to heat stress.

Weather Conditions During the Present Field Study

Given the equivalent temperature index (ETIC) for cattle (Wang et al., 2018) this reference tool [mild-- 23° C ≤ETIC<26 ° C, moderate--26° C ≤ETIC<31 ° C, severe-- 31° C ≤ETIC<37 ° C and emergency-- ETIC>37 ° C] was taken into consideration while performing this field trial. In this field study present data was obtained at 12 pm and 00 am with temperature records of 42°C and 31°C respectively, on 5 August, Friday 2021, indicated that cows enrolled were severe and emergency affected, respectively, by HS.

Blood Sampling and Analytes

Blood was withdrawn from *Vena jugularis* into anticoagulated tubes twice a day at 12 pm and 00 am at 05.08.2021. Sera was freshly dispersed and thereafter kept at refrigerator. Bovine zonulin ELISA Kit (MyBiosource ELISA kits) were purchased commercially. ELISA analysis of serum zonulin levels were performed.

Statistical Analyses

All data was tabulated as mean and standard deviation. Normality tests of the data within the hours in same animals were determined by Shapiro-Wilk test. Comparisons between different measurement times were conducted by Wilcoxin test. All statistical analyses were performed by program SPSS 22.0 (IBM, USA) and $p < 0.05$ was accepted as statistically significant.

RESULTS

Serum zonulin concentrations to those of apparently healthy 7 Holstein calves were deemed available to observe on liner graphic at Fig 2. To those of calves serum zonulin (ng/ml) $\bar{X}$ ± SD levels at midnight 00.0, as end point, were whole lower than what else measured at basal values at mid-day 12.00, as starting point, showing that HS markedly influence on circulating zonulin levels. Table 1 presented statistical interpretation of serum zonulin (ng/ml) $\bar{X}$ ± SD levels prior to and there after.

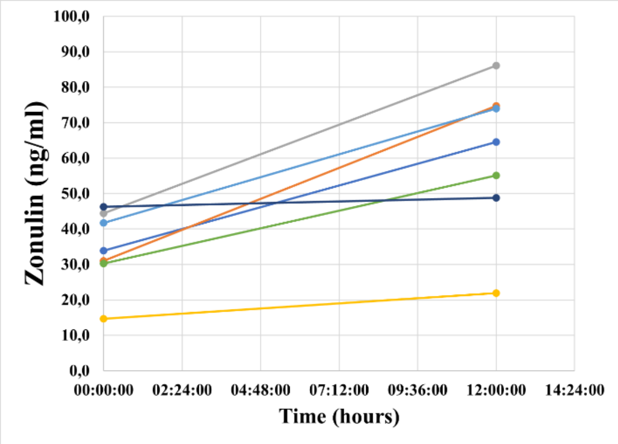

Fig.2. Linear graphic showing evidenced proof of circulating (and thereof fluctuating) serum zonulin levels (measured at mid-day 12.00 as starting point and midnight 00.0 as end point) in 7 calves enrolled at the present study.

Table 1. Statistical interpretation of serum Zonulin (ng/ml) $\bar{X}$ ± SD levels prior to measurement at mid-day 12.00 as starting point and there after midnight 00.0 as end point

	Hour		
	12:00	**00:00**	***p value***
Zonulin (ng/ml) $\bar{X}$ ± SD	60,07 ± 21,20	34,60 ± 10,90	0,018

DISCUSSION

Vulnerability to high climatic conditions could probably foist health and physiological stress-related conditions both in humans and animals. Furthermore, the gastrointestinal system is one of the foremost organs affected (Lambet, 2009). In the present study as natural model, Aydin Municipality presents natural climatic conditions, in which obtained results would have probably change management practices, hastening probable expected preventive measures. By our natural design, our HS protocol involved marked hyperthermia as evidenced by elevated rectal temperatures (not the subject of this field trial, however would be the purpose of our subsequent study and probable projects) and respiration rates (this data was also not necessary to shown) as was also reported previously. Other relevant effect of HS was diminished feed intake. This was briefly explained by the link between decreased appetite as a probable strategy for minimizing metabolic heat production (Pearce et al., 2013). Dairy calves were born in summer were prone to present lower average daily gain in contrast to those were born in winter (Place et al., 1998). As calves devour a certain volume of milk/milk replacer and starter *ad libitum* daily, HS could probably alter dry matter intake in calves at the starter. Calves were born in summer presented lower starter dry matter intake in contrast to others were born in winter (Rauba et al., 2019). Calves under HS existed diminished starter intake in comparison to others growth under moderate conditions (Broucek et al., 2009). Holstein heifers under HS (32.5 to 34 °C environment) presented lower feed intake, average daily weight gain and feed efficiency in contrast to other ones at cooler conditions (18 to 20 °C environment) (Baccari et al., 1983). Although not reported in our study (data not analyzed) decreased starter intake and thereafter decreased appetite was observed by the field veterinarian during study, which may be briefly related to HS.

The proposed mechanisms in which HS disrupts intestinal permeability, although not clearly elucidated, might involve inflammation and hypoxia modulate intestinal tight junction (tJ) proteins heat shock proteins and hypoxia-inducible factor (Yamagata et al., 2004; Turner, 2006; Qi et al., 2011). Furthermore, sequel of intestinal permeability changes involves nutrient digestibility alterations and absorption across the intestinal epithelium along with a hypothesis of an acute heat-load could deleteriously change intestinal integrity causing endotoxemia and inflammation (Pearce et al., 2013). In the present study serum zonulin (ng/ml) levels $\bar{X} \pm$ SD decreased (60,07 ± 21,20) at mid night 00.00 am in contrast to mid-day values at 12.00 pm (34,60 ± 10,90) (p=0,018). Elevated zonulin levels indicated that disrupted intestinal barrier and increasing intestinal permeability, as was below proposed mechanisms might participate.

One might speculate that calves and probably heifers engender fewer metabolic heat and exist larger body surface area in association with body mass, furthermore efficiently vanishing body heat and furthermore suggested to be more tolerant of HS in contrast to cattle (West, 2003). On the other hand, scientific data evidenced that HS might affect physiology, feed conversion efficiency, rumen of calves and heifers (Colditz and Kellaway, 1972). All aforementioned factors might alter their future productive life, in which calves under HS should be monetarized. A better understanding of HS influence on calves should be of beneficial (Beede and Collier, 1986, Wang et al., 2020). The purpose of our subsequent study would handle this idea.

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Ethical approval: This study was approved by Local Ethical Committee of University with 64583101/2021/107.

Conflict of interest: There is no conflict of interest between the authors

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