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RESEARCH ARTICLE

Chemical composition, hormonal levels and immunoglobin G concentration in colostrums, milk and blood plasma of Egyptian buffaloes following calving.

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Abstract

The formation of colostrum in buffalo udder occurs during the first 5−7 days after calving. Its composition is similar to that of blood and differs significantly from milk. The present study was planned to study the variations in the levels of some hormones in colostrum, milk and blood plasma of Egyptian buffaloes. Results demonstrate that, the chemical composition of colostrum (dry matter, solid non-fat extract, lactose, milk fat and protein) changes very rapidly with time, so that by few days post partum it is already similar to that of normal milk. Concentrations of IGF-1 were higher in colostrum than in mature milk. leptin concentration was 69% lower in mature milk than in colostrum (5.53±1.01) at birth vs. 1.68±0.69 ng/ml at one week), while no significant differences were observed during the first month of lactation. Leptin daily secretion in mature milk was lower than in colostrum . Concentrations of IgG in colostrum averaged 3260.5mg/dl at the zero time, and then decreased to 2654.0, 1900.5 and 1325.25 at 3, 6 and 24 hours later after parturition. Plasma IGF-1 concentrations were increased during one week then fell slightly .The plasma leptin concentrations showed obvious decrease from(2.38±0.93 ng/ml) at birth, to(1.87±0.32 ng/ml) at four weeks.

INTRODUCTION

The intake of colostrum during the first hours after birth is extremely important to provide the needed nutrients (proteins, carbohydrates, lipids, vitamins, minerals etc.) and for the normal growth and the morphological and functional maturation of the gastrointestinal tract of the neonatal calf, i.e. for the adequate adaptation of newborns to the new environment, especially in the early postnatal period when the abrupt change from parenteral nutrition in the fetal period to exceptionally enteral nutrition after delivery (Blum, 2006). Compared to milk, colostrum contains higher levels of proteins , lactalbumins, lactoglobulins and especially immunoglobulins (IgG1, IgG2, IgM, IgA), peptides (lactoferrin, transferrin), hormones (insulin, prolactin, thyroid hormones, cortisol), growth factors, prostaglandins, enzymes, cytokines (tumor necrosis factor- C), acute-phase proteins (C1-glycoprotein), nucleotides, polyamines, minerals (iron, magnesium and sodium salts), (pro)vitamins: especially D-carotene, vitamins A, E, D, B, cell elements - lymphocytes, monocytes, epithelial cells etc.(Blum and Hammon, 2000; Ontsouka *et al*., 2003; Blum, 2006). In buffalo, colostrum provides newborns with great amounts of nutrients, vitamins, and non-nutrient biologically active substances, such as immunoglobulin's, hormones, growth factors, cytokines, and other peptides with biological action (Blum and Hammon, 2000; Blum, 2006; Gauthier *et al*., 2006; Blum and Baumrucker, 2008). Besides the great importance of colostral immunoglobulin's for passive immunity of the neonate (Godden, 2008), colostrum has a broad impact on postnatal intestinal development. Several studies have identified a number of biologically active hormones and growth-promoting proteins present in colostrum, including insulin-like growth factors (IGF-I and IGF-II), (Francis *et al* (1988) and Vega *et al* (1991).In mammals, non-nutritional or bioactive factors, such as insulin, IGF-I and leptin, are present in high concentrations in first colostrum and affect postnatal intestinal development (Sangild, 2001; Blum, 2006; Blum and Baumrucker, 2008). Most non-nutritional components of colostrum are accumulated in the mammary gland during the prepartum period. Colostrogenesis ends abruptly at parturition (Barrington *et al.*, 2001; Godden, 2008). Therefore, concentrations (and often also mass) of many of its components are greatest in the first secretion after calving (first colostrum milking), then decline steadily over the next milking to much lower concentrations after about one week in mature milk. Colostrum, in comparison with milk, is known to be rich in immunologic components such as secretory immunoglobulin. Natural source of immunoglobulin's which protect the newborn and provide passive immunity. Contains: IgA, IgM and IgG, actoferrin, leukocytes, and bioactive growth factors such as epidermal growth factor (EGF), Castellote *et al*, (2011); Pang and Hartmann, (2007) and Kulski and Hartmann, (1981).Colostrum also contains relatively low concentrations of lactose, indicating its primary functions to be immunologic and trophic rather than nutritional. Levels of sodium, chloride, and magnesium are higher and levels of potassium and calcium are lower in colostrum than in later milk. Pang and Hartmann. (2007) and Kulski and Hartmann,(1981).Immunoglobulin's (60x cow), as well as hormones and growth factors such as relaxin (19x pig), prolactin (18x cow), insulin (65x cow), IGF-1 (155x cow), IGF-2 (7x cow), and leptin (90x humans) (Blum and Hammon, 2000; Wolinski *et al*, 2003; Bartol *et al*., 2008) among many other factors that have biological activity in the neonate. Leptin is also produced by the placenta, Kawai *et al*, (1997) and mammary gland (Smith−Kirwin *et al*, 1998; Smith and Sheffield ,2002; and Bartha *et al* ,2005) of various mammals, and is known to be present in milk from cows, goats, ewes, sows, and mares (Rosi *et al*, 2003; Chilliard *et al*, 2001; and Estienne *et al*, 2003). Leptin, the product of the OB gene, is a protein secreted predominantly by white adipose tissue (WAT) (Flier 1997, Friedman and Halaas 1998, Houseknecht and Portocarrero 1998). Leptin acts on the central nervous system and perhaps on peripheral tissues to regulate food intake, the storage and dissipation of energy and the coordination of metabolism during periods of suboptimal nutrition (Flier 1997; Friedman and Halaas, 1998; Houseknecht and Portocarrero 1998). Leptin also plays important roles in regulating processes critically dependent on energy supply such as reproductive and immune functions (Ahima *et al*, 1997; Finn *et al*, 1998; Lord *et al*, 1998; Cunningham *et al*, 1999). The few published papers report that, leptin may be produced by different cell types in the mammary tissue, and may act as a paracrine factor on mammary epithelial cell proliferation, differentiation and/or apoptosis via adipose-epithelial and/or myoepithelial-epithelial cellular interactions. In addition to leptin synthesis, epithelial cells may transfer leptin from the blood, and these two mechanisms may account for the presence of leptin in the milk. If leptin levels in milk (and specially colostrum) are found to be significant, this hormone could be involved in neonate physiology. In dairy ruminants, leptin and the leptin receptor expression within mammary tissue varies with physiological state (Silva *et al*, 2002) and stage of lactation (Laud *et al*, 1999), and it is possible that these variations are responsible for variations in milk leptin content. Milk leptin may also be produced by various cells types in mammary tissue (depending on lactation stage), or transferred from blood, or both, although the relative contributions of these sources are unclear (Bonnet et al, 2002).

Materials and methods

This study was carried out at Mehlet Moussa Experimental station, which belongs to Animal Production Research Institute, north part of the Nile Delta, Egypt**.** Eight multiparous buffalo dairy cows homogenous for parity were used. The experimental animals were kept under normal feeding and management conditions applied on the farm. Colostrum, milk and blood samples were collected just at birth of the buffalo (T0), and then at 3, 6, and 24 h later (T3, T6, and T24, respectively), then at biweekly intervals following one month of lactation and chemically analyzed for total solids, total proteins, lactose, fat and SNF in milk and colostrum by milk scan apparatus Tm FT2. Another samples of colostrum and milk were collected into tubes contain two drop of rennin enzyme to separate whey was used for measuring colostrum and milk hormones and IgG. Blood samples (10 mL) were centrifuged at 3000 r.p.m. for 20 minutes to separate plasma which was used for measuring plasma hormones (IGF-I and Leptin) and IgG. A double antibody radioimmunoassay was used to quantify insulin like-growth factor-1 (IGF-1) according to Daughaday and Rotwin (1989). BioSource IGF-1-RIA-CT kit (Cat. No. KIP1588, BioSource Europe S.A. - Rue de I' Industrie, 8-B- 1400 Nivelles Belgium) was used. The immunoglobulin G (IgG) content was quantified using Single Radial Immuno Diffusion Technique (SRID) as described by Fahey and Mackelvey (1965) SRID plates containing antibodies to IgG (Cat. No. RL 2003, the Binding Site LTTDR, UK) were used. The determination of leptin concentration was performed by ELISA reader (BIO TEK ELX808), using Leptin ELISA kit sandwich (DRG Instruments GmbH, Germany) according to the manufacturer's guideline. The standard curve was between 0 and 100 ng/ml. The sensitivity of the curve was reported to be 1.0 ng/ml.

RESULTS

1-Milk composition of buffalo during transition period from colostrum to normal milk.

Data demonstrate that, the chemical composition of colostrum (dry matter, solid non-fat extract, lactose, milk fat and protein) changes very rapidly with time, so that by few days post partum it is already similar to that of normal milk. Changes in total solids, total proteins lactose, fat and SNF concentrations from birth to one month are recorded in (Table, 1). There is obvious change in buffalo colostrum composition from the first milking until one week of parturition. At calving total solids, total proteins lactose, fat and solid non-fat extract percentage of buffalo colostrum were 20.48, 12.50, 3.44, 3.70and 16.54while at one week were 15.26, 3.94, 5.22, 6.61 and 9.16% respectively. The most consistent changes occur in milk protein content that is reduced more than twice post partum day compared to initial values.

2-Milk hormones (IGF-I, Leptin) and IgG concentration of buffalo during transition period from colostrum to normal milk.

(a)Insulin like growth factor-1(IGF-1)

Results in table 2 indicated that, the concentrations of IGF-1 were higher in colostrum than in mature milk. Georglev (2008) indicated that, the concentrations of IGFs and insulin were higher in colostrum than in blood unlike some hormones (somatotropin, glucagon and thyroid hormones). The levels of growth factors, insulin and other peptides is different in the various colostrum portions, being the highest in the cisternal fraction, then decreasing and rising again by the end of milking, respectively suckling. Georglev (2008) recorded that, the concentration of IGF-1 in cow colostrum is (383-500 μg/L), the lowest IGF-1 level is that of cow milk (4−10 μg/L).

(b)leptin

The present study indicated that, leptin concentration was 69% lower in mature milk than in colostrum (5.53±1.01at birth vs. 1.68±0.69 ng/ml at one week), while significant differences were observed during the first month of lactation. Leptin daily secretion in mature milk was lower than in colostrum . Plasma leptin at calving was 2.38±0.93 ng/ml, decreasing during post-partum (2.58±0.33, 2.24±0.28ng/ml at 6 and 24 hours and2.04±0.05ng/ml at one week respectively. Colostrum leptin concentrations showed increasing trend during colostrum period than leptin level in plasma and mature milk, suggesting that transfer of leptin from the blood account only partially for its milk content(Tables 2and,3).

(c)Immunoglobulin (IgG)

The present study indicated that, concentrations of IgG in colostrum averaged 3260.5mg/dl at the zero time, and then decreased to 2654.0, 1900.5, 1325.25 at 3,6 and 24 hours later after parturition (Table,2).The same trend was observed in plasma IgG.

3-Plasma hormones (IGF-I, Leptin) and IgG concentrations of buffalo during transition from colostrum to normal milk periods.

(a)Insulin like growth factor-1(IGF-1)

Plasma IGF-1 concentrations were increased during one week then fell slightly (Table,3).

(b)leptin

Data in Table 3 indicated that, the plasma leptin concentrations showed obvious decrease from birth (T0) 2.38±0.93 ng/ml, to Four weeks 1.87±0.32 ng/ml.During lactation period, plasma and milk leptin concentrations showed a similar decreasing time trend.

(c)Immunoglobulin (IgG)

The present study indicated that, concentrations of IgG in plasma averaged 25.98 μg/ml at the zero time, and then decreased to 22.25 μg/ml at four weeks (Table, 3).

Table (1): Milk composition of buffalo during transition period from colostrum to normal milk. (Mean±SE).

Milk composition	Total solids%	protein%	lactose%	fat%	SNF%
At birth(T0)	**20.48± 0.53^{a}**	**12.50± 0.22 ^{b}**	**3.44±0.07^{c}**	**3.70± 0.05 ^{b}**	**16.54±0.21 ^{b}**
(T3)h	**20.18± 0.24 ^{a}**	**12.94± 0.09 ^{b}**	**3.17±0.23 ^{c}**	**3.72± 0.39 ^{b}**	**16.71±0.11 ^{b}**
(T6)h	**21.01± 0.23^{a}**	**13.52± 0.08 ^{a}**	**3.18±0.12 ^{c}**	**3.72± 0.36 ^{b}**	**17.30±0.13 ^{a}**

(T24)h	**21.29± 0.73[a]**	**10.60± 0.14 [c]**	**3.45±0.10 [c]**	**6.32± 0.75 [a]**	**14.99±0.06 [c]**
one week	**15.26± 0.35 [b]**	**3.94± 0.02 [d]**	**5.22±0.11[a]**	**6.61± 0.19 [a]**	**9.16±0.10 [d]**
Two weeks	**15.26±0.39 [b]**	**3.72± 0.24 [d]**	**4.74±0.13[b]**	**6.40± 0.10 [a]**	**8.61±0.42 [de]**
Three weeks	**15.64±0.63 [b]**	**3.71± 0.14 [d]**	**4.69±0.15[b]**	**7.09± 0.44 [a]**	**8.55±0.20 [de]**
Four weeks	**13.34±0.60 [c]**	**3.19± 0.22 [e]**	**4.68±0.21[b]**	**4.95± 0.76 [b]**	**8.39±0.19 [e]**

a,b Means within the same column with different superscript differ significantly ($p<0.05$).
T3= 3 hours after birth, T6= 6 hours after birth, T24= 24 hours after birth

Table (2): Milk hormones (IGF-I, Leptin) and IgG concentration of buffalo during transition period from colostrum to normal milk (Mean±SE).

Hormones	**IGF-1**	**Leptin**	**IgG**
Constituent unit	**ng/ml**	**ng/ml**	**mg/dl**
At birth(T0)	**733.48±87.89[a]**	**5.53±1.01[a]**	**3260.5±428.20[a]**
(T3)h	**433.08±77.53[b]**	**3.08±0.63[abc]**	**2654.0±304.7[a]**
(T6)h	**227.25±24.49[c]**	**4.50±1.01[a]**	**1900.5±294.32[b]**
(T24)h	**190.73±9.98[cd]**	**3.43±1.14[ad]**	**1325.25±221.95[b]**
one week	**100.6±24.82[d]**	**1.68±0.69[bc]**	**462.5±71.22[c]**
Two weeks	**52.68±10.30[d]**	**1.98±0.50[bc]**	**397.5±94.90[c]**
Three weeks	**48.25±9.90[d]**	**0.85±0.38[bc]**	**322.5±75.97[c]**
Four weeks	**82.53±7.08[d]**	**0.65±0.15[c]**	**374.75±79.08[c]**

a,b,c,d Means within column with group with different superscript differ significantly($p<0.05$).
T3= 3 hours after birth, T6= 6 hours after birth, T24= 24 hours after birth

Table (3): plasma hormones (IGF-I, Leptin) and IgG concentration of buffalo during transition period from colostrum to normal milk (Mean±SE).

Hormones	**IGF-1**	**Leptin**	**IgG**
Constituent unit	**(μ/100ml)**	**ng/ml**	**μg/ml**
At birth(T0)	**13.86±2.14[a]**	**2.38±0.93[a]**	**25.98±7.06 [a]**
(T3)h	**15.31±2.55[a]**	**2.30±0.47[a]**	**24.18±4.31 [a]**
(T6)h	**14.76±2.83[a]**	**2.58±0.33[a]**	**28.4±4.51 [a]**
(T24)h	**14.39±1.54[a]**	**2.24±0.28[a]**	**23.98±5.19 [a]**
one week	**16.85±1.81[a]**	**2.04±0.05[a]**	**18.6±1.78 [a]**
Two weeks	**13.36±1.27[a]**	**2.06±0.07[a]**	**22.85±3.66 [a]**
Three weeks	**14.11±1.77[a]**	**1.89±0.07[a]**	**31.3±4.40 [a]**
Four weeks	**12.82±0.63[a]**	**1.87±0.32[a]**	**22.25±2.70 [a]**

Means within each column do not differ significantly from each other.
T3= 3 hours after birth, T6= 6 hours after birth, T24= 24 hours after birth

Discussion

1-Milk composition of buffalo during transition period from colostrum to normal milk.

The most consistent changes occur in milk protein content that is reduced more than twice postpartum day compared to initial values. This is mostly due to the sharp decrease in Ig fractions (Ontsouka et al., 2003), whose concentration, as already mentioned, was the highest in the first colostrum portions (Ontsouka et al., 2003). It was also found that the differences in milk secretion rates had no significant effect upon the chemical composition of colostrum as the differences in the concentrations of fats, proteins, lactose; dry matter and the solid non-fat extract among cows with different milk yields were low and statistically insignificant.

The concentrations of most ingredients, especially those of immunoglobulin's (Ig) and growth factors were the highest in the first portions colostrum immediately after calving and there after are rapidly decreasing (Table, 2).

At the same time, the contents of lactose and fat in colostrum are lower than those in milk. This findings is in agreement with previous studies (Rauprich et al., 2000a; 2000b; Blum and Hammon, 2000; Playford et al., 2000; Blum, 2006). It should be noted that Ig account for more than 50% of the total amount of colostrum proteins and contain almost all antibodies, encountered in maternal blood, about 90% of colostrum Ig being from the IgG1 type. At the same time, the contents of lactose and casein in colostrum are lower than those in milk (Ontsouka et al., 2003).

2-Milk hormones (IGF-I, Leptin) and IgG concentration of buffalo during transition period from colostrum to normal milk.

The highest proportion of buffaloes colostrum growth factors is that of insulin-like growth factors (IGFs), IGFs could originate from blood or be synthesized in the udder. Ontsouka et al., (2003) indicated that, there are species-related differences in the content of growth factors in colostrum. The concentrations of IGFs and insulin are higher in colostrum than in blood unlike some hormones (somatotropin, glucagon and thyroid hormones). The levels of growth factors, insulin and other peptides is different in the various colostrum portions, being the highest in the cisternal fraction, then decreasing and rising again by the end of milking, respectively suckling.

(b)leptin

The lowered trend in Leptin concentrations in milk with time during lactation might be due to leptin is produced by different cell types of the mammary gland, and could act as a paracrine factor on mammary cell proliferation, differentiation and apoptosis via adipose-epithelial and myoepithelial cellular interactions. Besides synthesizing leptin, secretory epithelial cells may transfer leptin from the blood, and these two mechanisms may account for the presence of leptin in milk. The respective part of these two processes remains to be clarified, as well as the true levels of milk leptin. Feuermann, et al (2006) found that, prolactin is the key factor signaling the mammary gland to interact with leptin in the regulation of milk synthesis during lactation. They evidence that, prolactin can alter leptin secretion and expression in the bovine mammary fat, and leptin expression in the bovine mammary gland of the lactating cows. Alice et al (2008) found no evidence of accumulation of leptin in colostrum pre-partum. Pre- and post-partum milk leptin concentrations were similar, but interestingly, leptin increased markedly post-partum to reach a peak 2 days after parturition.

(c)Immunoglobulin (IgG)

The lowered trend in Immunoglobulin (IgG) concentrations in milk with time during lactation might be due to about 90% of colostrum Ig being from the IgG1 type. Calves obtain antibodies ready-to-use under the form of Ig, mainly from the IgG1, IgG2, IgM and IgI classes with colostrum the so-called colostrum antibodies, bound to the globulin protein fraction (Blum,2006). Colostrum globulins are identical to those of maternal blood serum and during the first days of life, pass in the blood of calves through alimentary tract epithelium. The same trend was observed in plasma IgG. This findings is in agreement with previous studies (Rauprich et al., 2000a; 2000b; Blum and Hammon, 2000; Playford et al., 2000; Blum, 2006). According to Tomov et al. (1989), during the first hours after birth, IgM are absorbed more rapidly whereas IgG are mostly retained on the apical surface of the intestinal mucous coat, and exert there a local protective function. Also, there is a correlation between blood serum Ig of newborn calves and both peripheral blood cortisol and maternal blood cortisol, confirming the view that in physiological concentrations, glucocorticoids stimulate antibody formation (Tomov et al., 1989). The earliest colostrum intake is of primary importance for the passive immunization of calves, when colostrum's value is the most complete from biological pointof view (high titre of colostrum Ig, high lysozyme, bactericidal and high content of growth factors), the permeability of the epithelium of small intestine is the highest, and the acidity of abomasum content the lowest due to the lack of hydrochloric acid. The class M immunoglobulins (IgM) in colostrum vary between 5 mg/mL and 8.7 mg/mL whereas in milk their concentrations are 0.04–0.05 mg/mL (Levieux, 1999).

3-Plasma hormones (IGF-I, Leptin) and IgG concentrations of buffalo during transition from colostrum to normal milk periods.

(a)Insulin like growth factor-1(IGF-1)

The growth factor concentrations are highest in the first milk after parturition and decline rapidly thereafter. It is probable that the IGF-1 in the first milk has an important role in the prevention of autoimmunity and anti-inflammatory processes at an early age. Also, acting as a growth-promoting activityfactor.Penchev (2008) found that, the concentrations of IGFs and insulin are higher in colostrum than in blood unlike some hormones (somatotropin, glucagon and thyroid hormones).

(b)leptin

Although, both plasma and milk leptin concentrations showed a similar decreasing time trend during the first month of lactation, colostrum and milk showed a higher leptin level than plasma, suggesting that transfer of leptin from the blood account only partially for its milk content. Pinotti and Rosi, (2003) found that, Plasma leptin at calving was 2.64 microg/l, decreasing by 18% during post-partum (2.17 microg/l). Brogan et al. (1999) reported that, during lactation, when the level of prolactin is high, the level of serum leptin is low, results which may be considered contradictory to ours. Alice et al (2008) found that, plasma leptin concentrations were higher pre-partum than post-partum, decreased at parturition and arterio-venous differences for leptin across the mammary gland were at no time significantly different from zero. Plasma leptin does thus not appear to be involved in regulation of milk leptin. Both leptin and the short cytoplasmic form of its receptor were expressed in the mammary gland. The highest leptin receptor expression was observed pre-partum and decreased post-partum. Expression of leptin was relatively constant except for an increase in the last week prior to parturition.

(c)Immunoglobulin (IgG)

The higher trend in Immunoglobulin (IgG) concentrations in blood plasma at postpartum might be due to there is a correlation between blood plasma (IgG) of newborn calves and maternal (IgG) in both blood plasma and colostrum. Also,(Tomov et al., 1989)found that there is a correlation between blood serum (IgG) of newborn calves and both peripheral blood cortisol and maternal blood cortisol, confirming the view that in physiological concentrations, glucocorticoids stimulate antibody formation. (IgG) are absorbed by small intestine mucosa by pinocytosis for a relatively short time (8−12 hours after birth). Then, the permeability of intestinal mucosa in calves strongly decreased and becomes entirely impermeable after the 36th hour, in lambs after the 3rd day (Tomov, 1984; Gerov et al, 1987). The absorption times of the different Ig classes are different. Thus, the absorption of IgG stops after the 27th hour and that of IgA after the 16th hour following birth.

Conclusions:

Buffalo milk is an inriched source of major and minor components which are essential to provide the nutritional requirements to newborn.

Leptin concentrations in milk decrease with time during lactation and show relation with other maternal hormones. The endogenous leptin of the young is limited. Although these topics remain to be studied, it can be suggested that leptin may act on neonate physiology before and after its digestive absorption .Before its absorption, leptin may modulate gastro-intestinal functions of the neonate

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