Theriogenology of Pre and Post-parturient Downer Syndrome and Persistent or Recurrent Hypocalcaemia, in Cows and Buffaloes of Small Farmers, in Rural Areas of Rayalaseema Region

Bala Krishna Rao Dabbir1* and Venkata Siva Reddy Santimalla2

1Sreepathi Veterinary Services, Kadapa, Andhra Pradesh, India
2Assistant Director, Veterinary Hospital, Sambepalli, Andhra Pradesh, India

*Corresponding author: bdabbin@gmail.com

ABSTRACT

Theriogenology of pre and post parturient downer syndrome and persistent or recurrent hypocalcaemia, in 20 cows and 2 buffaloes of Small farmers, during July to October 2018, in rural areas of Rayalaseema Region, were intervened. After witnessing the poor response of conventional treatment which included an infusion of either Calboral or Mifex and Tonophosphan, parenteral phosphorus, all the 22 dairy farmers adopted the new intervention of infusion of calcium enriched Taurine (Taurocal). The recovery was dramatic with a cure rate at 86%. The possible therapeutic effect with regard to calcium homeostasis, stress factors, serotonin modulation and energy metabolism were discussed.

Keywords: Pre and post parturient downer syndrome, persistent hypocalcemia, infusion of Taurocal-dramatic response – intervention study

Parturient paresis (hypocalcemia) is most likely to affect dairy cattle around the time of parturition. It causes progressive neuromuscular dysfunction and flaccid paralysis. Older dairy cows, cows with a history of parturient paresis during a previous lactation, high-producing cows, and cows from the Jersey and Guernsey breeds are at highest risk for developing parturient paresis (Oetzel 1988).

In most cows, a complete recovery follows a single iv calcium treatment to correct the acute hypocalcemia. However, about 20% of cows treated for parturient paresis experience recurring episodes of hypocalcemia (relapses) requiring further treatment (Goff et al. 1989).

An attempt was made to investigate the reasons for these varied responses after infusion of calcium Boro gluconate and to find out a suitable and fitting intervention to improve the efficacy of calcium Boro gluconate by enriching with Taurine. The ailing 20 downers or recurrent cows and 2 buffaloes, referred to Sreepathi veterinary services, Kadapa for intervention, formed the clinical material, for the study. Taurine, 2-aminoethanesulfonic acid, is an endogenous end metabolite that is distributed in various tissues at high concentration. It is a sulfur-containing amino acid synthesized from cysteine and is excreted without any further metabolism. Since the first discovery of Taurine in 1827, many of its functions have been elucidated in experiments focusing on skeletal muscle, the retina and the central nervous and cardiovascular systems. The cytoprotective actions of taurine contribute to the improvement in the clinical and nutritional health of humans and animals through various
mechanisms, including antioxidation, energy production, neuromodulation, Ca^{2+} homeostasis and osmoregulation. The combination of one or more of these cytoprotective effects of taurine act to diminish the pathology and symptoms of a host of diseases ranging from those of the CNS, cardiovascular system, skeletal muscle and defective metabolism (Schaffer and Kim, 2018).

MATERIALS AND METHODS
Ailing twenty one cows and two buffaloes, were given conventional treatment with either Calboral or Mifex, Tonophospan, Mecobalmin, injectable Phosphorus, and after poor response, were referred to Sreepathi veterinary services, Kadapa for intervention. The dairy farmers were supplemented neither acidogenic diet nor calcium binders during the transition period. Taurocal, a product with calcium Borogluconate, enriched with Taurine, developed by ABT Corporation, Bangalore, were obtained free of cost and infused to the suffering cows. One bottle of Taurocal containing 25% calcium Borogluconate and Taurine, was injected intravenously. Rarely second injection was administered.

RESULTS AND OBSERVATION
Out of 22 referred cases, nineteen animals were recovered eventually. The cure rate 86%. Out of 19 recovered cases, only 3 animals were given second Injection of Taurocal (Table 1). The impact of infusion of Taurocal noticed as some downers got up immediately. The others got up within 6 to 12 hours. There was no recurrence of persistent hypocalcemia. The infusion brought out tremendous energy in downers.

DISCUSSION
The reasons for the outstanding results of Taurocal are multifold. The first reason is minimizing the stress of gestation. During the periparturient period, dairy cows suffer marked immune suppression as well as moderate to severe hypocalcemia (Reinhardt et al. 1988; Goff and Horst, 1997). The function of peripheral blood mononuclear cells (PBMC) and neutrophils declines as cows approach parturition and does not recover until 2 to 3 wk after parturition (Kehri et al., 1989a,b). A key early feature in immune cell activation is an increase in intracellular ionized calcium concentration ([Ca^{2+}]), which acts as a second messenger of signal transduction (Grafton and Thwaite, 2001; Lewis, 2001) The decrease in PBMC intracellular Ca stores before parturition and the development of hypocalcemia contributes to periparturient immune suppression (Kimura et al. 2006). The important mechanism of taurine cytoprotection is attenuation of endoplasmic reticular (ER) stress. ER stress is an important regulatory mechanism designed to restore ER function and re-establish a balance between protein degradation and protein biosynthesis/folding. When a cell experiences excessive ER stress, pathways are stimulated that can kill the cell (Prentice et al. 2015).

The second reason is the effect of Taurine on calcium homeostasis. Ca^{2+} is a universal carrier of biological information: it controls cell life from its origin at fertilization to its end in the process of programmed cell death. Precise maintenance of the physiologic levels of both extracellular and intracellular ionized calcium is essential to life. Ca^{2+} is a conventional diffusible second messenger released inside cells by the interaction of first messengers with plasma membrane receptors. However, it can also penetrate directly into cells to deliver information without the intermediation of first or second messengers. Ca^{2+} is controlled by reversible complexation to specific proteins, which could be pure Ca^{2+} buffers, or which, in addition to buffering Ca^{2+}, also decode its signal to pass it on to targets Taurine serves as buffer to maintain equilibrium between intracellular and extra cellular ionized calcium (Idrissi 2008).
Table 1

| Sl. No. | Village/Mandal                  | Month/ Year | Description                      | Before Treatment                          | After Treatment                          | Remarks            |
|---------|---------------------------------|-------------|-----------------------------------|-------------------------------------------|------------------------------------------|--------------------|
| 1       | Lakkireddipalli                 | 7/2018      | Hf 4 Th Calver                    | Downer for 10 Days                        | Taurocall. One Bottle, Got up after 6 Hours | Recovered          |
| 2       | Palannagaripalli/ Ramapuram     | 8/2018      | H.f Cow, 3rd Calving              | Downer Since 4 Days, Mifex Given, One Per Day but No Relief | Taurocall One Bottle Given, Animal Got up Immediately | Recovered          |
| 3       | Rachapalli/Lakki Reddi Palli    | 8/2018      | Hf Cow, 5th Calving               | Mifex 3 Bottles, One for 3 Days, No Response | Taurocall, One Bottle Got Up Immediately | Recovered          |
| 4       | Avulavandla Palli/ Rayachoti    | 8/2018      | She Buffaloe, 3rd Calving         | Recurrent Hypocalcemia, Given Oral and Intravenous Calcium for 2 Days but No Response | Taurocall One Bottle, Got Up After 6 Hours but No Recurrence | Recovered          |
| 5       | Devapatla/ Sambeppali           | 8/2018      | Jersey, 2nd Calver                | Bottle of Cal Mag No Response             | Taurocall One Bottle, Got Up Immediately | Recovered          |
| 6       | Peddakodivadlapalli/ Sambeppali | 8/2018      | Jersey, 2nd Calver                | Downer after One Day Calving, Mifex One Bottles for 2 Days But Recurrence | Taurocall L One Bottles Got Up Immediately, No Recurrence | Recovered          |
| 7       | Kathivandlapalli/ Sambeppali    | 8/2018      | Hf Heifer                         | Downer for 8 Days, Mifex, Mecolabin, Tonophaphan for 8 Days No Relief | Taurocall One Bottle No Response but after 2nd Injection Animal Normal | Recovered          |
| 8       | Gundrevandlapalli/ Sambeppali   | 8/2018      | Hf 3rd Calving                    | Pregnant Downer for One Week, Conventional Treatment Gave No Relief | Taurocal Got Up after 24 Hours | Recovered          |
| 9       | Gundrevandlapalli/ Sambeppali   | 8/2018      | Hf 2nd Calver                     | Downer for 3 Days, Conventional Treatment Failed | Taurocal C 2nd Injection On 2nd Day Got Up | Recovered          |
| 10      | Cherukuvandlapalli/ Sambeppali  | 8/2018      | Hf Cow                            | Pain, Shivering Milking                   | Taurocal Relived | Recovered          |
| 11      | Chakrayapet                     | 8/2018      | She Buffaloe, 2nd Calving         | Persistent Hypocalcemia. no Relief After Infusion of 4 Bottles | Taurocall One Bottle Relieved the Persistency | Recovered          |
| 12      | Kavaliandla Palli-Chinnamandem  | 8/2018      | Hf 2nd Calver                     | Downer Since 10 Days 2 Bottels of Mifex was Given but No Response | Taurocal 2 Bottles of Mifex was Given but No Response | Not Recovered      |
| 13      | Gollapalli/ Ramapuram           | 9/2018      | Hf 4th Calver                     | Downer for 4 Days, Mifex 2 Bottles for 3 Days, No Relief | Taurocall One Bottle, Cow Got Up Immediately | Recovered          |
| 14      | Madhavaram/ Raychoti            | 9/2018      | Hf 4th Calver                     | Downer 4 Days                            | Taurocal L Got Up after 4 Hours | Recovered          |
| 15      | Gopalapuram/ Kalakada           | 9/2018      | Hf Cow, 3rd Calver, Relived Dystokia, Downer, for 10 Day, Mifex @ One Bottles Per Day for 7 Days but No Relief | Taurocall One Bottle, Cow Got Again, and Became Downer, 2nd Tec Given Animal Got and Became Study. | Recovered          |
| 16      | Devapla/Sambepalli              | 9/2018      | Jersey Heifer, Calved, One Month, Persistent Hypocalcemia | 4 Bottles Calboral but Hypocalcemia Recurrence | Taurocall One Bottle Up Immediately but Nourrence Reoc | Recovered          |
of mammary derived parathyroid hormone-related protein (PTHrP) PTHrP, which can then act on bone to release calcium for transfer into milk: a process that is regulated by serotonin. Calcium and serotonin are positively correlated on the day of parturition in both Holstein and Jersey breeds (Samantha et al. 2016). Taurine modulates serotonin production and maintains serum calcium concentration (Wheler et al. 1967)

The fourth reason is induction of energy- Taurine deficiency-mediated impairment of complex I activity also affects energy metabolism, largely through elevations in the NADH/NAD+ ratio, which regulate energy metabolism by feedback inhibiting key dehydrogenases. The citric acid cycle is very sensitive to increases in the NADH/NAD+ ratio, as three NADH sensitive enzymes (α-ketoglutarate dehydrogenase, isocitrate dehydrogenase and citrate synthase) are subject to inhibition by elevations in the NADH/NAD+ ratio. For example, oxidation of pyruvate by the taurine deficient heart falls, as elevations in the NADH/NAD+ ratio inhibits pyruvate dehydrogenase activity and causes a deficiency in pyruvate, arising from the massive conversion of pyruvate to lactate (Schaffer et al. 2016).

CONCLUSION

After poor response to conventional treatment, twenty two farmers in the rural Rayalaseema region during July to October 2018, adopted new intervention. The treatment comprises infusion of 450 ml of 25% calcium Borogluconate with Taurine (Taurocal). It was observed the animals showed high energy stance and got up within 10 minutes to 12 hours. The cure rate was 86%. The possible therapeutic action of Taurine was based on calcium homeostasis, minimization of stress, serotonin modulation and energy metabolism.

ACKNOWLEDGEMENTS

We acknowledge Dr Paranjyothi Kanni, MSc PhD, research head, ABT Corporation, Bangalore and Dr Narayana K. M,V, Sc PhD, Retired professor of Veterinary pharmacology, Bangalore for their valuable guidance and Mr Nanjundaiah, technical head, ABT Corporation, Bangalore for his technical support.

REFERENCES

Goff, J.P., Reinhardt, T.A. and Horst, R.L. 1989. Recurring hypocalcemia of bovine parturient
Paresis is associated with failure to produce 1, 25-dihydroxyvitamin D. Endocrinology, **125**(1): 49-53.

Goff, J.P., and R.L. Horst. 1997. Physiological changes at parturition and their relationship to metabolic disorders. *J. Dairy Sci.*, **80**: 1260–1268.

Grafton, G. and Thwaite, L. 2001. Calcium channels in lymphocytes. *Immunology*, **104**: 119–126.

Idrissi, A.E. 2008. Taurine increases mitochondrial buffering of calcium: role in neuroprotection, Amino acids, **34**(2): 321–328.

Kehrli, M.E., Jr., Nonnecke, B.J. and Roth J.A. 1989a. Alterations in bovine lymphocyte function during the periparturient period. *Am. J. Vet. Res.*, **50**: 215–220.

Kehrli, M.E., Jr., Nonnecke, B.J. and Roth, J.A. 1989b. Alterations bovine neutrophil function during the periparturient period. *Am. J. Vet. Res.*, **50**: 207–214.

Lewis, R.S. 2001. Calcium signaling mechanisms in T lymphocytes. *Annu. Rev. Immunol.*, **19**: 497–5.

Kimura, K., Reinhardt, T.A. and Goff, J.P. 2006. Parturition and Hypocalcemia Blunts Calcium Signals in Immune Cells of Dairy Cattle. *J. Dairy Sci.*, **89**: 2588–2595.

Oetzel, G.R. 1988. Parturient paresis and hypocalcemia in ruminant livestock. *Vet. Clin. North Am Food Anim. Pract.*, **4**(2): 351-64.

Prentice, H., Modi, J.P. and Wu, J.Y. 2015. Mechanisms of neuronal protection against excitotoxicity, endoplasmic reticulum stress, and mitochondrial dysfunction in stroke and neurodegenerative diseases. *Oxid. Med. Cell. Longev.*, 964518.

Reinhardt, T.A., Horst, R.L. and Goff, J.P. 1988. Calcium, phosphorus, and magnesium homeostasis in ruminants. *Vet. Clin. North Am Food Anim. Pract.*, **4**: 331–350.

Samantha, R.W., Austin, P.P., Elizabeth, L.E., Stefanie, A.N., Tonia, L.P., Peter, M., Matthew, S.A., Thomas, D.C., Rupert, M.B. and Laura, L.H. 2016. Elevation of circulating serotonin improves calcium dynamics in the dairy cow. *J. Endocrinol.*, **230**: 105–123.

Schaffer, S.W., Shimada-Takaura, K., Jong, C.J., Ito, T. and Takahashi, K. 2016. Impaired energy metabolism of the taurine-deficient heart. *Amino Acids*, **48**: 549-558.

Schaffer, S. and Kim, H.W. 2018. Effects and Mechanisms of Taurine as a Therapeutic Agent. *Biomol. Ther.*, **26**(3): 225-241.

Wheler, J.H.T., Weller, L. and Klein, D.C. 1979. Taurine stimulates the production of serotonin and simulates the effects of 5-HTP. *Brain Research*, **166**(1): 20.
