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Ammonia and urea levels in blood and ovarian follicular fluid in cattle fed with normal and protein rich or imbalanced diet: A meta-analysis

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Meta-analysis is an analysis of analysis, the statistical analysis of large collection of results from individual studies for the purpose of integrating the findings. The present study was aimed to conduct a meta-analysis study on ammonia and urea concentrations in bovine serum and ovarian follicular fluid under normal and high protein or imbalance diet. Our study may throw some lights on ammonia and urea metabolism in ovarian follicle.

About 23 articles (Armstrong *et al.* 2001, Bruckental *et al.* 1989, Butler 1998, Butler 1996, Canfield *et al.* 1990, Claypool *et al.* 1980, Elrod and Butler 1993, Fahey *et al.* 2001, Ferguson *et al.* 1993, Gupta *et al.* 2008, Hammon *et al.* 2000, Hammon *et al.* 2005, Kenny *et al.* 2002, Larson *et al.* 1997, Law *et al.* 2009, Leroy *et al.* 2004, McEvoy *et al.* 1997, Mikkola *et al.* 2005, Rhoads *et al.* 2006, Roseler *et al.* 1993, Santos *et al.* 2009, Sinclair *et al.* 2000, Sklan and Tinsky 1993) with global impact on ammonia or urea concentrations in bovines published in reputed journals were searched and results were subjected to meta-analysis to determine the treatment variations without any biasness. The method applied for meta-analysis was similar to Suresh *et al.* (2010).

The meta-analysis of studies showed that the ammonia concentration in serum and ovarian follicular fluid were 99.01 ±3.48 and 209.11±4.54 μM respectively in normal conditions. Under feeding of protein rich diet the concentrations were 136.75 ±5.02 and 708.66±4.63 μM. The ratios of follicular fluid ammonia concentration to serum ammonia concentration were 2.01 and 5.20 under normal and protein feeding conditions respectively. The values for urea in serum and ovarian follicular fluid were 5.14± 0.39 and 5.13 ±1.42 mM respectively under normal conditions. The corresponding values for urea were 10.90±0.47 and 11.21 ±0.48 mM when animals were fed with protein rich diets. The ratios of follicular fluid urea concentration to serum urea concentration were 0.99 and 1.02 under normal and protein feeding conditions respectively.

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An increment in the concentration of ammonia and urea in blood as well as in ovarian follicular fluid was observed in cattle fed with rumen degradable protein or in an animal with negative energy balance (Armstrong *et al.* 2001, Sinclair *et al.* 2000). This has been associated with altered follicular growth patterns and a reduction in both the number of oocyte that cleave following insemination and the proportion that develop to the blastocyst. An excess of protein and a deficit of energy in the feed ration increases the production of ammonia that, when converted into urea in the liver, causes embryo mortality through an exacerbation of negative energy balance and reduced plasma prtogesterone levels, an alteration of uterine pH and increased secretion of PGF-2á (Butler 1998) .

Ammonia concentrations in follicular fluid are high relative to concentrations in plasma (Sinclair *et al.* 2000). Blood ammonia concentrations in cows fed high protein diets and with increase blood urea nitrogen vary from normal to high (Butler 1998). Although follicular fluid ammonia concentrations appear to be related to protein intake and blood urea nitrogen level, the exact mechanisms responsible for elevated concentrations of ammonia in follicular are unknown. Decreased uterine pH in cows fed high protein diets cause elevation of ammonia in the uterine fluids of cows with elevated blood urea nitrogen.

Outcomes from a meta-analysis include more precise estimate of the effect of treatment than any individual studies contributing to the pooled analysis. Identification of source of variation in responses or heterogeneity of group of studies and generalizability of responses can lead to more effective treatment or modification of management. Examination of heterogeneity is the most important task in meta-analysis. Major contributions include the development of protocol that provides the structure for literature search methods and analytical methods for evaluating the outcome of meta-analysis. Meta-analysis places a less emphasis on significance testing and larger emphasis on determining the magnitude and precision of an effect of interest. In the present study, we observed that high concentration gradients exist among ammonia levels in blood and follicular fluid, however, this gradient is not that much among urea levels compared to ammonia levels. This concludes that complex multi-step ammonia and a negligible urea metabolism exist in ovary (Jozwik *et al.* 2006). Blood and follicular fluid ammonia concentration rather than blood urea nitrogen, can better illustrate the toxic effects of elevated protein on reproductive parameters (Law *et al.* 2009). Our data provided some information on composition and physiological environment to which oocytes and other follicular cells are exposed in relation to ammonia and urea concentrations. Our result may show some light for further investigation of ammonia and urea metabolism in different size class ovarian follicle.

SUMMARY

A meta-analysis was conducted to determine the ammonia and urea levels in blood and ovarian follicular fluid in cattle fed with normal and protein rich or imbalanced diet. Results showed that the ammonia concentration in blood and ovarian follicular fluid were 99.01 ±3.48 and 209.11±4.54 µM respectively in normal condition and were 136.75 ±5.02 and 708.66±4.63 µM respectively in protein rich diet. The corresponding values for urea were 5.14± 0.39 and 5.13 ±1.42 mM in normal conditions and 0.90±0.47 and 11.21 ±0.48 mM in protein rich diet. Hence, high concentration gradients exist among ammonia levels in blood and follicular fluid, however, this gradient is not that much among urea levels compared to ammonia levels. This suggested that complex multi-step ammonia and a negligible urea metabolism may exist in an ovarian follicle.

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