Guest Editorial

Seasonal changes in bone metabolism in sheep: Further characterization of an animal model for human osteoporosis

The paper by Daniel Arens and colleagues, published in this issue of *The Veterinary Journal*, is one of several that are further characterising the sheep as a model for osteoporosis – a severe debilitating metabolic disease that affects mainly women (Arens et al., 2007). Why do we need an animal model for osteoporosis when there is an abundance of human subjects, especially as baby boomers age? Animal models have played an important role in history for the benefit of human health and greater understanding osteoporosis is just one of many examples of this. The ovariectomised rat has occupied a vital niche in the early screening of pharmaceutical agents for osteoporosis and the economics of research dictates the use of this model. However, if a particular compound is likely to help the human condition, a larger animal, higher up the phylogenetic scale – such as the aged ovariectomised ewe, will be needed before this drug can be used in a human clinical trial.

The other need for a relatively large animal model with some of the characteristics of human osteoporosis, is the design of prosthetic devices (joint replacements, spinal instrumentation, external fixator pins, etc.), with different coatings to promote osseointegration. These devices must be able to perform and not loosen in the presence of decreased bone mass (Turner, 2002). Smaller sized animals (rats, mice and rabbits) cannot be used when implants of the size used in humans, must be tested.

A variety of factors can cause bone loss in sheep. To mimic the human condition of post-menopausal osteoporosis, a number of studies in sheep from laboratories around the world initially investigated the effects of an acute estrogen deficiency associated with ovariectomy (Chavassieux, 1990; O’Connell, 1999; Turner et al., 1995). The results in from these studies were encouraging but it was clear that more information was necessary to characterize the model. Specifically, what information was missing from the sheep model that was well known in human osteoporosis?

Corticosteroid-induced bone loss is seen in humans treated for allergies, rheumatoid arthritis, and asthma to name but a few. Subsequent to the studies of the effect of acute estrogen deficiency in sheep came work in search of better bone-sparing corticosteroids (O’Connell et al., 1993). This was followed by studies of bone loss in sheep following prednisolone administration along with dietary changes (Lill et al., 2002).

Inducing bone loss in sheep following the dietary changes used by researchers using monogastric animals (e.g. calcium restriction) sounded attractive, but presented a challenge because of the differences in gastrointestinal systems and mineral homeostasis (O’Connell, 1999). Osteoporosis in humans has a variety of causes that all contribute to varying degrees such as age, genetics and diet. More recently, dietary-induced metabolic acidosis (DIMA) has been implicated as a contributor in human osteoporosis (New, 2002). This diet, combined with ovariectomy in sheep, has become a useful model to study the influence of diet in human osteoporosis (MacLeay et al., 2004, 2006).

Another factor that is well documented in humans is the seasonal change of bone mineral density (BMD) related to exposure to sunlight (vitamin D production in the skin) and therefore daytime length and season of the year. This has been mentioned in passing by researchers studying BMD in sheep but the study by Arens et al. (2007) is the most comprehensive study of this variable so far. In this study, attention was paid to changes in trabecular architecture (measured by micro-computed tomography, or µCT), bone histological parameters, bone markers and hormones as well as BMD. As hypothesised, BMD (a strong predictor for fractures in humans) was lowest in winter and this was supported by trends in histological changes and biochemical markers. The message in the study is clear to researchers studying small ruminants as a model for human osteoporosis; seasonal variations do occur and this needs to be factored into studies where alterations in diet (e.g. DIMA), corticosteroids, with or without ovariectomy, are used to induce osteopenia.

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References


