What’s new in rabbit medicine?

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Rabbits have become the third most common mammalian pet in Europe and the standards of care of this species have improved over the past decade.

The increasing interest towards this species has also lead to an increase in research. As practising vets we should look with interest into these studies as results may be of clinical interest and applicable in our everyday job.

Pharmacokinetics of penicillin G after IM administration in rabbits

Bacterial diseases are very common in pet rabbits and successful treatment is based on accurate diagnosis, as well as correction of underlying husbandry issues and management of concurrent diseases.

Inappropriate or excessive antibiotic use can be detrimental, leading to bacterial resistance and ineffective treatment.

Benzylpenicillin potassium (penicillin G) is a narrow-spectrum penicillin (active against Gram-positive aerobes, facultative aerobes and obligate anaerobes), often used in rabbits for treatment of pasteurellosis, odontogenic abscesses and treponematosis. However, several dosages and treatment regimes have been advocated; three times daily, once a day, or once every two or seven days (Welch et al, 1987; Varga, 2014).

Jekl et al (2016) studied the pharmacokinetics of this drug after a single IM administration of 38mg/kg (60,000IU/kg) to six clinically normal New Zealand white rabbits with the aim to determine the plasma concentration of the drug and recommend optimal dosing intervals. Results indicated the maximal plasma concentration of the drug was reached after 36 minutes.

In another study, Welch et al (1987) showed that rabbits infected with Pasteurella multocida showed higher serum concentration of penicillin G, compared to P multocida-free rabbits and suggested a dosing interval of eight hours (in cases of pasteurellosis), to ensure optimal blood and nasal concentration.

The length of time the tissue concentrations of penicillin remain at bactericidal level is essential for the effective therapeutic use of the drug. However, there are different minimal inhibitory
concentrations (MIC) for different Pasteurella isolates/serotypes in rabbits. Therefore, the penicillin G interval may vary between 8 to 14 hours based on the isolated bacteria.

Another study (Jekl et al, 2012), determined the MIC of isolates from odontogenic abscesses sensitive to penicillin G ranged between 0.2?g/ml to 0.3?g/ml and, therefore, concluded the suggested dosing interval for penicillin should be between 8 to 18 hours. The main limitation of this study was the low number of lab rabbits used and their supposed healthy conditions. This situation may be different to that of pet rabbits often suffering from underlying conditions. Furthermore, IM administration is not routinely used in this species in practice for antibiotic administration. The subcutaneous route is often preferred.

According to Morris (1995), the bioavailability through the subcutaneous route may not be dissimilar to that achieved via IM. However, this fact was not investigated in the present study.

Jekl et al (2016) concluded culture and sensitivity testing with determination of the exact MIC for the specific pathogen isolated is recommended in all cases of bacterial infection. A dosing interval of 12 hours for penicillin G may, in fact, not be sufficient against pathogen with high MIC.

**Factors influencing tooth and jaw malformations in rabbits**

Dental disease is extremely common in domestic rabbits and a controversial topic in the scientific literature. Possible aetiologies vary from congenital anomalies, inappropriate dietary and husbandry practices to a genetic background.

A study was undertaken by Korn et al (2016) to document the appearance of tooth and jaw pathologies in growing rabbits until adulthood in breeds of different sizes, and to explore if conscious oral examinations of rabbits at a young age can be used as a screening method for selecting animals that do not develop dental disease. In addition, different methods of assessing x-rays of the rabbit skull were applied.

Finally, the heritability of enamel defects, edge-to-edge bite and brachygnathia superior (disproportions in jaw lengths between maxilla and mandible) were estimated to supply rabbit breeders with information about the appropriate age to select future breeding animals.

For this study, animals of 10 different breeds were included to represent the variety of rabbits kept as pets and breeding rabbits to investigate if tooth and jaw anomalies are predominantly a problem in dwarf breeds, as previously postulated in the literature. All rabbits had free access to water and hay, but restricted access to pelleted feed. A full clinical examination of teeth and jaw was performed before the animals’ first breeding.

The offspring were examined weekly between the age of three weeks and weaning at eight weeks, then every second week thereafter until fully grown.
Animals were x-rayed if suspicion of dental disease arose from clinical examination and following the recommendation in Böhmer (2011). Radiographs were evaluated using different methodologies (Holtgrave and Müller, 1993; de Abreu et al 2006; Böhmer and Crossley, 2009).

According to the study’s results, three weeks of age was the earliest time to determine tooth status, unlike Fox and Crary (1971), who postulated four weeks as the earliest age for diagnosing brachygnathia superior, and Jekl and Redrobe (2013), who also stated the age of more than three weeks as earliest visible onset of incisor malocclusion in general.

The most common finding on clinical examination was a gap between the mandibular incisors, which was not seen only in animals with an edge-to-edge bite or a brachygnathia superior, but also occurred in animals without any other tooth and jaw alterations.

Trauma as a cause of this phenotype was not considered likely because of the high incidence, and no clinical sign of a loosened symphysis occurred in the clinical examinations and the assessments of the x-rays. The authors suspected an alteration in the early development of the dental germ since a gap between the mandibular incisors could be detected at three weeks of age.

Another common finding was the evidence of enamel defects, such as horizontal ridges and discolouration, despite providing a pelleted feed with a calcium and phosphorus content according to literature recommendation, and at least partial exposition to UV light.

The prevalence of a brachygnathia superior was 3.4% in all examinations, compared with 21.25% in the study by Jekl et al (2008), but in the latter study the patient population was presented to the veterinary practitioner because of tooth associated clinical signs.

Considering the development of the frequencies of different jaw and tooth pathologies, the authors suggest 12 weeks can be recommended as an appropriate age to preselect future breeding animals as no further increase is reported past this point.

The rabbit breeding standard (Jakobs et al, 2004) allows showing of young rabbits from the age of three months or six weeks onwards with the doe.

However, the authors point to a critical factor – the evaluation of the cheek teeth and associated bone structures, which cannot be performed by solely inspecting the incisors.

Therefore, it would be advisable to perform meaningful facial and oral examinations and present rabbits in inconclusive cases to a vet for further diagnosis.

A sole clinical examination concerning the tooth status of rabbits can lead to false-negative results and, therefore, is not sufficient, and x-rays are strongly recommended to gain vital information for a reasonable prognosis and therapy.
Dwarf and small rabbits were statistically more significantly affected, but intermediate and larger breeds affected by tooth and jaw alterations were still numerous. A possible reason could be mostly smaller breed rabbits are kept as pets and are, therefore, presented to vets more frequently.

In conclusion, the screening method proposed by Korn et al (2016) points at performing an oral examination at 12 weeks of age, focusing on incisor malocclusions and brachygnathia superior, with a follow-up screening at 20 weeks in dwarf and small breeds.

Although they failed to establish a correlation between dental pathologies and anatomical reference lines defined by Böhmer and Crossley (2009), the authors still underlined acquired dental disease is a chronic and progressive syndrome; therefore, clinical signs or abnormal findings from examination may be evidenced later in a rabbit’s life, and a single examination when rabbits reach maturity cannot distinguish between healthy and unhealthy animals.

**Use of a commercial CIGM in rabbits**

Continuous interstitial glucose monitoring (CIGM) systems are considered an essential tool in diabetes therapy in humans as an alternative to traditional blood-glucose monitoring methods. It aims to improve glycaemic control, prevent hyperglycaemia and hypoglycaemia, and to delay the onset of diabetic complications, thereby improving patients’ quality of life (Mayer et al, 2016). These systems are also used in veterinary medicine to monitor insulin response in cats and dogs hospitalised for the diagnosis of diabetes mellitus or, in critically ill animals without diabetes, by monitoring glucose concentration changes over time without interference from handling or other stressors (Surman and Fleeman, 2013).

In the study by Mayer et al (2016), seven New Zealand white rabbits were implanted (between their scapulae and under manual restraint) with CIGM devices which continuously recorded glucose data for five to seven days, to provide information about the normal longitudinal pattern of interstitial glucose. The animals underwent routine ovariohysterectomy and were given two different analgesic regimes as part of another study.

The data confirmed the normal glucose concentration was 5.5mmol/L to 11.5mmol/L. These values did not change substantially (as expected for hindgut fermenters) during the day or postprandially, but elevations were seen during surgery (up to 15.5mmol/L), with values that decreased to normal levels two to three hours post-surgery.

Harcourt-Brown and Harcourt-Brown (2012) also reported that rabbits presented with persistent, severe hyperglycaemia (>20mmol/L) had outcomes and a poorer prognosis for recovery.

Interestingly, none of the animals showed a drastic change in glucose concentrations during short periods of mild stress, such as restraint for phlebotomy, hospitalisation or transport.
The authors concluded the use of this system is feasible and provided initial insight into glucose metabolism of this species.

Further studies are necessary to evaluate the potential application of this technology in pet rabbits in clinical settings and in the home environment.

References

- Welch WD, Lu YS and Bawdon RE (1987). Pharmacokinetics of penicillin-G in serum and