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Patxi Sarasola qualified as a veterinary surgeon from Zaragoza Veterinary School, Spain in 1989 and obtained a PhD in veterinary pharmacology from Glasgow Veterinary School in 1993. He subsequently joined Pfizer Animal Health (UK), where he held different positions in Clinical Development (R&D) and was responsible for the European development and registration of different antimicrobials and antiparasitics in livestock and companion animals. Following his career in the pharmaceutical industry, Dr Sarasola launched ONDAX Scientific, a clinical research organisation (CRO) located in the UK and Spain. ONDAX provides clinical development services for the pharmaceutical industry with a particular emphasis on multinational clinical trials. Patxi Sarasola has published extensively in different areas of clinical pharmacology and pharmacokinetics and is a member of the editorial board of the Journal of Veterinary Pharmacology and Therapeutics.

Efficacy of Catosal® in the treatment of subclinical ketosis in dairy cows

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Subclinical ketosis – the silent profit killer

The ever increasing milk production in dairy cows has long been recognised to have a high impact on cattle health, fertility and thus farming economy. A major risk factor in this vicious circle is the negative energy balance associated with increased milk yield and decreased dry matter intake in the early postparturient period, often resulting in subclinical ketosis (1). This condition in turn is a predisposing factor for puerperal disorders and may lead to fertility impairments.

Catosal®

Catosal® (synonyms Coforta® and Phosphorum B12®, trademarks of Bayer Animal Health) has been successfully used in the treatment of metabolic disorders for more than five decades. This tonic and metabolic stimulant contains 10 g butafosfan (a phosphorus-based metabolic stimulant) and 5 mg cyanocobalamin (vitamin B12) per 100 ml solution as active ingredients. It is available as a ready-to-use solution for parenteral injection and is currently registered in about 60 nations worldwide.

Previous efficacy studies in cattle

Based on Sommer's pioneer work (2), the prophylactic effect of Catosal® during the dry period in the prevention of puerperal complications and fertility disorders has been demonstrated in numerous clinical studies (e.g., 3–5). Another study by Krdžalić and Čurčić (6) provided evidence for the efficacy of Catosal® on subclinical ketosis in cows, and two additional recent clinical studies confirmed the efficacy of Catosal® in the treatment of ketosis associated with abomasal dislocation (7,8).

In support of the documented clinical benefits associated with the well-established use of Catosal® in the adjunct treatment of clinical ketosis (primary or secondary to other conditions such as abomasal displacement, hypocalcaemic paresis, afterbirth retention or endometritis) or disorders of mineral homeostasis such as hypocalcaemic paresis, two further negative-controlled, blinded, multicentre and randomised clinical studies were recently performed in order to further evaluate the efficacy of the product in the treatment of subclinical ketosis in dairy cows.

New clinical results in subclinical ketosis

In the first of such studies, performed in Italy, 79 primiparous and multiparous cows were enrolled and monitored for the development of BHB levels in milk, appetite, rectal temperature, bovine activity score and concomitant diseases (9). Milk beta-hydroxybutyrate (BHB) levels of ≥ 200 $\mu\text{mol/l}$ were used as the criterion for subclinical ketosis. One group of 42 cows was treated with Catosal® at a dose of 25 ml per animal intramuscularly once a day for five consecutive days. The other group (control, n = 37) was not treated. Catosal® treatment mediated a significantly faster and better recovery of milk BHB levels than placebo treatment (Fig. 1). This effect was accompanied by an increased milk production and appetite (9).

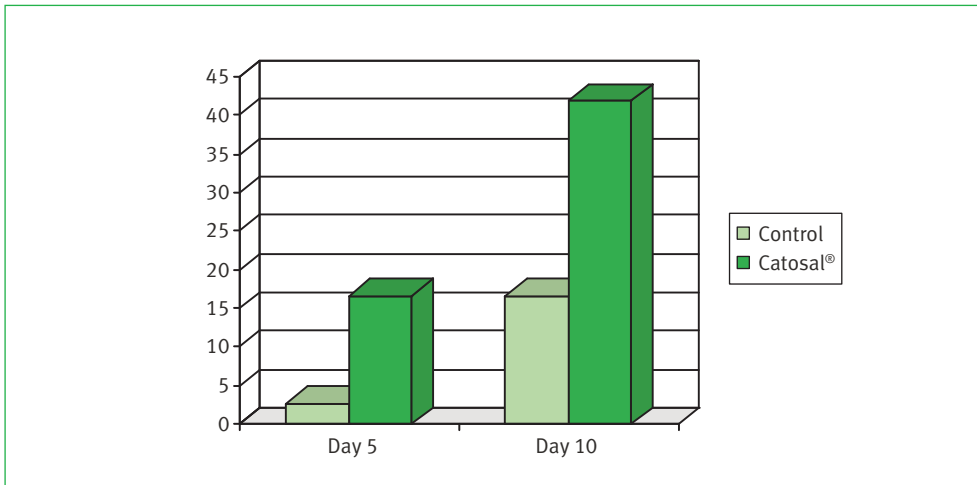


Figure 1: Prevalence of healthy cows (milk BHB < 100 mmol/l) after treatment with Catosal® (9).

These observations were corroborated in a second, still ongoing study in cows with subclinical ketosis (10). In this study, dairy cows were screened for elevated milk BHB levels (≥ 200 $\mu\text{mol/l}$) just as in the above-mentioned study. Then, they were randomised into either a group treated twice (study day 0 and day 3) with Catosal® (5 ml/100 kg body weight intravenously) or a group treated only on day 0 with Catosal®, followed by a treatment with saline on day 3, or a group treated only with saline, respectively. Blood samples for assessments of changes in BHB, glucose, glutamate-dehydrogenase activity and cholesterol levels were collected on study days 0, 3 and 6, respectively. Although the treatment effect of Catosal® in the target population (i.e., animals with BHB serum levels at inclusion > 1.2 mmol/l and < 3.2 mmol/l) is still being evaluated, preliminary results from this study indicate that Catosal®, given twice at an interval of 3 days apart, is safe and effective in the treatment of subclinical ketosis in dairy cows with serum BHB level ≥ 3.2 mmol/l at inclusion. These animals (i.e., BHB serum levels ≥ 3.2 mmol/l) showed a significant decrease in serum BHB levels after two treatments with Catosal®. Serum glucose levels increased in parallel (10). The proportion of animals with serum BHB levels of ≤ 1.2 mmol/l, defined as the criterion of treatment success, was 30 and 60% on study days 3 and 6, respectively, in animals with BHB level ≥ 3.2 mmol/l at inclusion, while none of the corresponding control animals (i.e., animals treated with saline only) achieved the criterion of treatment success (Fig. 2)(10). A single injection of Catosal® on study day 0 did, however, not appear to be sufficiently effective, indicating that it is necessary to give repeated administration of the metabolic stimulant in order to achieve optimal results.

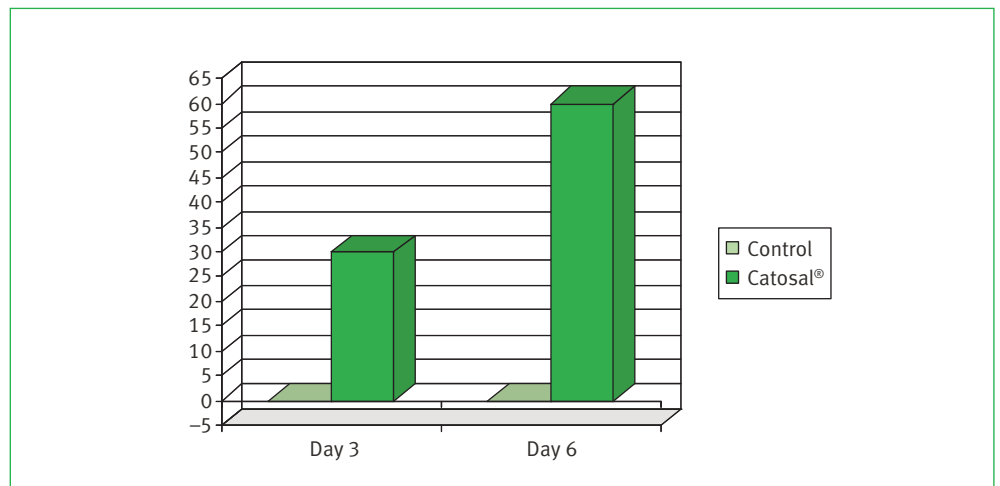


Figure 2: Prevalence of healthy cows (serum BHB < 1.2 mmol/l) after the treatment with Catosal® (10).

Conclusion and outlook

Both new clinical studies summarised in this review provide substantial evidence for the efficacy and safety of Catosal® in the supportive treatment of subclinical ketosis in dairy cows. They also indicate that repeated administration may provide superior results to a single injection. Overall, these studies further confirm the general perception of clinical efficacy of Catosal®, as demonstrated by the well-established use of this metabolic stimulant in the field.

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