Controlled clinical trial of the effect of a homoeopathic nosode on the somatic cell counts in the milk of clinically normal dairy cows

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Cows in a 250-cow Holstein-Friesian herd were allocated at random to be treated with either a homoeopathic nosode or a negative control, both treatments being applied by means of an aerosol spray to the vulval mucous membranes. A total of six treatments were given over a period of three days and milk samples were taken for the determination of somatic cell counts (SCC) on days –3, 3, 7, 9, 14, 21 and 28. Individuals applying the treatments or carrying out the SCC determination were unaware of which animals were receiving which treatment. Owing to the wide natural variations in SCC, the trial had only a 71 per cent possibility of detecting a 30 per cent difference in SCC between the two groups. There were no significant differences between the SCC of the two groups on any sample day, but there were significant variations between the SCC on different days (P=0·003) in both groups.

HIGH somatic cell counts (SCCs) in the milk of dairy cows are an indicator of subclinical mastitis and may have serious financial implications as a result of the penalties imposed by milk wholesalers and reductions in yield (Eberhart and others 1982, Philpot 1984, Beck and others 1992). Controlling mastitis and maintaining low cell counts depends mainly on good management and milking parlour hygiene, and the prompt recognition and treatment of mastitic cows is also important. On conventional farms mastitic cows are usually treated with intramammary antibiotics, but increasing numbers of farms are producing milk to an 'organic' standard (Hovi and Plate 2000), avoiding, whenever possible, the use of antibiotics. Several non-antibiotic products are being marketed with claims to treat or prevent mastitis and to reduce SCCs. This paper describes a controlled clinical trial designed to determine whether a homoeopathic nosode affected the SCCs of milk from dairy cows.

Homoeopathic remedies have been used for the treatment or prophylaxis of mastitis (Day 1986, May and Reinhart 1993, Andersson and others 1997) but the trials have not been appropriately controlled, randomised and blinded to provide objective evidence of their efficacy. The objective of this trial was not to establish the validity of veterinary homoeopathy but solely to examine the claims made for a specific commercially available remedy, Ainsworth's Udder Care, a homoeopathic nosode. This treatment is described as 'a broad-spectrum treatment regime for both subclinical and clinical mastitis', the use of which will be advantageous 'in respect of lowering cell counts and maintaining both low counts and reduced incidence of mastitis' (Hansford and Pinkus 1998). This product was chosen because it was widely available at the time of the study and because its manufacturer is a highly respected and long-established homoeopathic pharmacy. The trial was restricted to the investigation of SCC in non-mastitic cows and subclinically infected cows, first, because a specific claim was made for the treatment of such cows, and secondly, because clinical cases of mastitis could not ethically be left untreated.

MATERIALS AND METHODS

A 250-cow Holstein-Friesian herd located in Essex was used, and all the milking cows not due to be dried off before the end of the treatment period were included in the trial; they were randomly allocated into two groups of approximately equal size by using a randomising function on an Excel spreadsheet (Microsoft). The toss of a coin was used to decide which group should receive the nosode treatment and which the placebo treatment, and the members of each group were identified by the use of coloured tail tags. The link between the colour code and the treatment was known only to the project manager, and not to the individuals applying the treatment and collecting the data. Cows identified by the farm as having clinical mastitis, those that were dried off, or any treated with drugs during the trial were excluded.

No clear instructions were provided with the nosode and the treatments were given following advice from the manufacturer which stated that a capful (2·6 ml) of the treatment (a nosode of potency 30c, supplied in a 30 per cent ethanol solution) should be placed in a proprietary spray bottle (capacity 138·5 ml supplied by the manufacturer) and the bottle filled with tap water. The control treatment was prepared by making a 30 per cent ethanol solution in tap water and using it in the same way. The nosode and the control solution were placed in identical brown glass bottles identified by the tail tag colours of the two groups. The manufacturer's instructions stated that the nosode should be applied by parting the lips of the vulva and applying two squirts from the bottle to the mucous membrane. Before first use each spray bottle was squirted five times away from any animals to achieve consistent sized squirts; the mean volume of a squirt from the spray bottles was 0·76 ml.

The individuals responsible for applying the treatments and collecting the data were unaware of which treatment was the nosode and which the negative control.

The trial began on July 9, 2001 (day 0). The treatments were applied at six consecutive milkings, the first being the morning milking on day 0 and the last being the afternoon milking on day 2. For the first milking the cows in each group were treated by one of the two investigators, to avoid contamination between groups, but they then treated the groups alternately at each subsequent milking, to balance the effects of any differences due to their different application techniques. Latex gloves were worn and changed frequently to avoid contamination of the vulvas by faecal material. After the six treatments had been given, the tail tags were removed.

Composite samples of the milk from all four quarters were taken from each cow by independent laboratory technicians from the National Milk Records (NMR), during the afternoon milkings on day –3 and on days 3, 7, 9, 14, 21 and 28.

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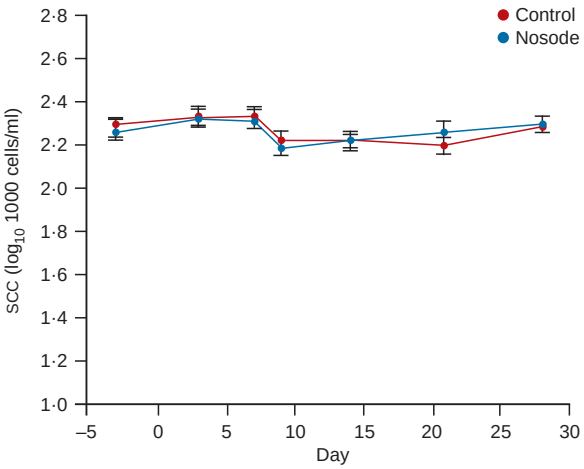

FIG 1: Mean (se) $\log_{10}$ somatic cell counts (SCCs) x 10^{-3}/ml of the nosode and negative control groups; treatments were given on days 0, 1 and 2

TABLE 1: Mean, minimum, maximum and median values of the somatic cell counts (x 10^{-3}/ml) recorded in the control and nosode-treated groups of cows during the trial; the treatments were given on days 0, 1 and 2

Group	Day –3	3	7	9	14	21	28
Control							
Number of samples	76	77	72	69	70	66	67
Mean	266	404	303	215	245	239	335
Minimum	30	26	49	24	25	28	48
Maximum	1614	7299	1229	795	1328	1427	4881
Median	203	178	218	157	165	159	166
Nosode							
Number of samples	76	76	74	73	72	69	68
Mean	251	296	346	215	239	264	308
Minimum	28	51	24	39	22	38	51
Maximum	1073	1330	3142	1018	1131	1604	2522
Median	192	215	187	140	150	177	165

Approximately 25 ml was collected from each cow into a sample bottle containing 0·75 ml bronopol preservative (Wychem). Twenty of the samples from the nosode group and 35 from the control group were found to have clotted and were discarded; they constituted 5 per cent of the total milk samples.

The SCCs were measured by NMR on a Fossamatic 360 (Foss Electric), and the data were analysed using SPSS Software.

Before the start of the trial, the SCCs of milk samples from the farm were examined to establish the likely distribution of the data and the likely discriminatory power of the trial. The initial data fitted a log normal distribution which indicated that the use of parametric statistical tests was appropriate and that the proposed trial would have a 71 per cent probability of revealing a 30 per cent change in cell counts (Buchner and others 1996).

RESULTS

Seventy-six cows received all six applications of the nosode and 76 cows were given the control treatment. In the 28 days after the treatment, eight cows in the nosode group and nine cows in the control group were withdrawn from the trial either because they developed mastitis or because they were dried off. No animals were withdrawn from the trial for any other reason. The data before their log transformation are summarised in Table 1, and the mean (sd) $\log_{10}$ cell counts for the treatment group and the control group on each sampling day are shown in Fig 1.

The largest differences between the two groups occurred on days 9 and 21, but a comparison of the means of the $\log_{10}$ data at each time point by an independent Student's *t* test (two-tailed) showed that there was no significant difference between the groups at any of the sample times.

A two-way analysis of variance was applied to the $\log_{10}$ data to investigate whether there were significant temporal variations. The results indicated that there was significant variation between sampling days ($P=0·003$), but no significant difference between the groups. A one-way analysis of variance (taking both groups together) suggested that the counts on days 3 and 7 were higher than on day 9 (Student-Newman-Keuls, $P<0·05$).

DISCUSSION

The presence of abnormally large numbers of inflammatory cells in the absence of clinical mastitis is widely accepted as an indicator of mammary gland pathology (Harmon 1994). Milk producers in the UK face financial penalties if the bulk milk SCC is high and producers adhering to 'organic' standards are required to minimise their use of antibiotics. For these reasons there is considerable interest in any pharmaceutical preparation that might lead to a reduction in SCCs and particular interest in products not requiring statutory licensing or withdrawal periods.

The trial was designed to try to eliminate an operator bias and to ensure that no confounding factors were present that might have influenced the results obtained from the two treatment groups. There have been reports of other trials of homoeopathic nosodes (Day 1986, Merck and others 1989, Stopes and Woodward 1990, Dorenkamp 1992, May and Reinhart 1993, Tiefenthaler 1994, 1995, Egan 1995, Searcy and others 1995, Andersson and others 1997, Kromker and Hamann 1999, Bohmer and Schneider 1999) but few have adhered to modern epidemiological standards for such trials and none has provided strong clinical evidence of their efficacy. It is not possible to undertake the perfect clinical trial and the veterinary pharmacopoeia contains many widely used products, for which there is little evidence for their efficacy in the treatment of specific conditions. However, when new treatments are made available, or there is increasing interest in traditional remedies, it is important to try to obtain evidence of their efficacy before promoting their use.

In fairness to the manufacturer of this particular remedy and the proponents of the homoeopathic treatment of mastitis, it is asking a lot of any treatment to affect the 'normal' level of a body constituent. However, the manufacturer's own publication, Hansford and Pinkus (1998), does make the claim that the product will reduce and maintain a low SCC in addition to providing a treatment for both subclinical and clinical mastitis. Furthermore, it is clear that the herd in the present study did suffer from some subclinical mastitis, as evidenced by a number of individual cell counts above 10^6/ml.

SCCs can provide an objective measure of udder health or disease. The milk samples were taken blind and the SCCs were measured by a well-established method. The trial was performed on healthy animals and any clinically diseased animals were removed from it. However, some of the cows had excessively high cell counts and it could be argued that SCCs above 10^6/ml should be defined as mastitic; however, when the results of the trial were re-analysed after the cows with SCCs above 2 x 10^6/ml had been eliminated, they remained unchanged. Variations in SCCs, both between individual cows and between samples taken from the same cow on different days, have been well documented (Brolund 1985) and, possibly owing to subclinical mastitis, they were responsible for the poor power of this study. There would be considerable value in a treatment that reduced cell counts by as little as 10

per cent, but this trial was unlikely to have revealed a reduction of less than 30 per cent.

It was not the intention to investigate the possible mode of action of the test treatment, although it is possible that even very small amounts of any agent could have a biological effect. The use of aerosols in a relatively confined space could have led to the control animals receiving tiny amounts of the treatment. Had this been the case some temporal effect might have been evident in both treatment groups. There were high SCCs on days 3 and 7, followed by a decrease on day 9. The analysis of variance suggests that these changes were statistically significant ($P<0{\cdot}05$), and that they affected both groups equally. There are many factors that might have caused such an effect in both groups, which is why any appropriate control group was an important component of the trial design.

Within the limits of the power of this trial there was no evidence to show that the homoeopathic nosode tested had any effect on the cows' SCCs. Further studies would be required to strengthen the evidence, either by using a single larger herd or by using several herds. On the basis of the normal variation of SCCs recorded in the trial herd, approximately 2400 animals in a single herd would be needed to have a 90 per cent chance of observing a 10 per cent change in cell numbers (Buchner and others 1996). Alternatively, the cell counts from herds receiving the nosode could be compared with those from herds receiving a control treatment, although the design of such a study would need to take into account other factors that directly or indirectly influence SCCs. Advice to farmers should continue to place emphasis on the meticulous application of milk parlour hygiene and the five-point plan for controlling mastitis (Blowey and Edmondson 1995).

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