

Critical appraisal – Randomised controlled trial Waelchi et al

Introduction	
Are the aims clearly stated?	Yes
Methods	
Is the study design suitable for the aims?	Yes
Which population was studied?	Multiparous cows and heifers with a single live calf with the placenta firmly attached requiring a caesarean section, carried out between 1992-1996, location of study is unknown.
Were the treatments randomly allocated? If yes, how was the randomisation done?	Yes, within pairs of cows Not stated
Were the groups comparable prior to intervention?	The basic data for the animals in the groups prior to intervention are not given (e.g. previous caesareans, breeds) so, for example, it is unclear how the cows and heifers are distributed within the groups
Was the person who administered the interventions blinded?	This is not stated but saline was used as a placebo.
Is it clear what measurements were carried out in the study?	The farmer was asked to note when the placenta was expelled post surgery. A vet was asked to examine the cow a minimum of 12 hours after surgery and confirm the findings from the farmer and treat as necessary.
Were the correct measurements chosen? Do they reflect (or are they strongly related to) the outcome of interest?	Yes Yes, although the 3 part question addresses all complications, only retained foetal membranes were assessed in this study.

Were previously established validated methods used to make the measurements? (e.g. Glasgow pain score, International Units etc)	Not applicable
What outcomes were measured?	Whether the placenta had been expelled or not by 12 hours post-caesarean. If not, it was considered to be retained.
Are the outcomes clinically relevant?	Yes
Were the outcomes assessed blind?	This was not stated but saline was used as a placebo.
Are the statistical methods described?	No
Was the statistical significance level stated?	Not exactly – the sequential analysis chart used $2\alpha=0.1$ (so can be considered as an equivalent of $p=0.05$)
Was the sample size justified?	No, but the sequential analysis enabled the trial to be limited to the minimum number of cows required. This was to avoid unnecessary harm.
Was ethical approval obtained?	Not stated
Are the methods described in enough detail that you could repeat them?	No, statistical methods not described
Results	
Were the basic data adequately described?	There are no basic data describing the two groups prior to intervention.
Do the numbers add up?	Yes

Are all subjects accounted for?	Yes
Was the statistical significance (p value) stated in the results? Is this consistent with the methods? (It should be stated in the sample size or power calculation)	Yes The p value was not explicitly stated in the methods but sequential analysis chart used $2\alpha=0.1$.
Were any side effects of the intervention reported if applicable?	No, but this study's primary aim was to examine the adverse events (prostaglandin inhibition) of NSAIDs
What were the main findings/key results?	22/49 (44.9%) of cows/heifers treated with flunixin and 35/49 (71.4%) of cows/heifers treated with saline (placebo) had completely passed the placenta within 12 hours of surgery 27/49 (55.1%) of cows/heifers treated with flunixin and 14/49 (28.6%) of cows/heifers treated with saline had retained foetal membranes at 12 hours post surgery Cows/heifers treated with flunixin were significantly more likely to have retained foetal membranes than patients treated with placebo (p = 0.014) The odds ratio was 3.07 (95% confidence interval, 1.33-7.09)
Discussion and conclusion	
What do the main findings/key results mean?	Flunixin appears to increase the risk of retained foetal membranes, although the lower end of the confidence interval is only 1.33, and other factors were not taken into consideration that could affect the outcome of the study.
Are the negative findings discussed? How are the negative findings interpreted?	No but this is not applicable
Does the discussion reflect the results?	Yes. In addition much discussion focused on the

	inhibition of prostaglandins in line with the aim.
Interpretation	
<p>What are the clinical implications of this study?</p> <p>Are the subjects in the study similar to those in the BET/your own?</p>	<p>Flunixin may increase the risk of retained foetal membranes. There may be a benefit to using prostaglandins routinely post operatively.</p> <p>There is not enough data to understand the signalment and history of the cows/heifers involved in this study to compare to the population described in the BET.</p>
General	
Who funded this study?	Not stated