International Platform of Registered Systematic Review and Meta-analysis Protocols

INPLASY

INPLASY202440104

doi: 10.37766/inplasy2024.4.0104

Received: 25 April 2024

Published: 25 April 2024

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Efficacy of monensin, 15 types of direct-fed microbials (DFM) or their fermentation products in milk performance in dairy cows: A systematic review and network meta-analysis (NMA)

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ADMINISTRATIVE INFORMATION

Support - National Natural Science Foundation of China (No. 32060774);Science and Technology Program of Inner Mongolia Autonomous Region (No. 2020GG0036; 2022YFDZ0051);Basic Scientific Research Business Project of Universities directly under the Inner Mongolia Autonomous Region (No. BR22-11-17);Discipline Project of College of Veterinary Medicine, Inner Mongolia Agricultural University (No. SYKJZD202302).

Review Stage at time of this submission - Preliminary searches.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202440104

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 25 April 2024 and was last updated on 25 April 2024.

INTRODUCTION

Review question / Objective The practice of administering antibiotics, such as monensin, to dairy cows during the perinatal and lactation periods has a long-standing history. However, in order to mitigate the potential harm and reduce antibiotic usage, various preparations with replacement effects have been developed and utilized. This review aims to assess whether direct-fed microbials (DFM) or their fermentation products , and possess the potential to substitute antibiotics in enhancing dairy milk performance.

The search strategy will be constructed around the PICOS tool: (P) Population: lactating cows; (I) Intervention: direct-fed microbials (DFM) or their fermentation products were added to the feed; (C) Comparator: control group with only usual feed or placebo treatment; (O) Outcomes: milk performance of cows(including dry matter intake, milk yield, feeding efficiency, energy correction milk, fat correction milk, fat yield, fat percentage, protein yield, protein percentage, lactose yield, lactose percentage). (S) Study type: RCTs.

Condition being studied The administration of antibiotics, such as monensin, to dairy cows during the perinatal and lactation periods has a long-established history. However, in order to mitigate potential harm and reduce antibiotic usage, various preparations with replacement effects have been developed and utilized. This review aims to evaluate whether direct-fed microbials (DFM) or their fermentation products possess the potential to serve as substitutes for

antibiotics in enhancing dairy milk performance.Through a network meta-analysis, we will conduct a comparative evaluation of the efficacy of monensin, direct-fed microbials (DFM) or their fermentation products on dairy milk performance in order to determine whether DFM or their fermentation products and phytonutrients possess the potential to serve as alternatives to antibiotics (monensin).

METHODS

Search strategy The researchers in this paper will search five electronic databases (PubMed, Embase, Cochrane, Web of Science and Ovid) from their creation to 2024. The search strategy was constructed around the PICOS tool: (P) Population: lactating cows; (I) Intervention: direct-fed microbials (DFM) or their fermentation products were added to the feed; (C) Comparator: control group with only usual feed or placebo treatment; (O) Outcomes: milk performance of cows(including dry matter intake, milk yield, feeding efficiency, energy correction milk, fat correction milk, fat yield, fat percentage, protein yield, protein percentage, lactose yield, lactose percentage). (S) Study type: RCTs.

Participant or population All lactating cows (female, no disease).

Intervention 1)Monensin, direct-fed microbials (DFM) or their fermentation products. 2)Dosage: No limit. 3)Timing: Lactating period of cow. 4)Frequency: No limit.

Comparator control group with only usual feed or placebo treatment.

Study designs to be included Randomized controlled trial.

Eligibility criteria 1. Inclusion criteria. (1) Experimental group with different direct-fed microbials (DFM) or their fermentation products for lactating cows; (2) Control group with routine feed or Placebo treatment; (3) Randomised controlled trial; (4) Outcome indicators including at least one of the following: dry matter intake, milk yield, feeding efficiency, energy correction milk, fat correction milk, fat yield, fat percentage, protein yield, protein percentage, lactose yield, lactose percentage. 2. Exclusion criteria. Title-abstract screening: (1) Not an original full research paper (e.g. review, editorial); (2)Non-randomized controlled trial (quasi-randomized controlled trials, animal studies, protocols, conference abstracts, case reports or correspondence); (3)Non-oral method feed; (4)cows with stress condition; (5)The timeframe predates 2005.Full text-screening(as above, with the addition of): (1) No relevant outcome measure reported; (2) Non-lactating healthy cows; (3) Phytonutrient content is inconsistent.

Information sources The researchers in this paper will search five electronic databases (PubMed, Embase, Cochrane, Web of Science and Ovid) from their creation to 2024.The data extraction process will be conducted independently by three reviewers (Pengxiang Bai, Lan Yang, Xiaohui Xu). Initially, we will attempt to extract numerical data from tables, text, or figures. If these are not reported, we will utilize Engauge Digitizer software for extracting information from graphs. If the data is still unreported or unclear, we will make an effort to contact the author via email (max. 2 attempts). Furthermore, if there are multiple time points or doses involved in the results measurement, we will extract data specifically from the time point or dose that exhibits the highest efficacy.

Main outcome(s) Milk performance of cows (including dry matter intake, milk yield, feeding efficiency, energy correction milk, fat correction milk, fat yield, fat percentage, protein yield, protein percentage, lactose yield, lactose percentage).The extracted data will be recorded in the form of mean and standard deviation.
Milk yield; continuous; kg/d; mean±sd (sem)
Energy correct milk(ECM); continuous; kg/d; mean±sd(sem)
Fat correcting milk (FCM); continuous; kg/d; mean±sd (sem)
Fat yield; continuous; kg/d; mean±sd (sem)
Protein yield; continuous; kg/d; mean±sd (sem)
Lactose yield; continuous; kg/d; mean±sd (sem)
Dry matter intake (DMI); continuous; kg/d; mean±sd (sem)
Milk yield/DMI; continuous; ratio; mean±sd(sem)
Fat%; continuous; %; mean±sd(sem)
Protein%; continuous; %; mean±sd (sem)
Lactose%; continuous; %; mean±sd (sem).

Additional outcome(s) Dose, timing of administration, frequency of administration, route of administration.

Data management The screening process will be conducted in two stages. Firstly, an initial screening based on the title and abstract will be carried out to identify articles that meet the screening criteria. Subsequently, a full-text screening of the retained articles will be performed. Throughout each stage, three independent observers (Pengxiang Bai, Lan Yang, Xiaohui Xu)

will independently assess each article. Any discrepancies will be resolved through discussion or consultation with Dacheng Liu.After the completion of the selection process, the three researchers will independently conduct fundamental feature extraction, risk assessment, and main outcome index data extraction. Subsequently, a meeting will be convened to verify, discuss, and determine the conformity data for subsequent analysis.

Quality assessment / Risk of bias analysis We will use the SYRCLE's ROB tool to assess the risk of bias in animal experiments (including (1)Randomization (selection bias); (2) Baseline characteristics (selection bias); (3) Allocation concealment (selection bias); (4) Random housing (performance bias); (5) Random housing (performance bias); (6) Random outcome assessment (detection bias); (7) Blinding (detection bias); (8) Incomplete outcomes data; (9) Selecting report; (10) Bias from other resources).

Strategy of data synthesis A network meta-analysis will be performed for all outcome measures reported in 30 or more articles. We will use Stata software (version 15.1) and performe NMA aggregation and analysis using Markov chain Monte Carlo simulation chains in a Bayesian-based framework according to the PRISMA NMA instruction manual. For subgroup analysis a minimum of 8 studies per subgroup is required. If meta-analysis is not possible, data will be reported through a descriptive summary(if appropriate). In studies , all variables are continuous variables and are expressed as means with standard deviation (SD). Continuous variables in the study will be reported as mean difference or standardised mean difference with 95% confidence intervals (CI) and analysis. Heterogeneity will be assessed using the (residual) I^2 and adjusted R^2 statistics. We will use the nodal method to quantify and demonstrate the agreement between indirect and direct comparisons, calculate through the instructions in the Stata software, and if the p-value > 0.05, the consistency was verified. If the necessary data is available, a subgroup analysis will be performed for lactating cows of different DIM. At each stage and overall, we also plan to perform subgroup analyses by parity. The robustness of our findings will be tested by re-running the analysis using multiple dose data (in studies that report multiple dose results), in order to select the most effective dose. If appropriate, we will test the robustness of linear regression of time-to-treatment by performing stratified analysis (treatment pre-ischemia vs during vs post-ischemia). We will evaluate the effect of our decision to aggregate all reported dairy cow lactation performance by re-running the analysis using only the study data from the Jablonski scale. To check for the presence of bias due to small-scale studies, which may lead to publication bias in NMA, a network funnel plot will be generated and visually inspected using the criterion of symmetry.

Subgroup analysis If the necessary data is available, a subgroup analysis will be performed for lactating cows of different DIM. At each stage and overall, we also plan to perform subgroup analyses by parity.

Sensitivity analysis The robustness of our findings will be tested by re-running the analysis using multiple dose data (in studies that report multiple dose results), in order to select the most effective dose.If appropriate, we will test the robustness of linear regression of time-to-treatment by performing stratified analysis (treatment pre-ischemia vs during vs post-ischemia). We will evaluate the effect of our decision to aggregate all reported dairy cow lactation performance by re-running the analysis using only the study data from the Jablonski scale.

Country(ies) involved China.

Other relevant information Data to be extracted:
1.Experimental groups, control group(s) and number of animals per group.
2.Author/year of publication
3.Duration of test
4.Breed of cows
5.Day in milk
6.Initial body weight
7.Initial milk production
8.Initial parity
9.The number of primiparous and multiparous cows.

Keywords Monensin; Direct-fed microbials(DFM); Network meta-analysis.

Contributions of each author
Author 1 - Pengxiang Bai - Pengxiang Bai will conduct data interpretation, draft the initial manuscript, and contribute to the data analysis.
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