Improving immune functions by innovative dairy cow management

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Is there any efficient alternative to treat clinical mastitis?

A systematic review of non-antimicrobial treatments of clinical mastitis in dairy cows.

- Studies selected from CAB Abstract, Pubmed and Web of Science from January 1970 to June 2014.
- A total of 2,451 manuscripts were first identified to finally reach 39 manuscripts corresponding to 41 studies.

➢ To date, no alternative therapies had consistently demonstrated efficacy for the treatment of clinical mastitis in clinical trials.
Transition period

The initiation of lactation causes a steep increase of nutrient requirements and a negative energy balance

- Massive mobilisation of body reserves
- Metabolic perturbations
  - High incidence of metabolic diseases
- Immunosuppression
  - Greater incidence of infectious diseases
A simple solution: reducing energy deficit by increasing energy intake

Despite decades of researches and progresses, the problem is still present because:

- Feed intake is limited in early lactation
- Rumen microflora takes several weeks to fully adapt to high starch diets, limiting the amount of grain that can be included in the diet
- Inclusion of fat in the diet will contribute to accumulation of fatty acid metabolites in blood
- Genetic progresses further increase milk production and energy requirement
Another solution: reducing energy deficit by decreasing energy requirement

- The amount of milk produced increases with the demand
  - In nature, milk production increases gradually with the demand by the offspring
  - With machine milking, the demand is maximum at first milking

- Our working hypothesis: slowing down the increase in milk production during the transition period would improve metabolic status and immune functions without compromising lactation performances
Does limiting milk production by milking once a day during the first week of lactation could reduce metabolic disturbances and immunosuppression?

Impact of postpartum milking frequency on the immune system and the blood metabolite concentration of dairy cows

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Effect of milking frequency during the first week of lactation on milk production

* Loiselle et al., J. Dairy Sci., 2009, 92:1900-1912
Effect of milking frequency during the first week of lactation on blood NEFA

* Loiselle et al., J. Dairy Sci., 2009, 92:1900-1912
Effect of milking frequency during the first week of lactation on blood BHBA

Effect of milking frequency during the first week of lactation on immune cells

- No clear cut immunosuppression observed
  - Neutrophils: no difference between the treatments or the sampling day for the different tested activities
  - PBMC: no difference between the 2 groups but lower proliferative activity during the first week of lactation

BUT

- Immune functions were always assayed with cells incubated in a standardised medium (with 5% FBS)

* Loiselle et al., J. Dairy Sci., 2009, 92:1900-1912
Does immunosuppression relate to the metabolic milieu (blood composition) of early lactation rather than autonomous immune cell defects?
Effect of sera harvested after calving on proliferation of PBMC from cow in mid-lactation

Relationship between serum composition and PBMC proliferation

- Negative correlation with NEFA
  \( r = -0.86, \ P < 0.001 \)

- Negative correlation with BHBA
  \( r = -0.54, \ P < 0.01 \)

Effect of NEFA and/or BHBA on proliferation of PBMC

Effect of NEFA on proliferation of PBMC

Effect of serum composition on neutrophils

- At a working concentration of 1 %, little effects
- At [NEFA] ≥ 0.5 mM, inhibition of oxidative burst
- No effect of BHBA

Conclusions of in vitro experiments:

- Depression of lymphocyte functions not related to cell defect but to the composition of their environment.
- NEFA concentration appears as the main cause of depression.

- Management and nutritional strategies that can limit the raise in NEFA concentration during the transition period are likely to improve cow’s immunity.

Once a day milking in early lactation: what other groups have found

A reduction in milking frequency and feed allowance improves dairy cow immune status

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Temporary alterations to postpartum milking frequency affect whole-lactation milk production and the energy status of pasture-grazed dairy cows

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Is it possible to get the benefits of reducing postpartum milk production without affecting the rest of lactation?

The effect of incomplete milking or nursing on milk production, blood metabolites, and immune functions of dairy cows

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Effect of partial milking during the first week of lactation

- 47 high yielding cows
- For the first 5 days of lactation, cows were:
  - Milked completely 2X (Control)
  - Milked incompletely 2X (Incomplete) (About 1/3 of expected milk production)
  - Left to nurse their calf until d5 and milked 1X from d3 to d5 (Nursing)
Effect of partial milking during the first week of lactation on milk production

![Graph showing milk yield in kg/d relative to days and weeks after parturition for different milking conditions: Control, Incomplete, and Nursing.](image-url)
Effect of partial milking during the first week of lactation on blood glucose and NEFA.
Effect of partial milking during the first week of lactation on incidence of hyperketonemia

- Control
- Incomplete Nursing
- Nursing

Number of cows

- >2400 μmol/L
- Between 1400 and 2400 μmol/L
- <1400 μmol/L
Effect of partial milking during the first week of lactation on immune cell functions

- Proliferation increases with number of DIM (2 < 5 < 61)
- Better proliferation with sera from cows incompletely milked
- Negative correlation between NEFA concentration and PBMC proliferation (r=-0.66) or IL-4 secretion (r=-0.44)

* Carbonneau et al., J. Dairy Sci., 2012, 95:6503-6512
Does this approach work on a commercial farm?
Partial milking in commercial farms

- 846 multiparous cows from 13 herds
- After calving, cows were either:
  - Completely milked twice a day
  - Incompletely milked twice a day (10 to 15 kg/d) for 5 days, then completely milked
- Blood samples were taken once a week for 5 weeks
- Reproduction, disease and milk production data were collected and are currently under analysis
Partial milking in commercial farms

Cows with BHBA > 1400µMol (%)

- 4-7 DIM
- 8-17 DIM

Legend:
- Red: Complete
- Blue: Incomplete
In summary

- At concentrations observed in early lactation, NEFA have negative effects on immune cell functions.

- Incomplete milking during the first days following calving reduces milk production during its application without affecting the rest of lactation.
Dry-off: a period of high risk for new IMI

- Involution is exceptionally slow in dairy cows
- Mammary gland continues to synthesize milk
- Milk accumulation and leakage
- High fat and casein contents of mammary secretion reduce immune cell functionality
- Risk of intra-mammary infection at calving increases with level of milk production at drying-off
Blanket dry cow therapy

- Important component of most mastitis control programs
- Prevents new IMI and cures existing infections
- However
  - not equally effective against all pathogens
  - risk of antibiotic contamination
  - Negative consumer perception
  - New regulations are limiting antibiotic usage in dairy production in some countries
- Treating only infected and high risk quarters would reduce antibiotic usage at drying-off but increases the number of new IMI at calving
Is it possible to prevent new intramammary infection at drying-off by stimulating mammary gland immunity?

Working hypothesis: a BRM that promotes sustained immune cell migration into the mammary teat after drying-off will hasten mammary gland involution and protect the gland from invading pathogens.
BRM development

- Chitosan formulations that are liquid at room temperature but form a hydrogel at body temperature have been developed.
- Chitosan hydrogels cause an increase in SCC and do not need to be supplemented to act as BRM.
- Glycerophosphate-based chitosan formulations are the most suitable for intramammary utilisation.
Effect of chitosan BRM on Indicators of mammary involution

Bovine Serum Albumin

Lactoferrin

Days

BSA (log10 ug/mL)

Lactoferrin (log10 ng/mL)

Low viscosity 2.5 mL

Low viscosity 5 mL

High viscosity 5 mL

control
Effect of chitosan BRM on Indicators of immune response

Somatic cell count

Lactate dehydrogenase

- Log10 scc / ml
- Days
- LDH (Log10 U/L)
- Days

- LV 2,5 mL
- LV 5 mL
- HV 5 mL
- control

Effect of chitosan BRM on Indicators of immune response
Effect of chitosan BRM on Indicators of immune response

- Expression of several genes related to immune response (IL-1, IL1β, TNF-α, CD14) in somatic cells are up-regulated by chitosan on the day following drying-off.
- Chitosan caused a transient inflammation of the quarter on the day of drying-off.
- Compatible with an internal teat sealant.
Conclusions

- Avoid, as much as possible, massive mobilisation of fat reserves
- Reducing temporarily milk production after calving may reduce the incidence of both metabolic and infectious diseases
- Stimulation of mammary gland immunity could be an alternative tool to facilitate drying-off of high yielding cows
Merci!