A parallel evaluation of five cost-effective indirect methods for assessing failure of passive immune transfer in neonatal calves

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Introduction

- Failure of transfer of passive immunity (FTPI)
  - Major risk factor for neonatal disease (diarrhea, respiratory disease) (Donovan et al, 1998)
  - Influence longevity, future milk production, weight gain (Raboisson et al, 2016)
  - Still remain a major issue in many herds, despite widely spread recommendations on colostrum management

- Assessment of FTPI in neonatal calves
  - Classically diagnosed when serum IgG concentration < 10.0 g/L (Buczinsky et al, 2018)
  - Historical gold standard for serum IgG concentration : radial immunodiffusion (RID)
  - Numerous indirect methods already evaluated
    - Serum Total Protein (STP) (direct or indirect), GGT… (Hernandez at al, 2016; Elsohaby et al, 2019)
      - Brix refractometer
    - Evaluated in controlled environments

Study objectives

- A study to evaluate methods for assessing FTPI in calves
  - By veterinary practitioners
  - In field conditions
  - 5 indirect and cost effective methods evaluated in parallel

Material and Methods

- Animals and samples
  - 245 2 to 6 day-old dairy and beef calves
  - random sampling from 93 herds (1 to 6 per herd, median 3)

  - Jugular venipuncuture in 2 vaccum tubes without anticoagulant
    - refrigerated for 24h00
    - centrigugated and serum frozen at -20°C

    - 1 aliquote used by vet practitioners (15 vets, 14 vet practices)
    - 1 aliquote send to ISAE 35 Laboratory

Material and Methods

- Serum analysis

What ?		How ?	Who ?
Serum IgG	RID-IgG g/L	Bov IgG Ring Test, IDBiotech, France	ISAE 35 Lab
Serum Total Protein	STP_OP (g/L)	Optical refractometer	Vet. practitioners
Serum Total Protein	% Brix	Digital Brix Refractometer (MA 882 Milwaukee)	
Serum Total Protein	STP_BA (g/L)	VetTest biochemistry analyzers	
Serum Albumin	ALB (g/L)		
GGT (EC 2.3.2.2)	GGT (UI/L)		
Serum Globulin	GLOB (g/L)	STP_BA - ALB	

Material and Methods

- Statistical analysis
  - Pearson correlations (r)

  - Evaluation of diagnostic characteristics for detecting FTPI (IgG < 10 g/L)
    - Sensitivity (Se) : conditional probability of correctly identifying animals with FTPI
    - Specificity (Sp) : conditional probability of correctly identifying animals without FTPI

    - ROC curves (pROC package R software, Robin et al, 2011)
      - Optimal cutoff points :
        - » Youden's J statistic
        - » Distance to the left-hand corner of ROC space (d^2)
      - Area under the curve (AUC)

Results

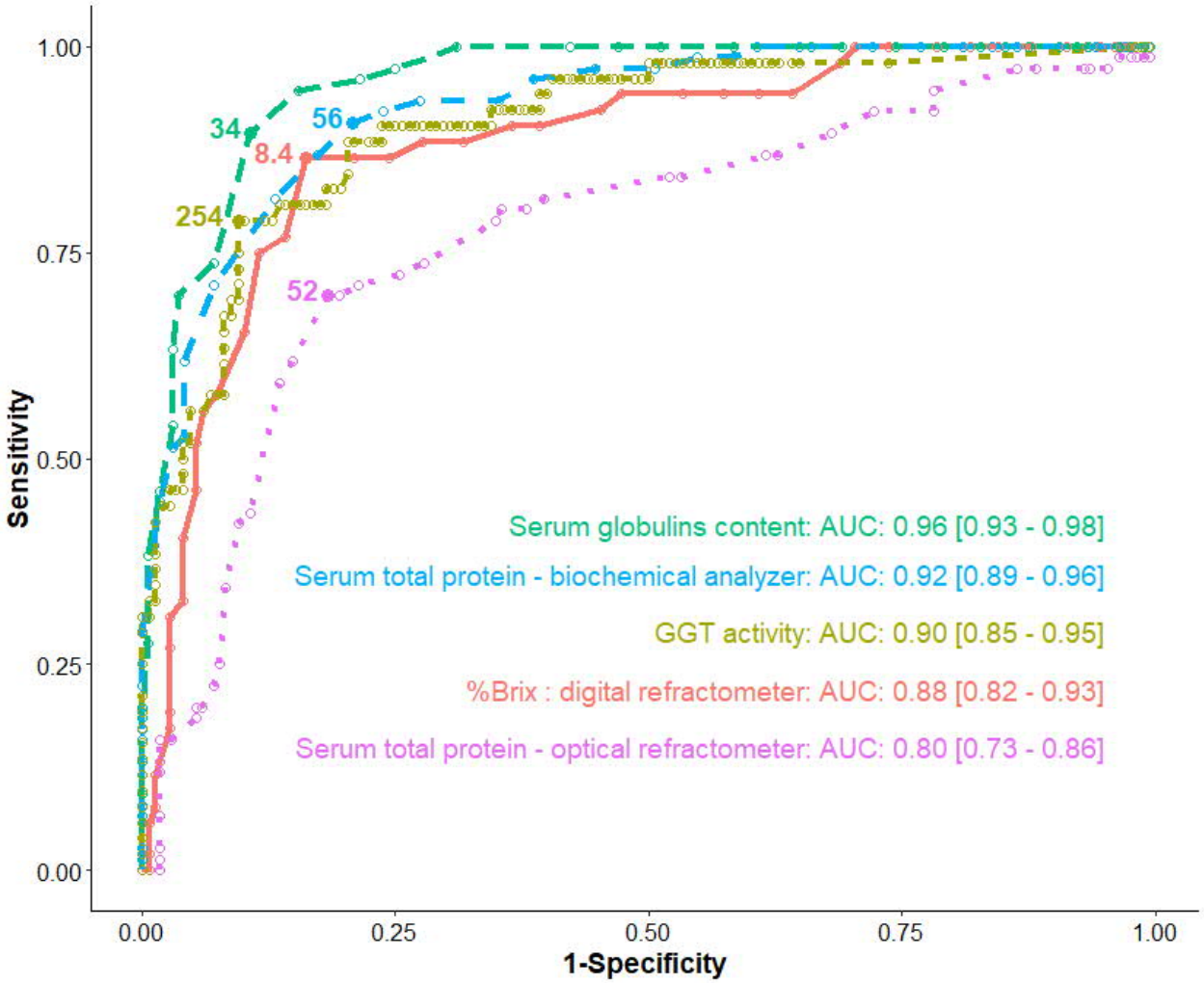
- Prevalence of FTPI
  - 76 calves (31.0%) with RID-IgG < 10 g/L : FTPI +
    - Post-hoc analysis : allows for a absolute precision of ±10% in Se and Sp estimates

- Pearson correlations r
  - with RID-IgG : all 5 methods significantly correlated ($p < 10^{-16}$)
    - r ranging from 0.67 to 0.89

  - Between indirect methods
    - STP_OP and %Brix: r = 0.78
    - STP_OP and STP_BA: r = 0.85
    - %Brix and STP_BA: r = 0.83

Results

- ROC curves



Results

- Diagnostic performance for assessing FTPI RID-IgG < 10g/ L

Test[1]	Optimal cutoff	Sensitivity (95% CI)	Specificity (95% CI)	Statistic[2]		
				J	d^2	AUC
STP_OP, g/L	52.0	69.7 (58.1–79.7)	81.6 (75.0–87.2)	0.51	0.35	0.80
%Brix, %	8.4	86.5 (74.2–94.4)	83.8 (76.8–89.3)	0.70	0.21	0.88
STP_BA, g/L	56.0	90.8 (81.9–96.2)	79.2 (72.2–85.0)	0.70	0.22	0.92
GLOB, g/L	34.0	89.4 (80.3–95.3)	89.3 (83.6–93.5)	0.79	0.15	0.96
GGT, IU/L						
All ages	254.0	78.8 (65.3–88.9)	90.5 (84.6–94.7)	0.69	0.23	0.90
2 and 3 d old	393.0	87.5 (71.0–96.5)	87.8 (78.7–94.0)	0.75	0.17	0.92
4 to 6 d old	254.0	90.0 (68.3–98.8)	86.4 (75.7–93.6)	0.76	0.17	0.91

Results

- Cut-point values with specificity greater than 95%

$$PPV = \frac{Se * P}{Se * P + (1-Sp) * (1-P)}$$

Test[1]	Threshold[2]	
	Having FTPI	Not having FTPI
STP_OP, g/L	43.0	68.0
%Brix, %	7.6	9.6
STP_BA, g/L	53.0	61.0
GLOB, g/L	32.0	35.0
GGT, IU/L		
All ages	201.0	583.0
2 and 3 d old	238.0	728.0
4 to 6 d old	164.0	373.0

[2]For FTPI = RID-IgG<10g/L

Discussion and conclusion

- Correlation of optical and digital Brix refractometers with RID-IgG
  - In accordance with other studies (Elsohaby et al., 2015, Hernandez et al., 2016, Cuttance et al., 2017; Elsohaby et al., 2019)
- Optimal cut-points
  - Optical (52.0 g/L) and digital Brix refractometer (8.4%) : in accordance with other studies
- Correlation between optical and digital Brix refractometers
  - r = 0.78 lower than other estimates (0.91 to 0.97, Hernandez et al., 2016)
  - Optical refractometer may lead to reading errors or imprecision (+/- 2 to 3 g/L)

Discussion and conclusion

- All indirect methods performed equally well
  - No significant difference in diagnostic accuracy / misclassification rate between them

- Brix refractometer or STP optical refractometer
  - Fast and inexpensive
  - Should be promoted
    - At the individual level
    - At the herd level

Interested in more details ?

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Thank you for your attention.

Any question ?

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