

EVALUATION OF AN ASSOCIATED INACTIVATED VACCINE AGAINST NEONATAL DIARRHOEAS CAUSED BY COLIBACILLI, ROTAVIRUS AND CORONAVIRUS

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Introduction

The major economic importance of neonatal infectious diarrhoeas in calves have justified for a few years the development of control programmes combining both sanitary and medical aspects [7]. The importance of immunity conferred through colostrum and milk has been demonstrated [1] [2] [8]. The vaccination of pregnant cows revealed, in the field, as the most efficient mean to reach a high colostrum and milk immunity [3] [4] [5] [10]. The etiology of neonatal infectious diarrhoeas in cattle is now well-determined ; different types of colibacilli having well-characterized attachment or virulence factors are now isolated ; viruses, rotavirus and coronavirus, have also been evidenced [6] [9] [11] [12]. The authors present the results obtained during a controlled clinical trial by using an inactivated vaccine, adjuvanted with aluminium hydroxyde and saponin. This vaccine is indicated for vaccination of pregnant cows.

Materials and methods

Herds : 40 french cattle farming units, in which those calves born during the weeks before the clinical trial presented symptoms of neonatal diarrhea.

Animals : 1685 pregnant cows were vaccinated. 728 cows were not vaccinated because they calved just before the beginning of the trial, or were on the time to do it. The calves born to these last cows allowed to identify the farm as infected and to calculate a morbidity rate in these calves born to non-vaccinated cows.

Vaccines : The under-study vaccine*, vaccine I, inactivated, adjuvanted with aluminium hydroxyde and saponin, and composed of antigens K99, Y, 31A, F41 of E.coli, and of bovine rotavirus and coronavirus. The dose is 5 ml, administered subcutaneously.

. The colibacillosis vaccine**, vaccine II, and the rota-coronavirus vaccine***, vaccine III, used according the recommendations of the manufacturer. These two last vaccines have been commercialized for many years.

Experimental design : The herds included in the clinical trial have been randomized into two groups : group A and group B.

Group A contained 22 herds (783 pregnant cows) ; Group B contained 18 herds (902 pregnant cows).

Group A animals were twice injected one dose of vaccine I, 15 to 90 days before calving for the first injection, and at the day of calving for the second injection.

Group B animals were simultaneously injected one dose of vaccine II and one dose of vaccine III (one injection on each side of the neck), 15 to 90 days before calving. They were then injected one dose of vaccine III the day of calving.

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. Criteria of analysis

The vaccine safety has been evaluated by checking local and general reactions after vaccination : inspection and palpation of the injection site, recording of rectal temperature after each injection.

The vaccine potency has been evaluated by serology : rotavirus antibody titers by inhibition of hemagglutination, coronavirus antibody titers by seroneutralisation, K 99, Y, 31A, F41 antibody titers by slow agglutination, in the serum, the colostrum and milk of vaccinated cows. From a clinical point of view, the clinical calf diarrhoea cases occurring between 0 and 30 days of age, and requiring specific veterinary treatment were recorded. The etiology of these clinical cases was checked by classical bacterial and viral isolation and identification techniques.

Results

. Local safety :

table 1 : Local reactions (in %)

Treatment	Nb of cows	% of animals per class of local reaction								
		1 day after						14 days after		
		1st injection			2nd injection			2nd injection		
		1	2	3	1	2	3	1	2	3
vaccine I	80	79	16	3	87	13	0	94	6	0
vaccine II	86	90	9	1	/	/	/	99	0	1
vaccine III		47	31	22	49	37	14	76	16	8

Class : 1 = no local reaction

2 = reaction ≤ 10 cm (largest dimension)

3 = reaction > 10 cm (largest dimension)

Statistical analysis (X²) confirms the following observations :

- the local reaction diminished with time for the 3 vaccines, I, II, III, P < 0.02
- 1 day and 14 days after injection , vaccine I induced less local reactions, and less important ones, than vaccine III, p < 0.001
- . There was no significant difference between vaccine I and vaccine II, one day or 14 days after injections.

. General safety :

table 2, cows rectal temperature (°C)

		1st injection				2nd injection			
		D.0	D.1	D.2	D.3	D.0	D.1	D.2	D.3
vaccine I	number	85	85	85	74	41	41	36	32
	mean	38,7	39,2	38,9	38,8	38,6	38,8	38,6	38,6
	variance	0,10	0,30	0,22	0,28	0,12	0,19	0,15	0,18
vaccine II +	number	88	88	83	55	53	53	52	45
	mean	38,8	39,3	38,9	38,6	38,6	38,7	38,7	38,6
vaccine III	variance	0,30	0,42	0,26	0,17	0,14	0,15	0,15	0,14

Mean rectal temperatures is 0.5 °C higher for both treatments, one day after the first injection, it is only 0.1 to 0.2°C higher one day after the second injection. There was no modification of the animals behaviour, and it was not possible to link this raise to the vaccine or to the attachment of the animals. No variation of the general status was noted.

. Serology :

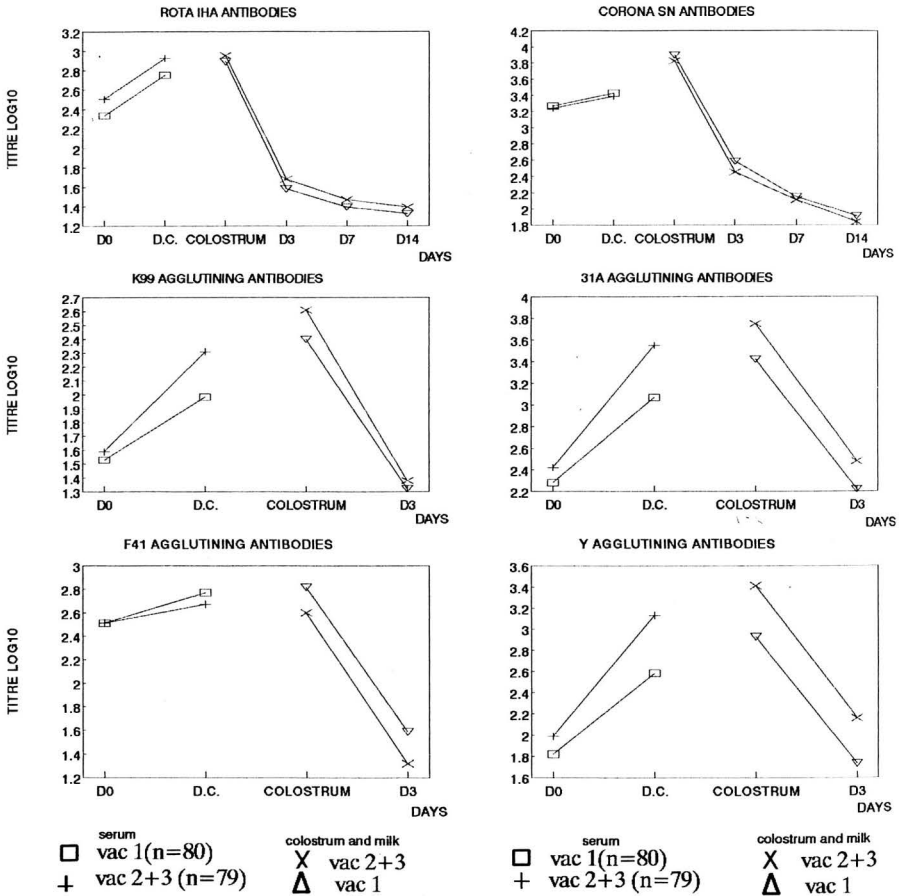


Figure 1

. Clinical study :

Table 3 : Morbidity rates (%) per treatment

	Controls	Vaccinates
vaccine I	17,5	4
vaccine II + vaccine III	10	4,2

Both treatments strongly diminished the incidence of neonatal diarrhoea in calves born to vaccinated cows. (X^2 HS $p < 0.001$). There was no significant difference between the two treatments.

Table 4 - Aetiology (%)

	vaccine I	vaccines II + III
Colibacilli	0	19
Rotavirus	21	25
Coronavirus	0	6
BVD	0	0
Cryptosporidiae	38	6
Others or unknow	41	44

Conclusion

Vaccine I, studied in 783 vaccinated pregnant cows in 22 herds, revealed totally safe as far as local and general tolerance were concerned. Local reactions, always mild, rapidly regressed. 14 days after the second injection, only 6 % of the animals presented a local reaction, which was always less than 10 cm in its largest dimension. None of the 85 controlled cows exhibited hyperthermia, neither after the first injection, nor the second. Vaccine I revealed at least as effective as the simultaneous use of vaccine II and vaccine III. Vaccine I induced seroconversion in vaccinated cows against all valencies. These antibodies are present at a high level in the colostrum of vaccinated cows, and decrease at the same rate than the ones induced by the simultaneous vaccination with vaccine II and vaccine III. The incidence of neonatal diarrhoea cases requiring veterinary treatment decreased from 17,5 % in the controls to 4 % in the calves born to vaccinated cows.

Summary

The development, for a few years now, of prophylactic programmes combining sanitary and medical aspects, was made necessary by the major economic importance of neonatal infectious diarrhoeas in calves. The importance of immunity conferred through colostrum and mil has been demonstrated. The vaccination of pregnant cows revealed, in the field, as the most efficient means to reach a high colostrum and milk immunity. The etiology of neonatal infectious diarrhoeas in cattle is now well determined ; different types of colibacilli bearing well-characterized attachment or virulence factors are now isolated. Viruses, rotaviruses and coronaviruses have also been evidenced. It seemed both important and useful to us to associate, within the same vaccine, different colibacilli (bearing the K99, Y, 31A, F41 antigens) as well as bovine rotavirus and coronavirus. This vaccine is inactivated and adjuvanted in aluminium hydroxyde and saponin. The authors report the results of a controlled clinical trial, conducted in blind versus a control group and a group of animals vaccinated with marketed vaccines. This trial involved 2,143 cows and 40 farms with a neonatal diarrhoea pathology, the etiology of which has been systematically defined. The vacine proved to be very well tolerated both locally and generally. Tis antigenicity is at least equal to that of the corresponding viral and bacterial vaccines sold at present. The vaccine further enabled the lowering of the percentage of diarrhoeic calves from 17.5% in the control group to 4% in the vaccinated group.

La importancia económica, en recientes años, de las diarreas infecciosas neonatales del ternero ha generado la elaboración de programas de profilaxis asociando aspectos sanitarios y médicos. Se ha demostrado la importancia de la inmunidad conferida por la ingestión de calostro y de leche. La vacunación de vacas gestantes se reveló, en el terreno, como el medio lo más eficaz para obtener una inmunidad elevada mediante la toma de calostro y la leche. La etiología de las diarreas infecciosas neonatales bovinas es ahora bien determinada. Se han aislado diferentes tipos de colibacilos portadores de factores de adhesión o de virulencia bien caracterizados. Virus, rotavirus y coronavirus han también sido evidenciados. Nos ha parecido importante y util asociar, en la misma vacuna, los antígenos K99, Y, 31A, F41 portados por diferentes colibacilos así como el rotavirus y el coronavirus bovinos. Dicha vacuna es inactivada y adyuvada con hidróxido de aluminio y saponina. Los autores presentan los resultados de un ensayo clínico controlado conducido a ciegas contra un grupo de animales testigos y un grupo de animales vacunados mediante vacunas del comercio. Dicho ensayo incluyó 2413 vacas procedentes de 40 crías en las que se había observado una patología de diarrea neonatal, cuya etiología fue sistemáticamente determinada. La vacuna fue muy bien tolerada tan localmente como generalmente. Su poder antigénico es al menos igual al de las vacunas virales y bacterianas correspondientes que son comercializadas actualmente. La vacuna permitió disminuir el porcentaje de terneros diarreicos de 17.5% para el grupo testigo a 4% para el grupo vacunado.

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