

EVALUATION OF AN INACTIVATED VACCINE AGAINST BVD-MD SYNDROME IN CATTLE

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Introduction

On account of the economic importance of the BVD-MD syndrome in cattle significant studies were performed concerning sanitary and medical prophylaxis. As far as medical prophylaxis is concerned, attenuated live and inactivated virus vaccines have been used in cattle [1] [4]. The safety of attenuated live vaccines has been considered doubtful more particularly in reproductive females. The efficacy of inactivated vaccines depends on the nature of the strains used and of the adjuvant [3] [4]. The results obtained with an inactivated vaccine in oil adjuvant so as to prevent the infection in breeding animals are presented by the authors.

Materials and methods

1. The vaccine : It is prepared from New-York strain (non cytopathogenic BVD strain) [5] and Aveyronite strain (non cytopathogenic BD strain) [2]. Both strains are cultured on ovine cell lines, inactivated by Betapropriolactone, and adjuvanted in oil. The volume of the dose is 2 ml.

2. Safety

2.1 : On adult cattle

5 adult cattle received a double dose (= 4ml) of vaccine via the subcutaneous route at day 0. At day 22 the same injection of vaccine was performed to the same animals. The body temperature was recorded during several days after each injection. 5 other cattle received 3 injections of 1 dose of vaccine via the subcutaneous route at a 7 day-interval, the temperature being recorded after each injection.

2.2 : On young cattle

4 susceptible animals 1 to 2 months of age, received two injections of 1 dose of vaccine via the subcutaneous route at a 21-day interval. The body temperature, and local reactions after each injection were noted.

3. Activity

3.1 : Serological study

4 groups of susceptible animals ie 4 calves from 1 to 2 months of age, 3 calves 3 months of age, 8 heifers 10 months of age and 3 calves 3 months of age, were twice injected at a 21-day interval via the subcutaneous route with 1 dose of vaccine. Blood samples were collected at various times after the first and second injection from non vaccinated controls and vaccinated animals.

Seroneutralising antibodies present in the serum of the animals were titrated on cells by indirect immunofluorescence towards both New-York and Aveyronite viral strains (about 300 DICC50 per ml). After one hour neutralisation at 37°C, reading is performed 48 hours incubation with cells. Seroneutralising antibody titres is given in log 10.

3.2 : Direct challenge exposure study

Two of mentioned groups of animals were challenge-exposed with New-York strain administered via the intravenous route in a volume of 1 ml and via the intranasal route with a volume of 0.5 ml per nostril ie $10^{5.5}$ DIC₅₀ per animal, 42 or 171 days after vaccination. The control and vaccinated animals are observed during 14 days after trial and blood samples are collected daily so as to detect viremia.

3.3 : By contact challenge exposure study

Two susceptible adult cows were twice injected with one dose of vaccine at a 21 day interval via the subcutaneous route. 9 months after the first injection, both of these animals and two control cows are inseminated. At two months of pregnancy, the 4 animals are put into contact with a viremic cattle permanently excreting BVD-MD virus.

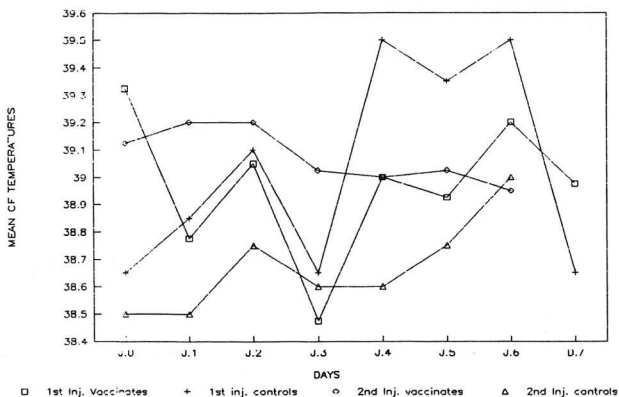
After calving of each female, blood samples are collected on calves before and after colostrum intake in order to detect viremia and to titrate neutralising antibodies. Blood samples were collected regularly on the 4 adult animals before and after challenge exposure in order to titrate antibodies. The same was applied to the viremic cattle in order to check the excretor status of this animal.

Results

1. Safety of the vaccine

1.1 : On adult cattle

The 5 cattle twice vaccinated with a double dose of vaccine did not show hyperthermia after each injection. The same applies to the 5 calves vaccinated three times with 1 dose of vaccine at a 7-day interval.



Graph 1 : Recording of temperature

1.2 : On young calves

The average temperature of the 4 vaccinated animals and of the 2 control animals is presented in graph 1. No change in both groups of animals was noted. At last no local reactions or only very mild ones are found after each injection of vaccine (see table 1).

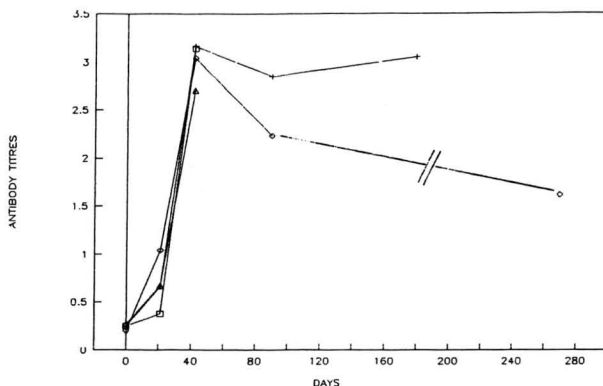
Table 1 : Local reaction results (cm)

Treatment	Calves n°	Local reaction results (cm)											
		following the first injection						following the second injection					
		D.0	D.3	D.4	D.5	D.6	D.7	D.21	D.24	D.25	D.26	D.27	D.28
Vaccinated	60	/	/	/	0.5	0.5	0.2	/	2	2	2	/	/
	100	/	/	/	/	/	/	/	1.5	1.5	1.5	1	/
	466	/	/	0.5	1.5	2	2.5	/	2.5	2.5	2.5	2	/
	472	/	/	/	/	/	0.2	/	3	3	3	2.5	2

2. Potency

2.1 : Serological results

The neutralising antibody response towards the New-York strain is presented in graph 2. Two injections of vaccine seem to be necessary in order to obtain a very clear seroconversion. These antibodies stay at a high level during several months. The neutralising antibodies titre towards the Aveyronite antigen after two injections is the same, at day 42, as the one observed towards the New-York antigen, ie 3.



Graph 2 : Seroneutralising antibody titres

2.2 : Direct challenge-exposure results

Out of the 3 vaccinated cattle challenge exposed 42 days after the first injection, only one presented viremia after challenge exposure at day 6. The 3 control animals presented a viremia from day 1 to day 8 (ie 20 days of viremia as a total for the 3 calves). Of the 3 vaccinated calves challenge exposed 171 days after the first injection none showed viremia whereas the 2 control animals showed positive viremia for 12 days (as a total for both animal).

2.3 : Indirect challenge exposure results

The kinetic of neutralising antibodies towards the New-York strain is given on table n°2. These results confirm those mentioned above. A very distinct and rapid increase of antibody rates of the 2 vaccinated cows is noted after they have been challenge exposed with the viremic cattle. But in control cattle seroconversion maximize only after two months. Serological and virological results after calving are collected in table 3.

The 2 calves born to vaccinated heifers are protected against a vertical infection in utero whereas the two control cows gave birth to 2 viremic excretors calves.

Table 2 : Seroneutralising antibody titres

1^o inj. 2d inj.

Treatment	Cattle n°	Seroneutralising antibody titres							
		After vaccination					After challenge exposure		
		D.0	D.21	D.42	6 month	9 month	D.15	1 month	6 month
vaccinés	18	0.2	0.7	2.9	2.5	1.9	3.1	4.1	3.8
	20	0.2	0.6	3.0	2.4	1.7	4.1	3.8	3.8
témoins	17	0.2	0.2	0.2	0.2	0.2	1.2	1.9	3.1
	19	0.2	0.2	0.2	0.2	0.2	2.2	2.7	3.4

Table 3 : Virological and Serological results after challenge

Treatment	Cattle n°	Cows Antibody titers at calving	Calves		
			Before colostrum intake Viremia	Antibodies	After colostrum intake Antibodies
vaccinés	18	3.8	-	0.2	3.4
	20	4.1	-	0.2	3.1
témoins	17	3.1	+	0.2	2.6
	19	3.4	+	0.2	3.1

Discussion / Conclusion

The safety and potency of MUCOBOVIN, inactivated vaccine in an oil adjuvant, were studied in cattle. Safety proved to be satisfactory with one dose, a double dose or repeated doses on young or adult animals :

- . Local reactions after vaccination via the subcutaneous route are inexistant or very mild and do not alter the general condition of these animals.

- . No general reaction, was observed, as demonstrated by the body temperatures followings after one or two injections.

The potency of the vaccine was demonstrated by :

- . The antigenic potency of the vaccine after a primovaccination (two injections at a 3-week interval) which induced a high seroneutralising antibody titres towards the two antigens.

- . The absence of viremia in vaccinated animals after challenge as compared to control animals.

- . The foetal protection of pregnant females vaccinated against an experimental challenge exposure.

Summary

The economic importance of the BVD-MD syndrome in cattle gave rise to very important studies concerning sanitary and medical prophylaxis. In the second case, reservations are made about attenuated live vaccines, though widely used worldwide, concerning in particular their safety. The authors report the results obtained using an inactivated vaccine in oil adjuvant intended for the prevention of infection in breeding animals. The vaccine safety was evaluated in young and adult cattle, whether administered as single or double dose, or as repeated injections. The vaccine potency was evaluated by titrating the post-vaccination seroneutralizing antibodies, by vaccination challenge of young susceptible cattle as well as by challenge of vaccinated pregnant cows by contact with a viremic cow. The vaccine proved to be very well tolerated both locally and generally. It induces high and persistent seroneutralizing antibody titres after two injections of vaccine. The virulent challenge of vaccinated animals shows the immunogenicity of this vaccine which further prevents pregnant cows against in utero contamination.

La importancia económica del síndrome BVD-MD en bóvidos ha generado búsquedas muy importantes en cuanto a los programas de profilaxis sanitaria y medical. En este segundo caso, las vacunas vivas atenuadas, aunque ampliamente utilizadas en el mundo, son objeto de reservas, particularmente en lo que se refiere a su inocuidad. Los autores presentan los resultados obtenidos al utilizar una vacuna inactivada en adyuvante oleoso destinada a la prevención de dicha infección en animales reproductores. Se evaluó la inocuidad de la vacuna en bóvidos jóvenes y adultos, inyectados con dosis única, doble, o iterativas de vacuna. Se determinó la actividad de la vacuna por titulación de los anticuerpos seroneutralizantes después de vacunación, por vacunación-prueba virulenta en bóvidos jóvenes sensibles y por prueba virulenta de vacas gestantes vacunadas por contacto con un bóvido virémico. La vacuna fue muy bien tolerada tan localmente como generalmente. Después de dos inyecciones, la vacuna induce títulos elevados y persistentes de anticuerpos seroneutralizantes. La prueba virulenta realizada en animales vacunados demuestra el poder inmunógeno de esta vacuna que además protege vacas gestantes contra una contaminación in utero.

References

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