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Understanding the epidemiology of sheep-pox outbreaks among vaccinated Algerian sheep and post vaccination evaluation of the antibodies kinetics of the commercially used vaccine

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ABSTRACT

Sheep pox is a disease of veterinary concern to small ruminant producers and veterinary diagnosticians, because of the associated tangible economic losses. The epidemiological analysis of sheep pox, among vaccinated sheep flock in Algeria from 2007 to 2016, showed that the disease outbreaks occurred every year and across all Algeria region with an average of 44.9 outbreaks per year, these outbreaks correlate with the region climate, the flocks' density and the transhumance practices. The one-year post vaccination antibody kinetics evaluation study of the commercially used vaccine in Algeria demonstrated a mild humoral response, the neutralization index range between 0.73 and 1.22. Therefore, the present study recommends a challenge study, using a virulent local strain, to evaluate the vaccine efficacy. Furthermore, quality control approach for the vaccine production processes is required.

1. Introduction

Sheep-pox virus (SPPV), goat-pox virus (GTPV), and lumpy skin disease virus (LSDV) of cattle are the three species in the genus *Capripoxvirus*, subfamily *Chordopoxvirinae*, family *Poxviridae* [1,2]. These diseases are economically important diseases of domestic ruminants and probably the most serious infectious disease of ruminants with substantial impact on livestock industries in endemic regions. These diseases inflicts substantial losses in terms of reduced productivity and lower quality of wool and leather [3].

Although no case of LSD and GTPV has been reported in Algeria, SPPV is considered by the Algerian veterinary services as a major transboundary diseases that threatened 27 million Algerian sheep [4,5]. Vaccination against sheep-pox disease has being conducted since the 1980s, and according to the Algerian Ministry of Agriculture and Rural Development (MADR), the vaccination rate during the last decade range between 68% and 75% with an average of 72%. However, SPPV is still responsible for several outbreaks in vaccinated sheep flocks [5].

Achour and Bouguedour [4] reported that SPPV is endemic in Algeria despite the implementation of a control program based on vaccination using live attenuated vaccines locally produced. Clinically, the virus affect only the sheep causing fever, nodules on the skin, mucous membranes and internal organs, emaciation, enlarged lymph nodes, edema of the skin, and sometimes death [6]. Therefore, the aim of this study is to i- investigate, through a retrospective descriptive study, the epidemiology of sheep-pox outbreaks among vaccinated Algerian sheep and ii- evaluate the post vaccination antibodies kinetics of the commercially used vaccine in Algeria.

2. Materials & methods

2.1. Study area

Algeria is the largest country in Africa. It is located between latitudes 19° and 37 °N and longitudes 9 °W and 12 °E. It is bounded by the Mediterranean Sea to the north, Tunisia and Libya to the east, Morocco and Western Sahara to the west, Mauritania, Mali and Niger to the south. Most of the coastal area (northern region) is hilly. South of the northern region is a steppe landscape; farther south, there is the Sahara desert. Administratively, Algeria is divided into 48 districts. However, according to climate and sheep flock management specificities, three regions were delimited. Each region contained 12–18 districts; North (35.3°–37 °N and 2 °W–8.5 °E), Steppe (33°–35.3 °N and 2 °W–8.5 °E) and Sahara region (19°–33 °N and 8.8 °W–12 °E).

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2.2. Epidemiology of sheep-pox outbreaks among vaccinated Algerian sheep

A 10 years national descriptive retrospective study of SPPV outbreaks in Algerian sheep was conducted. Data about the occurrences of these outbreaks per month/district/flock from 1st of January 2007 to 31th of December 2016 were collected from the Algerian Ministry of Agriculture and Rural Development (MADR). Count, data cleaning and analysis were performed using SPSS software version 20.0.

2.3. Evaluation of antibodies kinetics of the commercially used vaccine in Algeria

A total of 38 sheep aged between 3 and 12 months of different local breeds (Ouelad djellal and Hamra) and never been vaccinated before were included in the post vaccination antibodies kinetics evaluation of the SPPV commercially used vaccine in Algeria. The study was conducted between March 2011 and May 2012. Two groups were constituted; group A (11 sheep) and group B (27 sheep). The group A was placed under a closed experimental condition (with no contact with other animal) and the group B was placed with a vaccinated sheep flock under ordinary condition.

Both group received a live attenuated vaccine locally produced. According to the manufacture, each dose contains a minimum titer of $1 \times 10^{2,5}$ ($TCID_{50}$) of freeze dried live attenuated vaccine from the reference strain RM/65. The vaccine used was properly stored and the cold chain was well respected until utilization. Five blood samples were performed at Day 0, Day 30, Day 90, Day 180 and Day 365 post vaccination on each subjects. The collected sera were stored in a freezer at −20 °C until analyzed.

Antibodies levels conferred by the vaccine tested were determined by virus neutralization test using a Vero cells culture using the protocol described by Achour et al. [6] and according to the Manual of Diagnostic Tests and Vaccines for Terrestrial Animals recommendations [7]. The neutralization index is the log titer difference between the titer of the virus in the negative serum and in the test serum. Statistical analysis was performed at a 95% confidence level of statistical significance using SPSS software 20.0. Student test analysis was conducted to compare between the means of antibodies titers at Day 0, Day 30, Day 90, Day 180 and Day 365 post vaccination.

2.4. Ethical statement

Flocks owners participating in the study were informed about the purpose of the study and their verbal agreement was obtained. Veterinarian handling the subjects performed best practices. The study was permitted by the scientific council of the research laboratory “Santé et Productions Animales” at the Ecole Nationale Supérieure Vétérinaire (ENSV) of Algiers, and was performed according to the international rules considering the animal experiments and biodiversity rights.

3. Results & discussion

In Algeria, SPPV vaccination is conducted nationwide and annually using live attenuated vaccine locally produced. According to the manufacture, each dose contains a minimum titre of $1 \times 10^{2,5}$ ($TCID_{50}$) of freeze dried live attenuated vaccine from the reference strain RM/65. Annual vaccination campaigns concern small ruminants (for SPPV and Rev-1 brucellosis vaccine) and cattle (for FMD and rabies vaccine). It start in March-April every year; this period is much more acceptable to farmers as it does not coincide with either the lambing or the transhumance period [5].

According to the Algerian Ministry of Agriculture and Rural Development, the average SPPV vaccination rate reaches 72% every year during the last decades. The efficiency of the vaccine strain (RM/65) was worldwide established [3,6]. Thrusfield [8] stated that campaigns that vaccinate at least 70% of the target population are considered adequate to eliminate infection. However, SPPV is still responsible for several outbreaks even among vaccinated sheep flocks. Therefore, the present study aim to; understand the epidemiology of SPPV outbreaks among vaccinated Algerian sheep and evaluate the post vaccination antibodies kinetics of the commercially used vaccine

3.1. Epidemiology of sheep-pox outbreaks among vaccinated Algerian sheep

All the data regarding SPPV, gathered from the Algerian Ministry of Agriculture and Rural Development (MADR), are originated from passive surveillance of the disease. The number of outbreaks reported are often under-estimated, under-diagnosed and under-reported in Algeria mainly due to the lack of facilities and means to perform the laboratory diagnosis. Besides, an average of 28% of sheep population in Algeria are not vaccinated against SPPV especially in some mountainous areas where it is very difficult for veterinary services to access, witch deny these areas from the appropriate animal health monitoring including vaccination [5]. The status of the unvaccinated sheep population regarding SPPV is frightening and represents a significant source of contamination to other small ruminants. In this study, we limited our investigations to the vaccinated population, a SPPV outbreak is defined as the occurrence of new cases of SPPV in vaccinated sheep flocks.

Our analysis showed that SPPV outbreaks occurred every years, with the highest incidence occurring in 2008/2009 and 2014/2015, followed by 2011/2012 (Table 1). These peaks coincide with BTV, PPR and FMD epizootics that occurred in Algeria respectively in 2006–2009, 2011–2013 and 2014–2015 [7]. Indeed the emergence of theses TADs largely hampered veterinary efforts to continue SPPV vaccination as most of financial and personal means were focused towards controlling these epizootics. Most of the SPPV outbreaks declared during these periods were based only on clinical skin lesions without any laboratory diagnostic confirmation and could be considered as false-positive cases.

Our finding demonstrated that an average of 59, 24% of the reported outbreaks were occurred among transhumant flocks. During the study period, the number of outbreaks per year in transhumant flocks range between 9 and 43 with an average of 28, 6 outbreaks per year.

Table 1
Distribution of sheep pox outbreaks according to transhumance status, region and month post vaccination in Algeria.

Variables / Years		2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	Average (%)
Transhumance	Yes	9	43	39	20	24	24	18	41	36	32	28.6 (59.24%)
	No	4	18	18	17	17	19	13	20	21	16	16.3 (40.76%)
Region (climate)	North	4	16	15	11	11	12	8	17	14	11	11.9 (26.50%)
	Steppe	8	36	33	21	24	23	17	33	33	29	25.7 (57.23%)
	Sahara	1	9	9	5	6	8	6	11	10	8	7.3 (16.27%)
Month post vaccination	1- 6	5	11	9	10	12	9	9	11	10	12	9.8 (21.82%)
	6-9	5	42	38	23	21	29	16	42	39	30	28.5 (63.47%)
	10-12	3	8	10	4	8	5	6	8	8	6	6.6 (14.69%)
Overall		13	61	57	37	41	43	31	61	57	48	44.9 (100%)

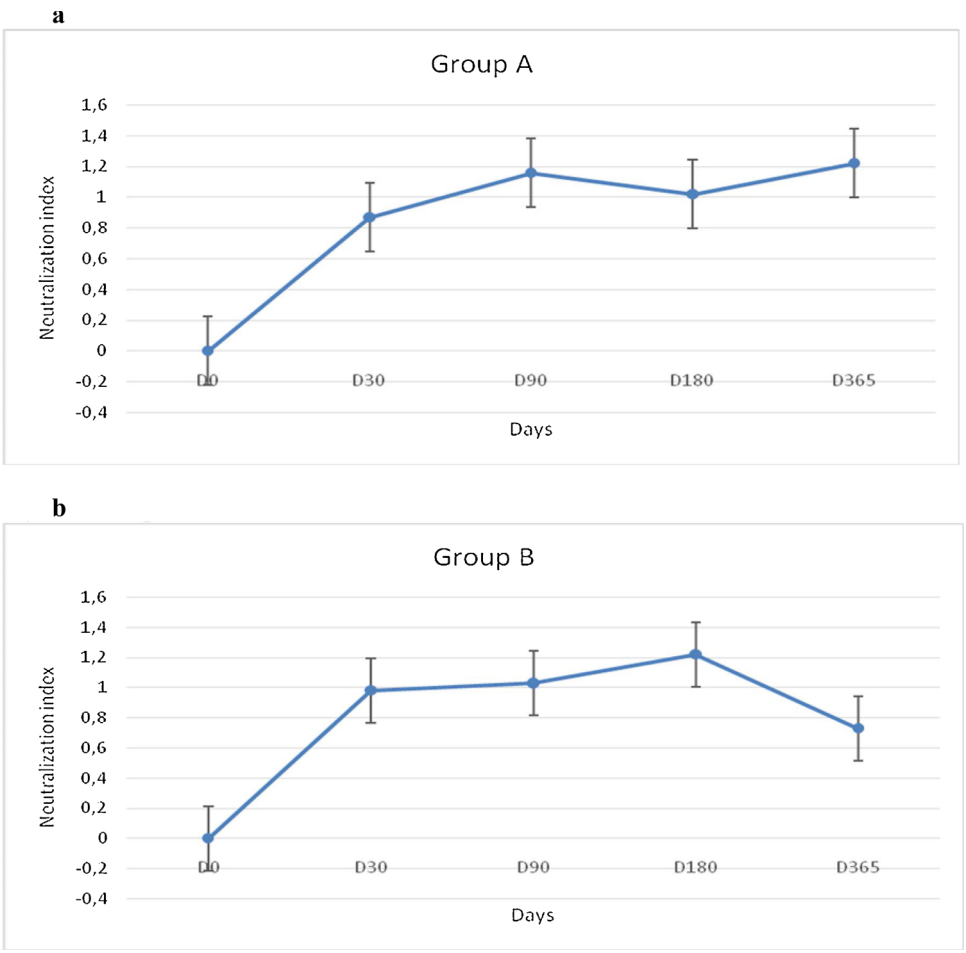

Fig. 1. Evolution of the neutralization index of the tested vaccine in Algeria.

Tuppurainen et al. [2] stated that viral infections such as SPPV occur predominantly in countries with extensive transhumant small ruminants breeding, and mainly in regions where uncontrolled movements of live animal are prevalent such as North Africa. This could be attributed to the fact that transhumant flocks experience transportation stress, underlying parasitic infection and other predisposing factors which may lower individual or herd immunity and thereby amplify the susceptibility of animals to the infection [4]. Ben Chehida et al [9] and Haegeman et al [10], made the same observations in neighboring Tunisia and Morocco, where SPPV outbreaks occurred mainly in transhumant regions.

The spatial distribution of SPPV in Algeria correlates with the region climate and the transhumance practices (Table 1). When SPPV outbreaks was compared between different region, it was found that the highest incidence of outbreaks occurred in steppe region (arid areas) with an average 5723% of the reported outbreaks during the study period, followed by northern region (humid coastal areas) with an average 2650% of the reported outbreaks. Then the dry areas (Sahara region) with an average 1627% of the reported outbreaks.

The reasons for the high incidence in the steppe region might be the high temperature, low humidity, high sheep density, low rainfall and the transhumance practices in this region. Haegeman et al [10] already indicated the steppe as risk factors for SPPV in Morocco. On the other hand, the low incidence in northern region might be due to heavy rainfall, low temperature and good vegetation, where sheep breeders do not need to drive their flocks long distances to access land with wild vegetation. Such conditions limit the transportation stress and the contact between animal, hence, the occurrence of infectious diseases.

The Sahara region receives less than 100 mm of rainfall per year. Grazing with wild vegetation are rare. The livestock system is mainly family size and of oasis type with less than 10 animals. The animals are kept permanently in stalls with very limited contact with other animals likely to be sources of transmissible infectious diseases [4]. These livestock production conditions may explain such a low number of SPPV outbreaks.

In spite of such a good vaccinated rate, an average of 2182% of the recorded SPPV outbreaks were occurred within 6 months post vaccination (Table 1). These periods correspond to spring and summer season, given the fact that vaccination campaigns start in March. The highest incidence of outbreaks was occurred between 6–9 month post vaccination which coincide with autumn through an average of 6346% of the reported outbreaks. Ben Chehida et al [9] reported that autumn and winter are the two main seasons for SPPV outbreaks in Tunisia. Surprisingly, the lowest incidence of outbreaks was recorded 10–12 month (1469%). Although, we could explain the reason for the high outbreaks incidence in the spring/summer and autumn season by the flocks departure and the return for and from transhumance, our data suggested a possible vaccination failure that need to be analyzed.

3.2. Evaluation of antibodies kinetics of the commercially used vaccine in Algeria

This study aims to evaluate the intensity of the humoral response of the SPPV commercial vaccines used in Algeria. The vaccine was properly stored and administrated to subjects according to the manufacture instructions. Analysis of sera obtained from the two group on day 0 was negative (Fig. 1), which indicates that the studied sheep were naïve to SPPV antibodies at least that SPPV antibodies are undetectable by the

method used.

The neutralization indexes obtained at day 30 post vaccination for the group A and group B were respectively 0.87 and 0.98. Subsequently, they increased at day 90 at an average of 1.02 and 1.22. At day 365 the neutralization indexes was 1.22 and 0.73 respectively for the group A (Fig. 1a) and group B (Fig. 1b). Statistical analysis reveals no significant difference between the means of antibodies titers of the group A and B (ANOVA test > 0.05).

In this study, the obtained results showed that the neutralization index never reaches the recommended value (1.5) at any time of the experience. However, the neutralization index obtained are similar to those observed by Achour et al [6] after vaccination with RM/65 strain. In Achour et al [6] study, all vaccines tested allowed a good protection measured by a specific challenge protocol comparing the titre of a virulent challenge virus on the flanks of vaccinated and control animals

According to the OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals recommendations [7], the immunity to SPPV is predominantly cell mediated, and therefore a weak post vaccination humoral response, does not imply that the animal from which the serum was taken is not protected. However, the present study recommends a challenge study, using a virulent local strain, to evaluate the vaccine efficacy. Furthermore, quality control approach for the vaccine production processes is required.

4. Conclusion

The present study revealed the occurrence of SPPV outbreaks among vaccinated sheep flock in Algeria. Our results suggested that the high density, contacts between animals and transhumance are the key factors in SPPV persistence in Algerian sheep flocks. Furthermore, the present study recommends that quality control approach for the vaccine production processes is required.

Conflict of interest

The authors declare no conflict of interest.

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