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Comparison of the efficacy of Neethling lumpy skin disease virus and x10RM65 sheep-pox live attenuated vaccines for the prevention of lumpy skin disease – The results of a randomized controlled field study

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ABSTRACT

Lumpy skin disease (LSD) is a viral disease of cattle and buffalo, caused by a Capripox virus. A field study was performed during an LSD epidemic which occurred in 2012–2013 in Israel, in order to assess the efficacy of two commercial vaccines for protection against LSD. Fifteen dairy herds, vaccinated 2–5 months prior to study onset with a single dose of $10^{2.5}$ $TCID_{50}$ of RM65 attenuated sheep-pox vaccine, and not affected previously, were enrolled in the study. 4694 cows were randomized to be either vaccinated with a $10^{3.5}$ $TCID_{50}$/dose of RM65 vaccine (x10RM65) or with a same dose of an attenuated Neethling LSD virus vaccine. A case of LSD was defined as the appearance of at least 5 lesions typical to LSD and a severe case was defined if this sign was accompanied by either fever (>39.5 °C) or/and a 20% reduction in milk production. Deep lesion biopsies and blood samples were collected from 64.5% of the cases in an attempt to detect DNA of LSD virus by PCR and to differentiate between the wild strain and the vaccine Neethling strain. Seventy-six cows were affected by LSD in 8 herds with an incidence of 0.3–5.7%. Mantel–Haenszel relative risk (RR_{MH}) for LSD morbidity at least 15 days after vaccination in x10RM65 vs. Neethling was 2.635 ($CI_{95\%}$ = 1.44–4.82) and 11.2 (2.3–54.7) for severe morbidity. RR_{MH} for laboratory confirmed cases was 4.28 (1.59–11.53). An incidence of 0.38% (9/2356) of Neethling associated disease was observed among Neethling vaccinated cows while no such disease occurred in x10RM65 vaccinated cows. We conclude that the Neethling vaccine is significantly more effective than x10RM65 in preventing LSD morbidity, though it might cause a low incidence of Neethling associated disease. No transmission of the Neethling strain to non-Neethling vaccinated cows was observed in this study.

1. Introduction

Lumpy skin disease (LSD) is a re-emerging economically significant disease of cattle, caused by the lumpy skin disease virus (LSDV), of the genus Capripoxvirus [1]. The virus is believed to be transmitted mechanically by blood feeding flying insects such as *Stomoxys* sp. and *Aedes* sp. [2] and potentially by ticks [3–8].

In Israel the disease was first recorded in 1989 [9] and afterwards in 2006–2007 [10]. In both epidemics it was suspected that the virus arrived from Egypt by wind borne arthropod vectors [11]. In 1989 all livestock in the infected village were culled, including sheep and goats. These control measures were followed by ring vaccination of the surrounding herds. In the epidemics which occurred during 2006–2007 only clinically infected animals were slaughtered and quarantine was applied to all affected herds. Along with this the entire southern region of Israel was vaccinated, using subcutaneous injection of 1 ml of an attenuated sheep pox vaccine of the RM65 strain (Abic®, Israel) ($10^{2.5}$ $TCID_{50}$/ml).

On late July, 2012 first suspected cases of LSD were reported from several beef herds located in north-eastern Israel, near the borders of Israel with Syria and Lebanon. The epidemic kept advancing southward despite the implementation of movement restrictions and emergency vaccination with an attenuated sheep pox vaccine of the RM-65 strain (Jovivac™, Jovac®, Jordan) ($10^{2.5}$ $TCID_{50}$/ml). On October, 2012 first cases began to appear among intensive zero-grazing high producing Holstein dairy cattle herds

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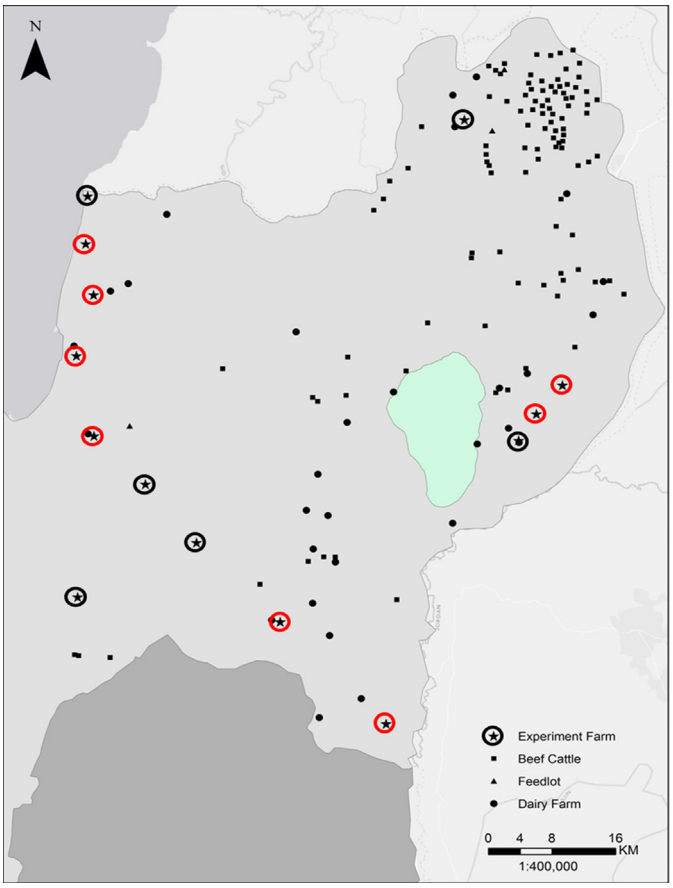

Fig. 1. Spread of lumpy skin disease among dairy and beef cattle in Israel during 2012–2013. Black stars represent the 15 dairy herds participating in the efficacy study during 2013 (affected herds are circled in red. Non-affected herds are circled in black).

and reached its peak at the spring of 2013. During April alone 70 new herds were affected, including more than 40 new dairy herds. At this stage the disease has spread among the herds in the entire northern part of Israel, with one isolated foci in the center of Israel more than 100 km south, probably due to unauthorized movement of sick cattle (the affected farms apart of this isolated foci are depicted in Fig. 1). The failure of controlling the outbreak by using the attenuated RM65 sheep-pox vaccine, in its original concentration ($10^{2.5}$ $TCID_{50}$/ml) led the Israeli Veterinary Services to take a decision, on March the 18th 2013, to vaccinate all cattle in Israel against LSD, using the attenuated RM65 sheep-pox vaccine in a 10× dose (x10RM65) and the attenuated Neethling lumpy skin disease vaccine (OBP®, Republic of South-Africa). Roughly, almost all dairy herds were vaccinated within 3 months with the Neethling vaccine while most of the feedlots and beef cattle herds were vaccinated with the x10RM65 vaccine.

The current study was planned, parallel to this campaign, aiming to evaluate the field efficacy and safety of the two vaccines during the ongoing LSD epidemic which occurred in Israel. Both vaccines were used for the first time in Israel, and to the best of our knowledge their efficacy was never compared previously under field conditions.

2. Materials and methods

2.1. Study population

The study was conducted in 15 commercial dairy herds in the north of Israel in which no LSD was documented prior to the study onset. (Fig. 1, Table 1). These herds accommodated a total of 8480 animals (cows, heifers, suckling calves). All participating herds held proper restriction facilities, which enabled animal identification and proper vaccination technique.

2.2. Prior vaccination

As a part of the initial attempts made by the veterinary services to mitigate the outbreak, all herds were vaccinated subcutaneously 2–5 months prior to the study with 1 ml of an attenuated sheep pox vaccine of the strain RM65 (Jovivac™, Jovac®, Jordan) ($10^{2.5}$ $TCID_{50}$/ml) (Table 1).

2.3. Study design

All the cattle in the 15 participating herds were vaccinated according to the following scheme with the exception of 29 animals that could not be restrained. Cows were allocated to two vaccination groups: Cows with an even brand number were vaccinated subcutaneously with 2 ml of an attenuated LSDV Neethling strain vaccine. In addition, in 7 herds (herds 1, 4, 5, 6, 9, 11 and 14, Table 1) all animals under 24 months of age (suckling calves, heifers) were vaccinated with 2 ml (as recommended by the manufacturer) of the Neethling strain vaccine (Lumpy Skin Disease Vaccine for Cattle, $10^{3.5}$ $TCID_{50}$/dose (according to data provided by the manufacturer in the registration file of the vaccine), OBP®, Republic of South-Africa, Lot numbers: 435, 8655). Cows with an odd brand numbers were vaccinated with the x10RM65 vaccine, which was prepared by diluting the RM65 vaccine (Jovivac™, Sheep *pox virus strain RM-65*, $5 \times 10^{2.5}$ $TCID_{50}$/ml = $10^{3.5}$ $TCID_{50}$/dose, Jovac®, Jordan, Lot numbers: 20DO310, 23D112) with fifth of the volume recommended by the manufacturer and injecting twice the recommended dose (i.e. 2 ml instead of 1 ml). In 8 herds the same preparation was administered to all animals aged under 24 months (suckling calves, heifers) (herds 2, 3, 7, 8, 10, 12, 13 and 15, Table 1). Both vaccines were injected subcutaneously in the neck region. All vaccinations were performed by trained veterinarians, using syringes and needles that were disposed after a single use.

2.4. Data collection

Age of all vaccinated animals and daily milk yield of all vaccinated milking cows were retrieved from the herd management software (NOA™, Israel Cattle Breeders Association). After vaccination, all cattle in the herds were monitored daily for any signs of LSD or other illness by the herdsmen and twice weekly by the attending veterinarian. When illness was suspected its date of identification was recorded and notified to the study veterinarian (JBG). The study veterinarian arrived at the farm to conduct physical examination and to collect blood samples and biopsies from some of the suspected animals, usually within a day from notification. Blood was sampled from the coccygeal or jugular vein (5 ml, EDTA tube). Full skin deep lesion biopsies were taken under local anesthesia. Samples were collected from 49 (64.5%) out of 76 clinically affected cows.

2.5. Case definition

Any animal with at least five typical LSD skin nodules was considered a positive case. Any cow, calve or heifer in which the appearance of typical skin nodules was accompanied by fever (>39.5 °C) was defined as a severe case. In milking cows severe case definition included also a decrease of over 20% in daily milk yield compared to average milk yield in the two preceding days. Such cases were defined as severe even when fever was not recorded.

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