Control of a foot-and-mouth disease epidemic in Argentina

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Abstract

A major epidemic of foot-and-mouth disease affected Argentina during 2001. The epidemic was controlled by mass-vaccination of the national herd and movement restrictions. The median herd disease reproduction ratio ($R_H$) decreased significantly from 2.4 (before the epidemic was officially recognized) to 1.2 during the mass-vaccination campaign and <1 following the mass-vaccination campaign. The largest distance between two outbreaks was similar during (1905 km) and after (1890 km) the mass-vaccination. However, after mass-vaccination was completed, the proportion of herd outbreaks clustered decreased from 70.4\% to 66.8\%, respectively. Although a combination of vaccination and livestock-movement restrictions was effective in controlling the epidemic, 112 herd outbreaks occurred up to 6 months after the end of the mass-vaccination campaign. Mass-vaccination and movement restrictions might be an effective strategy to control FMD; however, the time taken to end large, national epidemics might be >1 year.

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1. Introduction

Foot-and-mouth disease (FMD) probably has the greatest economic impact of any disease on global livestock production (James and Rushton, 2002). A major epidemic of FMD-virus affected Argentina from July 2000 through January 2002. Although initial reports indicated that the epidemic was controlled by December 2000 and that FMD-virus was reintroduced in February 2001 (Correa Melo et al., 2002; Perez et al., 2004), a review of the epidemic conducted by the Argentine Animal Health Service (SENASA) indicated that FMD outbreaks occurred throughout the period July 2000 through January 2002, with 2519 herds being affected. Only 11 of these outbreaks (which occurred in 2000) were associated with FMD-virus type O. The remaining outbreaks were associated with FMD-virus type A (Perez et al., 2004).

A combination of vaccination and livestock movement restrictions was used to control the 2000–2002 Argentine epidemic. However, the way in which this strategy was implemented varied. From the beginning of the epidemic (July 2000) through 17 September 2000, livestock movements were restricted throughout Argentina and herds in contact with outbreak herds were vaccinated twice (~21 days apart). The vaccine used during this period was bivalent (serotypes O1 Campos and A24 Cruzeiro). From January 2001, serotype A Argentina/2000 was included (SENASA, 2003). Although in-contact herds continued to be vaccinated between September 2000 and March 2001, movement restrictions were only imposed on outbreak and in-contact herds. These restrictions lasted for ≥30 days after detection of the last clinical sign of FMD within each herd. In early 2001, a new FMD-virus serotype was detected and the number of outbreaks in Argentina increased dramatically. As a consequence, the FMD epidemic was reported to the Office International des Épizooties and the disease-control strategy was redesigned. Between 13 March and 3 April 2001, a complete restriction on livestock movements nationwide was re-imposed. An initial round of mass-vaccination was conducted in the affected region of Argentina, north of the Negro river (Rio Negro) and Neuquen province (Anon., 2001) between April and July 2001. A vaccine containing four strains of FMD-virus (O1 Campos, A24 Cruzeiro, A Argentina/2000, A Argentina/2001) was used. A subsequent round of vaccination, using this vaccine, was conducted early in 2002 (Anon., 2002).

During a major FMD epidemic, the decisions about whether and how to vaccinate are complex. During 2001, several FMD epidemics affected Europe and South America and the control strategies used have been discussed. Technical, logistical, economic, political, cultural and historical reasons may affect such a decision (Leforban, 2002). When future epidemics occur, scientific and political debate regarding the merits of vaccination is likely to be repeated. Vaccination decisions typically are made quickly and are influenced greatly by previous experiences. However, because large FMD epidemics are extremely rare events, the opportunity to assess the effects of control strategies are very limited. To improve the success of future FMD-control activities, we evaluated the effect of control measures—mass-vaccination and restriction on livestock movements—on the herd reproduction ratio ($R_H$) and spatial distribution of FMD during the recent epidemic in Argentina.
2. Methods

2.1. Data source

The system used by the SENASA to report and collect the information related to the herd outbreaks has been described (Perez et al., 2004). Briefly, an outbreak was defined as a herd in which an FMD-virus infection was recognized officially—SENASA local veterinarians considered that clinical signs, lesions and results of field investigations were consistent with FMD. In some outbreaks, serological (ELISA) test-positive results also were obtained. From January through February 2001, occurrence of FMD outbreaks officially was denied and subsequently, no official records detailing the 268 outbreaks that occurred in that period were available for analysis. From March 2001 through December 2001, 2126 outbreaks occurred (Perez et al., 2004). These reports (SENASA, 2001), including the date of intervention (when the outbreak initially was detected by SENASA local veterinarians), date when the outbreak started (an estimate of the date when the first FMD lesion occurred in the herd, based on age of the clinical lesions observed) and herd location were published weekly. A grid system was used to describe the location of the outbreaks reported. Each of the 10,000 grid cells measured 0.25° longitude by 0.17° latitude. The average land area of these cells was approximately 410 km² (range 300–465 km²). For location-specific analysis, outbreaks were assumed to be located in the center of each corresponding cell.

2.2. Data analysis

Herd outbreaks were based on official SENASA reports collected during 2001 (SENASA, 2001). The epidemic was divided into three consecutive periods. The first corresponded to the period of time with incomplete reporting. Because the outbreaks were not officially recognized until March 2001, the accuracy of the reporting system was probably substantially lower during this period. To account for potential biases by missing reports, the 33 herds with an estimated (based on age of lesions observed) time of infection prior to the first officially recognized outbreak were grouped together in this period. The second period—corresponding to the application of intensive FMD-control strategies (vaccination of all the cattle nationwide and a ban on livestock movements from in-contact herds)—started with the first outbreak officially recognized in 2001 and finished with the official end of the first round of mass-vaccination on 31 July. During this 5-month period, 1968 herd outbreaks were reported. The third period was the 4 months between the end of the first round of mass-vaccination and the detection of the last outbreak; 112 outbreaks were identified during this period.

For each of the 3 epidemic periods, the spatial distribution, time-to-detection of herd outbreaks, and $R_H$ were estimated. Time-to-detection was calculated as the difference between the estimated start date (based on age of FMD lesions) and official date of reporting an outbreak. The coefficient of transmission—the $R_H$—during each epidemic period was estimated (Anderson and May, 1991) as $1 + (D/t_d) \ln 2$, where $D$ is the duration (days) of herd infectiousness and $t_d$ the time period (days) in which the number of herd outbreaks doubles. Assuming that $D$ and time-to-detection were approximately equal, the
mean estimates of time-to-detection were substituted for \( D \) and used to estimate \( R_H \). For each period of the epidemic, the number of consecutive \( R_H \)’s estimated is equal to the length of the period divided by \( t_d \). Values of time-to-detection and \( R_H \) before the epidemic was officially recognized, during vaccination and after the end of the first round of mass-vaccination were compared \((P < 0.05)\) using a Kruskal–Wallis test (Statistix 7, Analytical Software, Tallahassee, FL, USA).

The spatial distribution of herd outbreaks was described by estimating Ripley’s \((k)\) function (Cluster Seer 2.0, BioMedware, Ann Arbor, MI, USA). This function, \( k(h) \), based on the number of outbreaks that are located within a critical distance \((h)\) of each outbreak, was estimated as \( (R/n^2) \sum \sum I_0(d_{ij})/w_{ij} \), where \( R \) is the size \((\text{km}^2)\) of the study area, \( n \) the number of outbreaks within the region \( R \), \( I_0(d_{ij}) \) a correction factor \((1\ \text{if the distance between the } i\text{th and } j\text{th outbreaks, } (d_{ij}) \leq h; \ 0\ \text{otherwise}) \), and \( w_{ij} \) a weighting factor that corrects for edge effects. The study area was based on a rectangle formed by connecting the locations of the most northerly, western, eastern and southerly outbreaks during each epidemic period. The weighting factor \((w_{ij})\) was the conditional probability that locations at a distance \( h \) from \( i \) were in the study area \((R)\), and was estimated as the proportion of the circular area centered on \( i \) and with radius \( h \) that lay within the study area. For each of the three epidemic periods, \( k \) was assessed considering a radius \((h)\) of half the maximum distance between locations \( (\text{so that the diameter of the circle used to estimate the } k \text{ equaled the maximum distance between any two locations in the study area})\), allowing us to estimate the expected and observed number of outbreaks throughout the study area affected by the epidemic during each of the epidemic periods under study. \( k(h) \) was compared to the expected number of outbreaks \((L(h))\) assuming the occurrence of outbreaks were Poisson distributed \((\lambda = \text{the mean number of outbreaks per unit area})\). If the disease outbreaks were clustered, then, at some point, \( k(h) > L(h) \) and the distance at which the difference between \( k(h) \) and \( L(h) \) is maximum can be considered the distance at which outbreaks were most clustered within each period under study. In addition, overall clustering in each epidemic period was quantitatively described by the total area under the \( k(h) \) curve, an indirect measure of how the distribution of outbreaks deviates from an expected Poisson point process (Diggle, 2003).

3. Results

Median times to intervention before the occurrence of the first officially reported outbreaks, during the control period and after the end of the first round of mass-vaccination were 8 days \((\text{range } 1–21)\), 4 days \((\text{range } 0–30)\) and 3 days \((\text{range } 0–27)\), respectively. Differences between the three periods were significant \((\text{Kruskal–Wallis test statistic } = 21.88, P < 0.01)\).

Median coefficient of transmission \((\text{Fig. } 1)\) was 2.4 \((\text{range } 2.4–3.8)\) before the FMD epidemic was officially reported and 1.2 \((\text{range } 1.0–1.5)\) during the first round of mass-vaccination. After the first round of mass-vaccination was completed, \( R_H \) \((1.0)\) was estimated only once \( (\text{because the epidemic finished before the number of outbreaks doubled for a second time})\). Differences between the three periods of the epidemic were significant \((\text{Kruskal–Wallis test statistic } = 8.6, P < 0.05)\).
Fig. 1. Coefficient of transmission (herd reproduction ratio, \( R_H \)) of foot-and-mouth-disease during the epidemic in 2001 in Argentina.

Fig. 2. Location of herd outbreaks prior to the first officially recognized outbreak in the foot-and-mouth-disease epidemic in 2001 in Argentina. The number of outbreaks located within half of the maximum distance between outbreaks during the same period (■), the average (○) and 95% CI (...) of the expected number of outbreaks if the distribution follows a Poisson process and the identity function of no clustering (—) are shown in the insert.
The maximum distance between herd outbreaks before the FMD epidemic officially was reported was 769 km (Fig. 2). During and after the mass-vaccination campaign, maximum distances were 1890 and 1905 km, respectively (Figs. 3 and 4). The minimum distance was 0 km in each of the three periods—two or more herd outbreaks occurred in the same geographic cell. Maximum spatial clustering—maximum difference between $k(h)$ and $L(h)$—for the same periods occurred at distances of 45.4, 169.3 and 95.1 km, respectively. The area under the $k(h)$ curve—a relative estimate of overall clustering—was 60.7% before the epidemic was officially reported, 70.4% during vaccination and 66.8% after vaccination.

4. Discussion

Vaccination is an option for controlling FMD epidemics when the time between primary outbreak occurrence and index outbreak detection, and the number of and distance between outbreaks during this initial period, suggests that a slaughter (stamping-out) policy will be insufficient to control an epidemic (Leforban, 2002). Because large FMD epidemics are extremely rare events, the opportunity to explore the effects of different control strategies are limited. This paper described the effects of a combination of mass-vaccination and movements restrictions during a large FMD epidemic.
Although FMD outbreaks occurred in Argentina throughout 2001, the occurrence of an epidemic was not officially reported until March 2001. Thirty-three outbreaks over a distance of 769 km (Fig. 2) were reported in March, but were estimated to have started in January or February 2001, the first period analyzed in this study. Limited information on the number of outbreaks during this period probably lead to an underestimation of parameters, including coefficient of transmission, distance between outbreaks and clustering. To avoid measurement bias, these initial outbreaks were included in a separate group. The median time-to-intervention was significantly higher for herd outbreaks that started during this first epidemic period—suggesting that as the epidemic progressed and was reported officially, capability of the veterinary services to detect FMD-affected herds improved.

The mass-vaccination and movement restrictions applied to control this FMD epidemic resulted in a significant ($P < 0.01$) reduction in the herd reproduction ratio, even though the herd reproduction ratio probably was underestimated during the first period of the epidemic in Argentina. The reproduction ratio was probably below 1 following the end of the first round of mass-vaccination (indicating the success of the control activities conducted). However, reduction in herd-to-herd FMD-virus transmission was slow and 6 months were required to eliminate completely the occurrence of herd outbreaks. When mass-vaccination is applied, the herd reproductive ratio decreases (Fig. 1) due to a progressive increase in the
proportion of resistant herds, so that a rapid decrease in $R_H$ (as observed in the Argentine epidemic) is unlikely. The maximum distance (1905 km) between any two herd outbreaks after the mass-vaccination campaign was completed was similar to the maximum distance during the vaccination period (1890 km). The spatial distribution of the outbreaks was also similar in both periods—suggesting that the outbreaks that were identified after the end of mass-vaccination were a consequence of a lack of vaccine protection (rather than FMD-virus re introduction). Protection against infection conferred by vaccination never is 100%. In an experiment conducted in Argentina at the end of the epidemic, 85% of vaccinated cattle developed high serological titers (SENASA, 2002). Populations in which vaccine protection is incomplete remain susceptible (particularly to highly infectious diseases such as FMD). Incomplete protection of vaccinated herds is supported by the observation that after the end of the mass-vaccination campaign, the density of outbreaks in Buenos Aires Province was associated with the density of cattle and the density of large herds (Ward and Perez, 2004). However, when a critical proportion of the herd is immune (and herd immunity is reached) in a population, the reduction in $R_H$ will be sufficient to end the epidemic (although the actual time to the end of the epidemic can be long). Subsequently, 113 outbreaks (112 included in this study and 1 outbreak in January 2002) occurred after the end of the first round of mass-vaccination. After the second round of mass-vaccination, reports of outbreaks ceased.

The strategy used to control the epidemic also was associated with decreases both in the proportion of FMD outbreaks clustered (estimated in this study as the area under the $k(h)$ curve), and the maximum distance at which clustering occurred (estimated as the maximum difference between $k(h)$ and $L(h)$ during each period under study. Figs. 2–4). Distance of clustering decreased almost half after the end of the mass-vaccination campaign (95 km) compared to during the vaccination campaign (179 km). The proportion of outbreaks clustered (area under the $k(h)$ curve), decreased 5% after vaccination. The effect of vaccination on spatial clustering probably is related to its effect on $R_H$. During the vaccination period, $R_H$ progressively decreased. However, it still remained >1 during this phase and more herd outbreaks were reported—increasing the distance and amount of clustering. After the end of vaccination, the remaining outbreaks probably were limited by the distribution of a susceptible population. Subsequently, $R_H$ was < 1 and the distance and amount of clustering decreased.

Movement restrictions were imposed in the Argentine FMD epidemic. Subsequently, the estimated decrease in FMD-virus transmission should be considered a consequence of both vaccination and movement restrictions, rather than of vaccination alone. The FMD herd-outbreak definition used in this study was based on field investigations; serological confirmation was often unavailable. Lack of serological confirmation might have led to an overestimation of the number of outbreaks. However, under-reporting of outbreaks might have compensated for this overestimation. Median duration of herd infectiousness was assumed to be similar to the median time-to-detection for each epidemic period assessed in this study. Because this assumption does not account for latency, duration of infectiousness might have been overestimated. Alternatively, because herds were not depopulated in this epidemic, infected herds might have remained infectious even after imposition of vaccination and movement restrictions. We felt that selection of the median value during each period is more realistic that selecting arbitrary values from the literature.
Only approximate rather than exact locations of the herd outbreaks were reported. This lack of precision might have affected clustering estimates. For example, the minimum distance between outbreaks was 0 km, as a consequence of the aggregation of herd outbreaks to the center of their respective geographic cell. Similarly, definition of the radius \((h)\) used to assess the number of outbreaks located within a critical distance of each herd outbreak in the \(k\)-function analysis is subjective and likely to affect the results. The aim of this study was to assess the effect of mass-vaccination and movement restrictions on these parameters (rather than to estimate the exact value of the parameters), and to estimate the approximate time until \(R_H < 1\). Excluding the first epidemic time period (when underreporting of outbreaks probably occurred), we assumed that reporting bias was non-differential during and after the mass-vaccination campaign. Consequently, we believe that conclusions were not substantially affected by these potential biases.

5. Conclusion

Control methods—vaccination of cattle and restricted movement—during the 2001 foot-and-mouth-disease epidemic in Argentina significantly decreased the transmission of FMD-virus, the proportion of outbreaks that were clustered and the maximum distance of clustering. The epidemic was not controlled until \(~6\) months after the end of the first round of mass-vaccination. This suggests that although this strategy can be useful in controlling large epidemics, time elapsing until control is achieved can be very long in large FMD epidemics.

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