Molecular epidemiology research on foot-and-mouth disease (FMD) viruses typically requires information on the study population and a sufficient number of samples for accurate detection and trending of serotypes and lineages in a region or country. Based on the study of Abdel Rahman et al. [1], this commentary is to draw the attention to insufficient sample size and limited geographical locations that represent the circulating field strains of foot-and-mouth disease (FMD) virus in Egypt during 2016. Sequence analysis of one FMD vaccine sample produced locally in 2019 was compared to circulating strains in 2016, irrespective of time difference. While the epidemiological circumstances were different, the results showed absence of some viral vaccine antigens and suggested intertypic recombination and accidental virus release. These results may be associated with compromised sensitivities of the methods employed, irrelevant quality control procedures and improbable or far-fetched speculations. Also, anonymity of the analyzed product casts doubts on all locally produced vaccines in Egypt.

Keywords: FMD vaccine, sequence analysis, FMD Egypt.

Introduction

The article by Abdel Rahman et al. [1] reported that 62 clinical samples (blood, serum, white blood cells and swabs from the nose, mouth and saliva) were collected from two cattle and 2 buffaloes in 2016. Only saliva samples from the 4 animals were positive for FMDV serotype A by PCR, but the virus was detected in cell cultures from 3 samples. Statistically, if at least 3 FMD serotype lineages were circulating in Egypt, O, A and SAT-2 [2,3], a minimum of 10 animals should be sampled per serotype, making a total of 30 animals. However, with such limited number of samples and narrow zone of investigation, the authors concluded the circulation of A/AFRICA/G-IV in Egypt since 2012 based on a single episode. Other surveillance studies have shown this lineage to be sporadic, not occurring as part of any overwhelming outbreak. However, the strain may be included in some special batches that are labeled accordingly and used for internal epidemiological situations or exportation purposes. Until 2019, the authorities have only requested the inclusion of A-Iran 05 in the local vaccines following its emergence in 2006, being more rampant [4].

Further, the authors did not provide the vaccination history of the animals, although this may have been the case, with no sloughed tongue epithelium and negative PCR results from the blood and serum (Stenfeld et al.) [5]. The speculation that current vaccines in Egypt are not expected to necessarily protect from lineage A/AFRICA/G-IV is controversial, since cross protection by A-Iran 05 has been demonstrated before [6] and the authors themselves [1] have paradoxically reported that highly efficacious vaccines against FMDV serotype A could produce...
protection against heterologous strains, regardless of low matching results in vitro. However, the epidemiological situations during the 3 years interval between the field and vaccine analyses may not necessarily be the same, which explains the absence of A/AFRICA from the current local vaccines [3]. When challenge experiments are performed to evaluate cross-protection among strains within a specific FMD serotype, OIE guidelines are followed, contrary to the authors’ views. The guidelines require that 12 out of 16 vaccinated animals (75%) be protected (Saad and Deghaidy, 2012) [2]. However, other challenge experiments have been conducted using groups of 5 animals only to evaluate immunogenicity, potency and cross challenge studies before batch release [6,7].

At present, FMD vaccines produced in Egypt contain SAT2/EGY-2012 (topotype VII, lineage 2), which is sometimes referred to as SAT-2 Alex, SAT-2 Gharbia or SAT-2 Eritrea [6]. However, SAT-2 Libya (topotype VII, lineage 3) has been additionally included in the vaccines since 2018 [3, 4] after a severe outbreak and an official request to incorporate it. Nevertheless, the authors claimed absence of any other isolates of serotype SAT 2. Also, while the vaccine contained O ME SA/PanAsia-2 strain, the authors assumed the presence of O1 Sharqia/EGY/72 and quoted it as almost undistinguishable from O/Dakhalia/Egypt/2014, although both are rather old and less protective than O/PanAsia that was circulating in Egypt since 2010 [8]. Strain (O/EGY/10/2011) is commonly included in the current local vaccines. Sobhi et al. [9] observed two different strains of serotype O, one related to PanAsia-2 in Upper Egypt and the Delta (i.e., most of Egypt) and the other, was probably less immunodominant and related to the East African strains in Sharkia province. This is not in line with the conclusions of Abdel Rahman et al. [1], who reported that the vaccinal strain of serotype O has shown variable sequence alignment and phylogenecity profiles, being generally comparable to other O/ME-SA strains, while the leader protein-coding zone (five prime untranslated region) was more or less similar to those of some historical EURO-SA vaccine strains, including O1/Campos/BRA/58 and O1/BFS1860/UKG/67. The authors also report that the virus in the inactivated vaccine (of lineage O/ME-SA, box A) was very distant from the lineage O/EA-3 strains (box B). However, this lineage emerged between 2016 and 2017 in some areas of Egypt that suffered from limited or no vaccination [4], while ME-SA strains (O/PanAsia-2 or O/Manisa) could provide a sufficient broad coverage [8,10].

During the analysis of two local vaccines, the authors used a high-throughput sequencing protocol adjusted for short nucleic acid chains [11]. Based on a relatively lower Cq, they selected one vaccine for loading onto FTA cards and shipping for further research. The obtained negative results and anonymity of the select vaccine cast doubt on the quality of both products and cannot be linked to any. While the results of a European double emulsion vaccine were used for control purposes [11], the local vaccine of MEVAC is water-in-oil emulsions and would normally show stringent binding and slower antigen release. Also, loading of FTA cards and shipping at room temperature was not recommended by the producer (Sigma-Aldrich), which advises to perform the analysis as soon as possible and indicates that “frozen storage is helpful for RNA preservation”.

https://www.sigmaaldrich.com/catalog/product/sigma/whawb120205?lang=en&region=EG

The results also demonstrated an unexpected close relationship between the vaccine and field FMD isolates in Egypt, simply attributing this to accidental virus release, not knowing that there are safety and innocuity tests conducted by both the producers and the government reference laboratory before any batch release (OIE guidelines). The presumed lower payload in the analyzed vaccine vs. that produced in Europe might probably be due to lower RNA extraction from the select water-in-oil emulsion, long preservation of RNA at room temperature or use of unclean methods that could highly reduce the sensitivity of the assays, as per authors’ claim. We believe it would be interest to draw the attention to these points for consideration in future research.

Acknowledgement

The author wishes to thank the cell culture-based vaccines team of MEVAC for their outstanding efforts to provide quality FMD vaccines to the market.
Conflict of interest
None.

Funding statement
Funding for publication was provided by MEVAC.

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تعليقات على تحليل التسلسل الجزيئي لفيروس مرض الحمى القلاعية المصري في العترات الحقلية وعترات اللقاح: التهجين بين الأنماط المختلفة وإشارة إلى احتمال انفلات الفيروس عرضيا.

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تعتبر أبحاث علم الأوبئة الجزيئية الخاصة بفيروسات مرض الحمى القلاعية معلومات وافية عن قطاعات أو مجتمعات الدراسة وعددًا كافيا من العينات للكشف الدقيق عن الأنماط المصلية والأنواع والتأثير على انتشار في أي منطقة أو بلد. ومنذ بدء دراسة عبد الرحمن وآخرون [1], فإن هذه التعليقات تهدف إلى فهم الانتشار في الجسم، غير الكافي للعينة المتاحة، وحدودية المواقع الجغرافية التي تكشف عن السلالات الحقلية المتاحة من فيروس الحمى القلاعية في مصر خلال عام 2016. وقد تم تحذير التسلسل الجزيئي لعينة واحدة من فئات الحمى القلاعية المنطقة حديثًا عام 2019، وقورنت النتائج بالسلالات المتاحة في عام 2016، بخصوص الانتشار في الفضاء الزمني. وتذكر أن اختلاف الظروف البيئية، أظهرت النتائج عدم وجود بعض مستضدات (الإنترجينات) لللقاح الفيروسي كما أقرر الباحثون حديثًا تجلي أو إعادة تركيب بعض الأنماط الفيروسية المختلفة مع احتمال إنشاء الفيروسات في البيئة بشكل عرضي. وقد تظهر مثل هذه النتائج بخصوص الانتشار في الفضاء الزمني في التحليل فضلا عن نقص إجراءات مراقبة الجودة وفي الكهرباء أو بناءة المهن. كما أن عدم الكشف عن هوية المنتج الذي تم تحذيره يلقي بظلال من الشك على جميع اللقاحات المنتجة محليًا في مصر.

الكلمات المفتاحية: لقاح الحمى القلاعية، تحليل التسلسل الجزيئي، مرض الحمى القلاعية في مصر.

Egypt. J. Vet. Sci. Vol. 52 No.2 (2021)