Vacinação para gripe A (H1N1) em doentes com Lupus Eritematoso Sistémico

Influenza A (H1N1) vaccination in Systemic Lupus Erythematosus patients

Fernando Salvador, Sofia Ribeiro, Cátia Macedo, João Neves, Sofia Teixeira, Fátima Farinha, Isabel Almeida, Carlos Vasconcelos

Resumo

Objectivo: Avaliar retrospectivamente o uso da vacina para a gripe A e os seus efeitos na população de doentes adultos com Lupus Eritematoso Sistémico (LES) seguido na Unidade de Imunologia Clínica do Hospital Santo António – Porto, Portugal.

Material e Métodos: Efectuado um questionário telefónico, onde foi averiguado o número de indivíduos com o diagnóstico médico de gripe A. Foram também inquiridos se a vacina lhes havia sido proposta, se a tinham efectuado e se tinham apresentado reacções adversas locais e/ou sistémicas. Nos doentes aos quais foi administrada a vacina, foi avaliada a repercussão na actividade da doença numa escala numérica de 0 (doença não activa) a 10 (muito activa) no mês anterior e posterior à vacinação.

Resultados: Dos 318 doentes com LES seguidos na Unidade foram contactados 186 (idade média 43 ± 13; 91% do sexo feminino). A vacinação tinha sido proposta a 37% dos doentes (68), tendo sido administrada a 28 doentes (41%). Dos vacinados, 72% apresentaram reacções adversas locais e 31% sistémicas. Em nenhum destes foi diagnosticada gripe. A média da avaliação global da actividade da doença no mês precedente e subsequente à administração da vacina foi de 3. A variação média foi de 0.

Conclusão: Apesar das recomendações da Direcção Geral de Saúde, uma significativa parte dos doentes com LES não foram vacinados quer porque, aparentemente, não lhes ter sido proposto, quer pela sua fraca adesão. Apesar de uma importante incidência de efeitos laterais locais e sistémicos, não se verificou alteração da actividade do LES.

Palavras-chave: Lupus Eritematoso Sistémico, vírus H1N1, vacinação, segurança.

Abstract

Objective: To evaluate retrospectively the use of Influenza A (H1N1) vaccine and its effects on the Systemic Lupus Erythematosus (SLE) adult patients followed in the Clinical Immunology Unit of Hospital Santo Antonio – Porto, Portugal.

Material and Methods: A telephone survey was carried out, asking patients whether they had influenza A medical diagnosis. They were also asked whether the vaccine had been proposed and administered and if any local and/or systemic side effects had emerged. Patients who took the vaccine, were assessed regarding the effect of the disease activity on a numerical scale from 0 (no active disease) to 10 (very active) the month before and after vaccination.

Results: Of 318 SLE patients followed in the Unit, 186 (mean age 43 ± 13; 91% female) were contacted. Vaccination was offered to 37% of them (68) and was administered to 28 patients (41%). 72% of vaccinated patients had local adverse reactions and 31% systemic. No influenza infection was diagnosed in vaccinated patients. The mean global assessment of disease activity in the month preceding and following the administration of the vaccine was 3. The mean scale variation was 0.

Conclusion: Despite the Health Portuguese Department recommendations for H1N1 vaccine, a significant number of SLE patients were not vaccinated either because they had not been proposed to, either by their poor compliance. Although a significant incidence of local and systemic side effects there was no change in SLE activity.

Keywords: Systemic Lupus Erythematosus, H1N1 virus, vaccination, safety.

INTRODUCTION

Systemic erythematous lupus patients are at a higher risk (around twice regarding the general population) of developing infectious pathologies.[1-3] Such predisposition is also dependent on corticosteroid and/or other immunosuppressant drugs used for the disease control.[4,5]

Vaccines are a safe and effective way of preventing some types of infections. Since the 70ties that several authors debate the issue of vaccines and the possibility of autoimmune diseases to become acute.[6-10] Recently and after several years of discussion, it was demonstrated that the antibody production after vaccination can be reduced.[11,12] However, their safety and efficacy are kept.[13-15] In this sense it is strongly recommended

Clinical Immunology Unit, Hospital Santo António, Porto Hospital Centre, Porto, Portugal

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1. Flu diagnosis

a) Has a doctor made a flu diagnosis on your condition?

Yes	No

b) When was made the diagnosis?

c) Had you confirmed positive results for the Flu A virus (H1N1)?

Yes	No

2. Flu A vaccine?

a) Has a physician recommended the Flu A vaccine to you?

Yes	No

b) Has the Flu A vaccine been administered to you?

Yes	No

3. Adverse reactions to Flu A Vaccination

a) Did you have any of the local adverse reactions: swelling, redness, heat or pain?

Yes	No

b) TDid you have any of the following general adverse reactions> fever, muscular pain, joint pain or increased lymph nodes?

Sim	Não

4. Repercussion in the disease activity

a) How do you evaluate Lupus activity in the month preceding the vaccination?

0	1	2	3	4	5	6	7	8	9	10

The best possible — The worst possible

b) How do you evaluate Lupus activity in the month subsequent to the vaccination?

0	1	2	3	4	5	6	7	8	9	10

The best possible — The worst possible

Questionnaire.

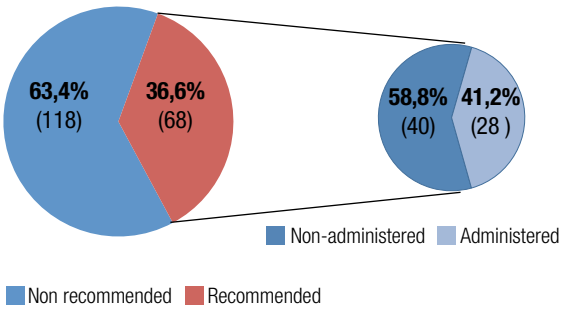
FIG. 1

the vaccinations against flu in patients with autoimmune pathology.[16, 17]

By the end of 2009, H1N1 infection has raised the alert in the world population. On the 11th June 2009, the World Health Organization has declared the first pandemia by influenza in the last 41 years. In Portugal, during the pandemic stage, 192.294 cases were reported, being the first on the 18th week of 2009 and the last in the 6th week of 2010.[18]

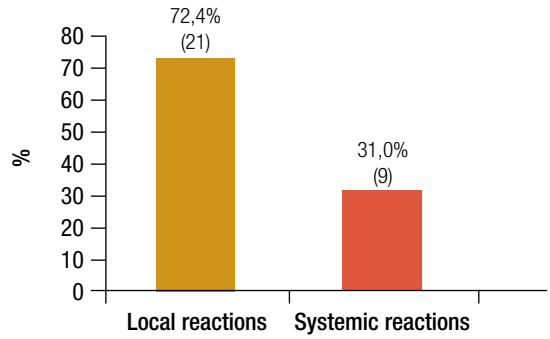
In a way to reduce the morbidity and mortality and the speed the disease is spreading, albeit the scarcity of the studies, it was proposed by the Health General Directorate, the vaccination to populations in risk, namely diseases under immunosuppression or with chronic pathology.[19]

The vaccine against the infection by flu A virus



Vacinação nos doentes com LES (n=186).

FIG. 2



Adverse reactions in vaccinated patients (n=28). Note: a patient may have simultaneously local/systemic adverse reactions

FIG. 3

acquired in Portugal had a commercial name of Pandemrix®. It was an inactive vaccine by fragmented virions with AS03 adjuvant, with a composition of squalene, DL-αtocopherol and polysorbate 80. It had residual traces of egg proteins, ovalbumin, formaldehyde, gentamicin sulphate and sodium deoxycholate. The vaccine was administered in a single dose by intramuscular route, in the deltoid muscles preferably in primary health care.[19]

In the sense of evaluating the use of the flu A vaccine and its repercussions in a Portuguese population with SLE was carried out such study.

MATERIAL AND METHODS

Retrospective study on the use of flu A vaccine in patients with a diagnosis of Systemic Erythematosus Lupus, according to the criteria of the *American College of Rheumatology* (ACR),[20] followed in the Clinical Immunology Unit of Hospital de Santo António, Porto Hospital Centre – Porto, Portugal. Demographic data were collected consulting the clinical files. In this stage were excluded all patients without a telephone contact. Subsequently a phone survey was carried out on 15th March 2010 where it was assessed the number of individuals with a flu diagnosis made by a doctor and with results confirming H1N1 in the period included from week 18 of 2009 and week six of 2010. They were also enquired whether the vaccination had been proposed to them, if they had taken it and if there had been any local adverse reactions (edema, redness, heat and pain) and/or systemic (fever, myalgia, arthralgia and adenopathies). In patients to whom the vaccine was given, the repercussion on the autoimmune disease activity was evaluated according to a score given by the patient in a number scale from zero (non-active disease) to 10 points (very active disease) in the previous and following month of vaccination (*Fig. 1*).

RESULTS

In the Clinical Immunology Unit 318 patients with an SLE diagnosis have been followed. From these 132 were excluded, 96 did not answer the phone and 36 did not show a contact telephone number in the clinical file. The average age of the 186 patients included in the current study was of 43 ± 13 years, with 91% female.

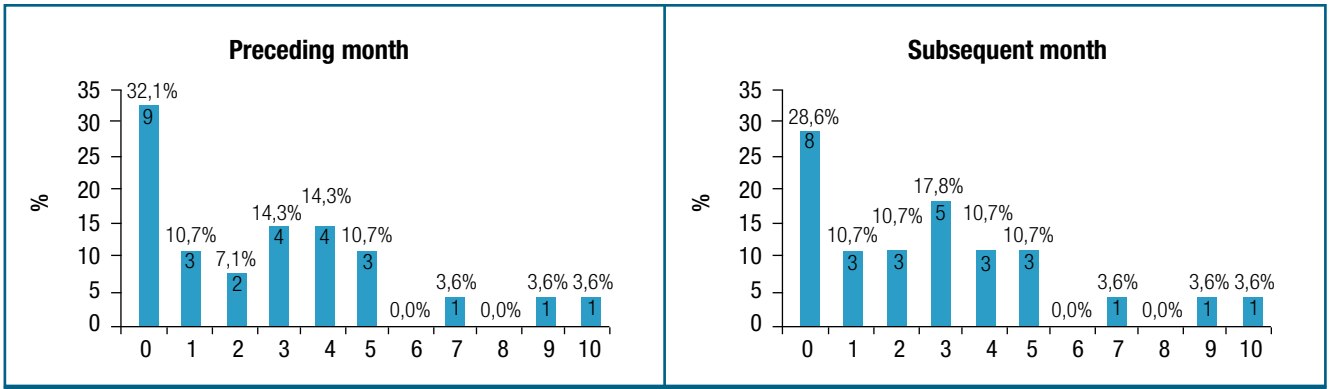
It was verified that the flu clinical diagnosis was made to 17% of the sample, in which 4% was confirmed in laboratory as H1N1 infection. In none of these vaccine was given.

It was verified that the vaccination had been recommended to 37% of the sample (68 patients), and given to 28 patients (41%) (*Figure 2*).

From the 28 patients vaccinated (15% of the total of contacted patients) 72% presented local adverse reactions and 31% systemic reactions. In none there was a diagnosis of flu.

Regarding the general evaluation of the autoimmune disease activity in the previous month to vaccination, most patients were at number zero of the numeric scale with an average of 3 (*Figure 4*). In the subsequent month evaluation, most patients were also at number zero with an average of 3 (*Figure 4*).

Therefore the mean variation of the numeric sca-



Distribution by numeric scale to the global evaluation of the autoimmune disease in the preceding and subsequent month to the vaccination.

FIG. 4

le was zero (*Table 1*) and the variation mode of the numeric scale was also zero.

DISCUSSION

The epidemiologic distribution of this sample is in accordance with the known for the disease, [21, 22] predominantly in the female gender (9:1) and in younger ages.

Flu A vaccine was proposed to less than half of patients (37%) both by hospital physicians as for primary health care physicians. Such fact may be due on one hand to some skepticism by the medical profession regarding the H1N1 infection, and on the other hand to the quick introduction of this vaccine in the market, overcoming some of the rules for its commercialization.

In the same way, only 41% of patients to whom the vaccine was recommended, took it. The pressure from the social media and the consequent disinformation conveyed by them, deteriorated by shorter and shorter periods of consultation making difficult the physician – patient relationship can explain such situation.

TABLE I

Average, mode and respective variation of the numeric scale to evaluate the autoimmune disease in the preceding/subsequent month

	Preceding month	Subsequent month
Average	3	3
Mode	0	0
Average of the numeric scale variation = 0		
Mode of the numeric scale variation = 0		

Vaccinated patients presented a high percentage of adverse reactions, both local (72%), as systemic (31%), when compared to the numbers emerging and a summary of product characteristics. However they are similar when compared with a reference study by Greenberg at al,[23] reporting 56.3% of local adverse reactions and 53.8% of systemic reactions in healthy individuals.

In spite of some heterogeneity in the distribution of a numeric scale typical of SLE patients, most of them are found to have a disease with low activity (average 3, mode 0) whether in the previous month or in the following month to the vaccine administration. As expected its use did not lead to a significant difference in the disease activity.

Other studies, carried out in similar periods testing the vaccine against flu A in a population of autoimmune patients, presented overlapping results. In the widest published cohort, in 572 SLE patients, no change in the disease activity following the vaccine administration was detected.[24] In cohorts by Gabay et al[25] and Elkayan et al[26] identical results were also reported.

In this sense the recommendation for vaccination against the flu in the SLE population is reinforced. The treble vaccine for the season 2011/2012 (carrying H1N1 strain) should be recommended to the lupus population.

Notwithstanding the agreement and importance of the results obtained, we chose to highlight some limitations on this study. The big sample dimension

and the need of a quick contact due to the urgency and actuality of the subject led to the option of carrying out a telephone survey. However, its consequent limitation to patients with a telephone and to those who answered it, associated to a retrospective evaluation of the disease activity after the vaccine, conditioned eventually to obtain some results in the survey carried out. In the same way, the use of a scale easy to interpret and apply in preference of an internationally validated scale to evaluate the disease activity, can limit some other conclusions reached and its generalization for the reminder of the LSE population. Lastly, we consider that the sample characterization regarding the L suppressants therapy would widen the range of conclusions.

CONCLUSION

With this study the concept that the vaccination in individuals with autoimmune diseases can be beneficial, avoiding occasional infections in the future and a possible deterioration of underlying diseases, without triggering any immunologic dysfunction after active immunization is reinforced.

One comes to the conclusion that in spite of the Health Directorate recommendations, a significant part of SLE patients were not vaccinated. Notwithstanding the incidence of local entities systemic adverse effects, no changes on SLE activity, at the time of the H1N1 vaccine were recorded.

The publication of the results obtained and a better clarification of the lupus population can improve the implementation and compliance of the vaccine against the flu. ■

References

1. Glück T, Muller-Ladner U. Vaccination in Patients with Chronic Rheumatic or Autoimmune Diseases. Clinical Infectious Diseases 2008;46:1459-1465.

2. Alarcon GS. Infections in systemic connective tissue diseases: systemic lupus erythematosus, scleroderma, and polymyositis/dermatomyositis. Infect Dis Clin North Am 2006;20:849-875.

3. Bouza E, Moya JG, Muñoz P. Infections in systemic lupus erythematosus and rheumatoid arthritis. Infec Dis Clin North Am 2001;15:335-361.

4. Bernatsky S, Hudson M, Suissa S. Anti-rheumatic drug use and risk of serious infections in rheumatoid arthritis. Rheumatology (Oxford) 2007;46:1157-1160.

5. Glück T, Kiefmann B, Grohmann M, Falk W, Straub RH, Scölmerich J. Immune status and risk for infection in patients receiving chronic immunosuppressive therapy. J Rheumatol 2005;32:1473-1480.

6. Ristow SC, Douglas RG Jr., Condemi JJ. Influenza vaccination of patients with systemic lupus erythematosus. Ann Intern Med 1978;88:786-789.

7. Louie JS, Nies KM, Shoji KT, et al. Clinical and antibody responses after influenza immunization in systemic lupus erythematosus. Ann Intern Med 1978;88:790-792.

8. Brodman R, Gilfillan R, Glass D, Shur PH. Influenza vaccine response in systemic lupus erythematosus. Ann Intern Med 1978;88:735-740.

9. Williams GW, Steinberg AD, Reinertsen JL, Klassen LW, Decker JL, Dolin R. Influenza immunization in systemic lupus erythematosus. A double-blind trial. Ann Intern Med 1978;88:729-734.

10. Herron A, Dettleff G, Hixon B et al. Influenza vaccination in patients with rheumatic diseases. Safety and efficacy. JAMA 1979;242:53-56.

11. Holvast A, Huckriede A, Wilschut J et al. Safety and efficacy of influenza vaccination in systemic lupus erythematosus patients with quiescent disease. Ann Rhem Dis 2006;65:913-918.

12. Abu-Shakra M, Press J, Varsano N, et al. Specific antibody response after influenza immunization in systemic lupus erythematosus. J Rheumatol 2003;30:2295-2296.

13. Wallin L, Quintilio W, Locatelli F, Cassel A, Silva MB, Skare TL. Safety and efficiency of influenza vaccination in systemic lupus erythematosus patients. Acta Reumatol Port 2009;34:498-502.

14. Stojanovich L. Influenza vaccination of patients with systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA). Clinical and Developmental Immunology 2006;13:373-375.

15. Mercado U, Acosta H, Avendaño L. Influenza vaccination of patients with systemic lupus erythematosus. Rev Invest Clin 2004;56:16-20.

16. Van Assen S, Agmone-Levin N, Elkayam O et al. EULAR recommendations for vaccination in adult patients with autoimmune inflammatory rheumatic diseases. Ann Rheum Dis 2011; 70(3):414-422.

17. Van Assen S, Elkayam O, Agmon-Levin N et al. Vaccination in adult patients with autoimmune inflammatory rheumatic diseases: a systemic literature review for the European League Against Rheumatism evidence-based recommendations for vaccination in adult patients with autoimmune inflammatory rheumatic diseases. Autoimmun Rev 2011 2011; 10(6):341-352.

18. Flu – Statistical Information. Direcção-Geral da Saúde 2010 http://www.portaldasaude.pt/NR/rdonlyres/E1F27E5D-3A2D-43DE-950A-26FEC84F6816/0/dadosestat%C3%ADsticosGripeA.pdf. Access on the 29th October 2011.

19. Vaccination campaign against the pandemic flu virus H1N1 (2009). Circular Normativa n.º17. Direcção-Geral da Saúde. 14th October 2009 http://www.dgs.pt. Access on the 29th October 2011.

20. Classification and Response Criteria for Rheumatic Diseases. American College of Rheumatology. 1997 http://www.rheumatology.org/practice/clinical/classification/index.asp. Access on the 23rd October 2010.

21. Wallace JD. Dubois' Lupus Erythematosus. Philadelphia: Lippincott Williams & Wilkins, 2007:34-44

22. Vasconcelos C. Epidemiologia Clínica do Lúpus Eritematoso Sistémico no Norte de Portugal:2007:71-73.

23. Greenber ME, Lai HM, Hartel GF et al. Response to a Monovalent 2009 Influenza A (H1N1) Vaccine. N Eng J Med 2009; 361:2405-2413.

24. Saad CG, Borba EF, Aikawa NE et al. Immunogenicity and safety of the 2009 non-adjuvanted influenza A/H1N1 vaccine in a large cohort of autoimmune rheumatic diseases. Ann Rheum Dis 2011; 70(6):1068-1073.

25. Gabay C, Bel M, Combescure C et al. Impact of synthetic and biologic disease-modifying anti-rheumatic drugs on antibody responses to the AS03--adjuvanted pandemic influenza vaccine: a prospective, open-label, parallel--cohort, single-center study. Arthritis Rheum 2011; 63(6):1486-1496.

26. Elkayam O, Amir S, Mendelson E et al. Efficacy and safety of vaccination against pandemic 2009 influenza A (H1N1) virus among patients with rheumatic diseases. Arthritis Care Res (Hoboken) 2011; 63(7):1062-1067.