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Association between chronic stress and immune response to influenza vaccine in healthcare workers

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ABSTRACT

Introduction: Chronic stress can influence immune response to vaccines. Healthcare workers are exposed to stressors and biological hazards, the health effects of which may be prevented through vaccination.

Objectives: This study aims to evaluate the association between stress in nurses and: (1) insufficient response to influenza vaccine, assessed one month after vaccination (T_1); (2) the drop in haemagglutination-inhibition (HAI) antibodies (ab) six months after vaccination (T_6).

Methods: A nested case–control study was carried out with 136 healthy hospital nurses. Individual interviews, the *General Health Questionnaire* (GHQ_{12}) and *Maslach Burnout Inventory* (MBI-HSS) were applied in order to determine the presence of stress, using the triangulation method at the beginning of the study (T_0). Influenza vaccine was administered and titres of HAI above each strain composing influenza vaccine before vaccination (T_0), at T_1 and T_6 were assessed.

Results: There was no statistically relevant (5%) relationship between stress and the insufficient immune response to the vaccine at T_1. Nevertheless, there was an association between stress and the drop in HAI ab AH_1 at T_6, when we assessed stress by the triangulation method using an interview ($p = 0.006$), GHQ_{12} ($p = 0.045$) and combination of criteria ($p = 0.001$), even after multivariate analysis (respectively, $p = 0.01$, $p < 0.05$ and $p = 0.002$). The odds ratios were, respectively, 3.64, 2.73 and 5.22.

Conclusions: The association we found, between chronic stress and the drop in HAI ab at T_6, corroborates the hypothesis that stress can negatively influence immune response. Therefore, it seems reasonable to consider this issue when we implement vaccination programmes for healthcare workers.

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Stresse crónico e a imunidade à vacina contra a gripe em profissionais de saúde

Palavras-chave:
Anticorpos
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Vacina contra a gripe
Stresse

R E S U M O

Introdução: O stresse crónico pode influenciar a resposta imunitária à vacinação. Os profissionais de saúde estão expostos a stressores de natureza profissional e ainda a agentes biológicos cujos efeitos poderão ser prevenidos pela vacinação.

Objetivos: Estudar a associação entre a presença de stresse e (1) a "insuficiente" resposta imunitária à vacina contra a gripe, avaliada um mês após a vacinação (T_1); (2) a redução dos títulos de anticorpos dirigidos às hemaglutininas (HAI) seis meses após a vacinação (T_6).

Métodos: Realizou-se um estudo caso-controlo incorporado num estudo de coortes com a participação de 136 enfermeiros hospitalares saudáveis. Realizaram-se entrevistas individuais e aplicaram-se os questionários *The General Health Questionnaire* (GHQ_{12}) e *Maslach Burnout Inventory* (MBI-HSS) para determinação da presença de stresse crónico pelo método da triangulação, no início do estudo (T_0). Foi administrada a vacina contra a gripe e determinou-se os títulos de HAI dirigidos a cada estirpe componentes da vacina contra a gripe, antes da vacinação(T_0), em T_1 e em T_6.

Resultados: Não se encontrou associação significativa (5%) entre a presença de stress e a "insuficiente" resposta à vacina contra a gripe em T_1. Contudo, encontrou-se uma associação entre a presença de stress e a diminuição do título de HAI dirigidos à estirpe A(H_1N_1) em T_6 quando se avaliou a presença de stresse pelo método da triangulação usando a entrevista (p=0,006), o GHQ_{12} (p=0,045) e a combinação dos três critérios (p=0,001), que se manteve após análise multivariada (respetivamente p=0,01, p<0.05 e p=0.002). Os *odds ratio* ajustados foram de 3,64, de 2,73 e de 5,22.

Conclusões: A associação encontrada entre a presença de stresse crónico e a redução do título de HAI em T_6 vem apoiar a hipótese de que o stresse poderá influenciar negativamente a manutenção dos títulos de anticorpos, mesmo em indivíduos adultos não idosos. Assim, parece razoável considerar este aspeto quando se pretende implementar programas de vacinação dirigidos a profissionais de saúde.

Introduction

Healthcare workers are exposed to many stressors, some of them related with organisational work conditions and others, more specific to this profession, related with their activity of caring for the ill.[1–3]

Chronic stress and burnout seem to be very common in nurses.[4–6] For example, López-Castillo and colleagues found high levels of emotional disturbance determined by the General Health Questionnaire (GHQ_{28}) in 39% of hospital nurses.[7]

Amongst the consequences of chronic distress, whether they are related or not with work, are the possible effects on the immune system, including effects on the immune response to vaccination.

Healthcare workers are strongly advised to be vaccinated against influenza in order to protect themselves against the disease, reduce staff absenteeism and minimise the risk of nosocomial transmission to the patients they take care of. Vaccination is a possible model for immune response, testing mostly the humoral immune response. Vaccinated people develop antibodies (ab) that bind and neutralise the virus, in most cases ab against the surface glycoprotein hemagglutinin. Those ab can be used as markers of protection against the disease,[8] caused by strains that are similar to the vaccine composition.

According to meta-analysis by Segerstrom and Miller, chronic exposure to stressors such as taking care of spouses with dementia, unemployment and suffering from physical disability is associated with a smaller ab response to influenza vaccine.[9] Some reviews also suggest that chronic stress is associated with a smaller ab response to influenza vaccine.[10–12]

Generally speaking, studies evaluating the association between chronic stress and immune response to influenza vaccine showed relatively consistent results in old people. In those people, chronic exposure to stressors was associated with chronic anxiety and symptoms of depression and a lower response to influenza vaccine, in comparison to a control group.[13–17]

The use of a standardized dose of antigen which promotes a good immune response in most adults, could make it difficult the detection of the influence of chronic stress in the immune response to vaccination in younger adults, with a robust immune system.

Older people have a weaker immune system, related with age, so this could be an explanation for the greater consistency of results showing a negative association between chronic stress and immune response to vaccines in them. Vedhara and colleagues did not find any association between taking care of spouses with multiple sclerosis and ab response to influenza vaccine in adults under the age of 55.[18]