Efficacy of The Influenza Vaccine in Multiple Sclerosis Patients: A Systematic Review and Meta-Analysis

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Background

Pathogenesis: Multiple sclerosis (MS) is a neurodegenerative disease thought to be of autoimmune origin.[1] An unknown environmental insult and genetic predisposition are believed to trigger MS.[1] The underlying immune mechanisms that mediate initiation and progression of MS are not fully elucidated, however, these mechanisms are thought to include inappropriate activation of lymphocytes and macrophages directed against nerve-insulating myelin sheaths autoantigens.[1] The resulting inflammatory response is thought to involve TNF-α, nitric oxide, and IL-6.[1] This continual attack can lead to myelin stripping and eventual axon breakage leading to neuron loss.[1]

Influenza risk: Due to the aberrant immune systems in MS patients and the immunosuppressive therapies often used as treatment, these patients are at high risk of infections.[2] One such infection with high morbidity and mortality in immunosuppressed patients is the influenza virus, which affects between 9.3-49 million people in the US every year. [3] There are four strains of the influenza virus with strains A and B causing the seasonal epidemics annually.[4] Influenza A can be further subdivided into H1N1 and H3N2.[4] There are two lineages of the influenza B virus – Victoria and Yamagata.[4]

Influenza vaccine: The seasonal influenza vaccine is either trivalent made up of both subtypes of influenza A viruses and one influenza B virus or quadrivalent that includes the addition of another influenza B virus.[4] The vaccine comes in inactivated, recombinant, or live-attenuated forms.[4] Yearly administration of the influenza vaccine is recommended for all healthy patients.[4]

Purpose: There has been previous research on multiple sclerosis patients who have received the influenza vaccine however, much of it focuses on safety and relapse rates.[5] Studies that focus on the immune response mounted against the vaccine in MS patients are scant. This study serves to compile this previous research into a systematic review and meta-analysis to provide a comprehensive picture of the efficacy of the influenza vaccine in MS patients.

Hypothesis: Patients with multiple sclerosis will be able to mount an adequate immune response comparable to that mounted by healthy controls against the influenza vaccine.

Methodology

Literature review: A literature review was conducted to identify studies focused on the efficacy of the influenza vaccination in MS patients. To find relevant articles, several keywords were used in various databases to search for the articles which include: ”multiple sclerosis,” “influenza,” “vaccine,” “vaccination,” “efficacy,” “seroprotection,” and “seroconversion.” Articles were initially selected based off titles and abstracts. Reference lists were manually scanned for additional studies that could be included.

The studies selected used multiple sclerosis patients as the population of interest irrespective of the disease duration, treatment regime, or severity of the disease. The studies also looked at the efficacy of the vaccination quantified by antibody titers. Selected articles were then rescreened based on their full text. Articles that did not meet the aforementioned criteria or duplicates were removed.

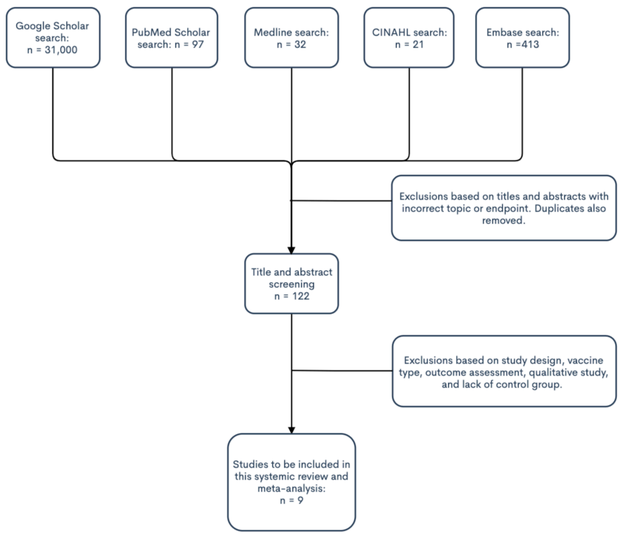

Figure 1: Flowchart of study selection process for systematic review and meta-analysis

Meta-analysis: The articles were then reviewed and the data extracted for the meta-analysis. Sample size, patient demographics, therapies, definitions of experimental groups, and vaccination types were pulled from all articles into an excel sheet. Articles reporting seroconversion and seroprotection were compiled into a separate excel sheet.

The risk differences were calculated with a 95% CI. The results were displayed on forest plots. To evaluate the studies for heterogeneity, chi-square tests and I^2 statistic were utilized. A value of 0.05 was the level of significance for the chi-square tests and I^2 values ≥ 75% was indicative of high heterogeneity.

Results

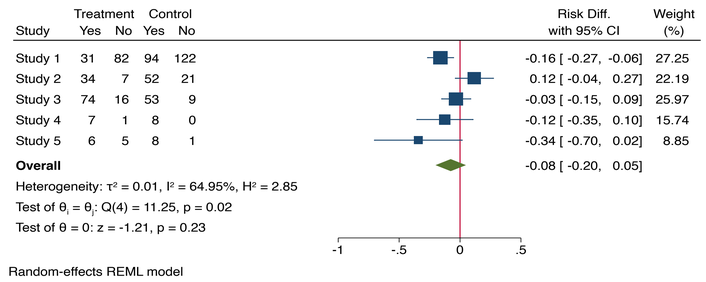

Figure 2: Forest plot for the risk difference of response rate for influenza H1N1 between MS patients and healthy controls

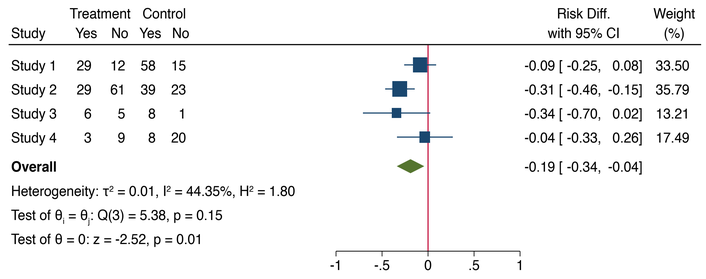

Figure 3: Forest plot for the risk difference of response rate for influenza H3N2 between MS patients and healthy controls

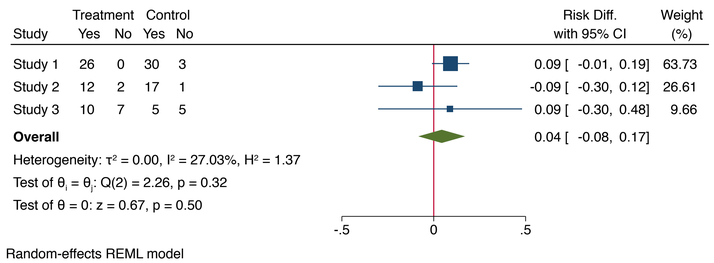

Figure 4: Forest plot for the risk difference of response rate for influenza A between MS patients and healthy controls

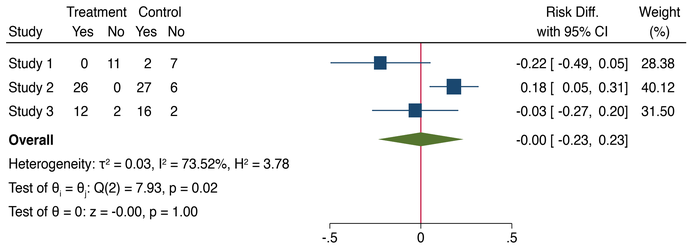

Figure 5: Forest plot for the risk difference of response rate for influenza B between MS patients and healthy controls

Results

- No overall significant treatment effect on H1N1
- No overall significant treatment effect on H3N2
- No overall significant treatment effect on influenza A
- No overall significant treatment effect on Influenza B
- The treatment affect, while not significant, was stronger (I^2) for the H1N1 and H3N2 virus than the influenza A of B virus
- Due to missing or incomplete data, study size varied by analysis

Conclusion

Discussion: Based on the results, MS patients appear to be able to mount an adequate immune response to the influenza vaccine compared to healthy controls consistent with previous literature. Although it appears the MS patients’ treatments may have some effect on this immune response. The vaccine should thus be continued to be recommended to these patients as the data shows it to be efficacious.

Limitations:

- The sample size was small due to the limited amount of studies weakening the statistical significance of the study.
- Article compilation and data extraction were not performed in duplicates
- Disease duration, sex, age, or medication regime was not corrected for during data analysis
- Data appears to be heterogenous

Future implications: Additional clinical trials measuring the efficacy of the influenza vaccine in MS patients are needed in order to have more conclusive data.

References