Effectiveness and safety of tetanus vaccine administration by intramuscular vs. subcutaneous route in anticoagulated patients: Randomized cinical trial in primary care

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BACKGROUND

Although tetanus is a disease of low incidence in Spain, it is an important public health problem due to the high associated mortality rate. Annual reports of registered cases show a gradual fall, with an average of 10 cases per year between 2009 and 2015, resulting in 18.4% being lethal.

METHODS AND MATERIALS

Design and study population

Prospective, double-blind clinical trial comparing tetanus-diphtheria vaccine administration routes, intramuscular (IM) vs. subcutaneous (SC) injection, in patients with oral anticoagulants. ISRCTN69942081. Patients treated with oral anticoagulants, 15 health centers, Vigo (Spain). Sample size, 117 in each group.

Outcome variables

Safety analysis: systemic reactions and, at the vaccine administration site, erythematic, swelling, hematoma, granuloma, pain. Efectiveness analysis: differences in tetanus toxoid antibody titers. Independent variables: route, sex, age, baseline serology, number of doses administered.

Analysis

We conducted a descriptive study of the variables included in both groups (117 in each group) and a bivariate analysis. Fewer than 5% of missing values. Imputation in baseline and final serology with the median was performed. Lost values were assumed to be values missing at random. We conducted a descriptive study of the variables and compared routes. For safety,multivariate logistic regression was applied, with each safety criterion as outcome and the independent variables.Odds ratios (ORs) were calculated. For effectiveness, a generalized additivemixedmodel, with the difference between final and initial antibody titers as outcome.

RESULTS

A previously published protocol was used across the 6-year study period. The breakdown by sex and route showed: 102 women and 132 men; and 117 IM and 117 SC, with one dose administered in over 80% of participants. There were no differences between groups in any independent variable. The second and third doses administered were not analyzed, due to the low number of cases. In terms of safety, there were no severe general reactions. Locally, significant adjusted differences were observed: in pain, by sex (male, OR: 0.39) and route (SC, OR: 0.55); in erythema, by sex (male, OR: 0.34) and route (SC, OR: 5.21); and in swelling, by sex (male, OR: 0.37) and route (SC, OR: 2.75). In terms of effectiveness, the model selected was the one adjusted for baseline serology.