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Epidemiology of snakebite in Europe: Comparison of data from the literature and case reporting

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ABSTRACT

A better assessment of the incidence and mortality due to envenomation should improve the antivenom supply and consequently management of snakebites. Currently, in most countries, notification of snakebite is insufficient and irregular. An alternative is to consider data from the literature to estimate the incidence and mortality. The gaps and bias resulting from this method can be corrected using a meta-analytic model adjusted with a randomized coefficient, which provides an average incidence and mortality taking into account the relative weight and representativeness of each sample. The aim of the present study is to compare the results of the application of the meta-analytic model with the national notifications of snakebites in different European countries. To achieve this goal, a questionnaire was sent to health services of all European countries asking for the incidence, mortality and some parameters defining the population at risk of snakebites in Europe. Notifications were compared with the results of a recently published meta-analysis of literature data. Results showed an acceptable agreement, although significant differences in the incidence of snakebites occurred in some countries. The discussion emphasizes the limitations regarding notifications and underlines the potential biases that restrict the reliability of data from the literature. Finally, pending reliable notification of snakebites in all European countries, analyzing data from the literature is likely to be an acceptable and simple solution.

1. Introduction

Snakebite is, even in Europe, an underestimated medical emergency (Chippaux, 2012). Treatment of envenomation requires the administration of antivenom, the supply of which is regulated and expensive (Chippaux, 2012; De Haro, 2012). A better estimate of the incidence and severity of envenomation could facilitate its management by health services (Chippaux, 2008) and could help in assessing therapeutic needs and optimizing care. In addition, it would provide a decisive argument in advocating the integration of envenomation in the overall strategy to control neglected tropical diseases, as requested by the World Health Organization (WHO, 2010). However, the irregular availability of reliable data is also observed in industrialized countries, including those in the European Union.

Without standardized notification of snakebites by health services, case report is irregular and insufficient. Currently most of the available information comes from medical literature in which the data are processed using a

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random meta-analytical model (Chippaux, 2012). This model provides the incidence and mortality of snakebites with a confidence interval of 95%, and estimates the prevalence of envenomation in children and other age groups, sex distribution, location of bites, clinical severity of the envenomation, frequency of the use of antivenoms, and occurrence of adverse events after administration of antivenom. However, these estimates have limitations assessed by the Higgins score (I^2), which reflects the heterogeneity of the studies in terms of methodology, number of patients and representativeness (Borenstein et al., 2009). First of all, publication bias - authors' motivations to publish their results - may overestimate the incidence and severity of envenomation by selecting either the most remarkable clinical cases from a medical standpoint, or hospitals which attract higher number of patients for specific reasons (such as: distribution of the ecological niches of snakes, better technical facilities, reputation of medical staff, etc.), which makes the random model ineffective. In addition, integration of geographic variability in the model is likely to be inadequate, even if studies are grouped into more or less homogeneous areas considering the local climate, ecology and economy. Finally, the patient's therapeutic choice and the peculiarities of snakebite management have no direct impact on the incidence, but affect the use of health care, which could have a significant impact on the catchment population of the health centers and thus, the denominators used to calculate incidence.

To undertake this study from a complementary standpoint, a questionnaire was sent to health authorities in each European country asking them to provide the number of snakebites treated in health facilities, and all information available, following the model of recently developed studies in Spain (Saz-Parkinson et al., 2012; Amate Blanco and Conde Espejo, 2012). These results were compared to data from a recently published meta-analysis (Chippaux, 2012) to assess the accuracy of the latter and analyze the reasons that could explain any discrepancy. This work aims to evaluate the relevance of the meta-analysis model and suggest some corrections to improve the predictions of the model.

2. Materials and methods

2.1. Questionnaire

We sent a questionnaire to the Ministry of Health of 20 countries of the European Union (EU), even those lacking venomous snakes, through the Institute of Health Information of the Ministry of Health, Social Policy and Equality of Spain, and its counterparts in each country of the EU.

The questionnaire explicitly regarded snakebites notified by hospitals to the national health services based on their coding system for hospital discharges. The questionnaire asked for all data, from the earliest date possible for which validated information was available. Details on snakebite notification were requested, notably if the diagnosis was known at the time of admission or if it was assessed during hospitalization. Different registration codes could be used in different countries, either ICD9 code (989.5 Venom: bites of venomous snakes, lizards, and spiders. Tick paralysis) or ICD10 (T63.0: Snake venom). In addition, the following information was also requested:

- Year of discharge
- Hospital location (region, province or city)
- Main diagnosis code (the diagnosis which led to hospital admission)
- Sex of patient
- Age of patient
- Code at the time of hospital admission (whether it was an emergency admission or a programmed admission)
- Code at the time of discharge (whether the discharge occurred due to cure, voluntary discharge, transfer to another institution, death or any other cause)
- Length of stay (number of days in hospital for each case or patient)

The information obtained from the health authorities is referred to as "reported" or "notified" data in this work.

2.2. Meta-analysis

The data, as well as the method used for the meta-analysis are detailed elsewhere (Chippaux, 2012). Briefly, a systematic search based on keywords within bibliographic databases (both Medline® and Inist®-CNRS) brought together 62 epidemiological articles (i.e. including at least 5 cases) covering the period 1980 to 2010. For each country, annual mean population during the period under review was obtained from official documents of the United Nations (http://www.un.org/esa/population). The data were analyzed using meta-analysis software (Comprehensive Meta Analysis v. 2.2.050 software; Biostat®, Englewood, NJ, USA). The meta-analysis provides the average of the variable, with a confidence interval of 95% according to the number of patients and total population covered in each study. The Higgins index reflects the respective weight of each study in the overall analysis and was used to assess the heterogeneity of the studies ($I^2 < 25\% =$ low heterogeneity; $25\% < I^2 < 50\%$ acceptable heterogeneity; $I^2 < 50\% =$ high heterogeneity).

Regional analyses were performed in the three main areas in Europe, North, Central and South, according to zoological (distribution of venomous species), climatic and economic criteria specified elsewhere (Chippaux, 2012). National analyses were performed using data from the same items for each country (Table 1). We did not find any article with data from Belgium, Lithuania and Romania. Regarding Denmark, on the one hand, we used historical data available between 1900 and 1947 (Marquart, 1951) and, on the other hand, studies published for Norway and Sweden, countries which are close by and have similar climatic, environmental and economic conditions, which showed a remarkably low heterogeneity (Chippaux, 2012).

Data calculated using the meta-analytical model are referred to as "forecasts", "estimates" or "predictions" in this work.

Finally, statistical comparisons were performed using the χ^2 when the variables had a normal distribution and non-parametric tests (Kruskal–Wallis) when the