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Dose-response modelling of staphylococcal enterotoxins using outbreak data

Laurent Guillier*, Hélène Bergis, Florence Guillier, Véronique Noel, Frédéric Auvray, Jacques-Antoine Hennekinne

ANSES, Food Safety Laboratory, Department of microbiological food contaminants, 14 rue Pierre et Marie Curie, 94706 Maisons-Alfort, France

Abstract

Staphylococcal food poisoning (SFP) is one of the most common food-borne diseases and results from the ingestion of staphylococcal enterotoxins (SEs). Yet, small amount of data are available for establishing a dose response. The objective of this work was to build a dose response relation based on the systematic investigations carried out during recent years in France. Over the period 2010-2014, more than 60 SFP outbreaks involving SEs, mainly from France, were microbiologically investigated. The enterotoxins were characterized as well as quantified. Attack rates, appearance times and natures of symptoms collected during epidemiological investigations were related to microbiological data. The outbreaks collected focused on enterotoxins SEA, SEB, SEC, and SED. Distribution of appearance times of symptoms and their natures were not influenced by the type of enterotoxins. The US EPA benchmark dose (BMD) methodology was then used to establish dose response. Attack rates of SFP outbreaks were modelled as a function of ingested doses and a BMD have been estimated for SEA.

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Keywords: benchmark dose; dichotomous data; uncertainty

1. Introduction

Staphylococcal food poisoning (SFP) is one of the most common food-borne diseases and results from the ingestion of staphylococcal enterotoxins (SEs). SEs are highly heat resistant, preformed, large peptides produced by some *S.*

* Corresponding author. Tel.: +33-(0)149772644.
E-mail address: laurent.guillier@anses.fr

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aureus strains. According to the official European Union data from 2013[1], 386 foodborne outbreaks were attributed to *Staphylococcus* spp. in 12 Member States, representing 7.4% of all reported foodborne outbreaks.

Doses of approximately 20 to 100 ng have been reported effective in causing SFP[2]. However, these concentrations are taken from a limited number of food outbreaks. Because SE concentrations are rarely measured, there here is small amount of data available for dose response. The objective of this work was to establish a dose response based on the systematic investigations carried out during recent years in France.

2. Materials and Methods

2.1. Enterotoxin identification and quantification

Food involved in SFP outbreaks were tested for the presence of enterotoxins (A to E) according to the European Screening Method of the European Union Reference Laboratory (EURL) for coagulase positive Staphylococci (CPS), consisting of an extraction followed by a dialysis concentration step coupled to detection with the Vidas SET2 kit, a combined qualitative detection test (BioMerieux, Marcy l'Etoile, France). SE-positive samples were further analyzed by quantitative double sandwich ELISA, the confirmatory method of the EURL for CPS[3] to quantify the amount of each enterotoxin produced.

2.2. Nature of effects

The distribution of reported symptoms for the selected SFP was represented with Venn diagrams. The diagrams were constructed using the venneuler R package. The distribution of mean incubation periods (i.e. the onset of symtoms after consuming contaminated food) observed in the 63 outbreaks as well as the distribution of individual incubation periods within an outbreak were characterized using R 3.1 software and the "fitdistrplus" package[4].

2.3. Dose response modelling

The benchmark dose (BMD) approach was used. It involves dose-response modeling to obtain BMDs, i.e. dose levels corresponding to specific response levels. For this, we selected (i) the outbreaks on which to base BMD calculations, (ii) the benchmark response value, (iii) tested the models to use in computing the BMD, (iv) assessed the models fit and carried out and model comparison and (v) computed the confidence limit for the BMD (i.e., the BMDL). The US EPA Benchmark Dose Software[5] was used.

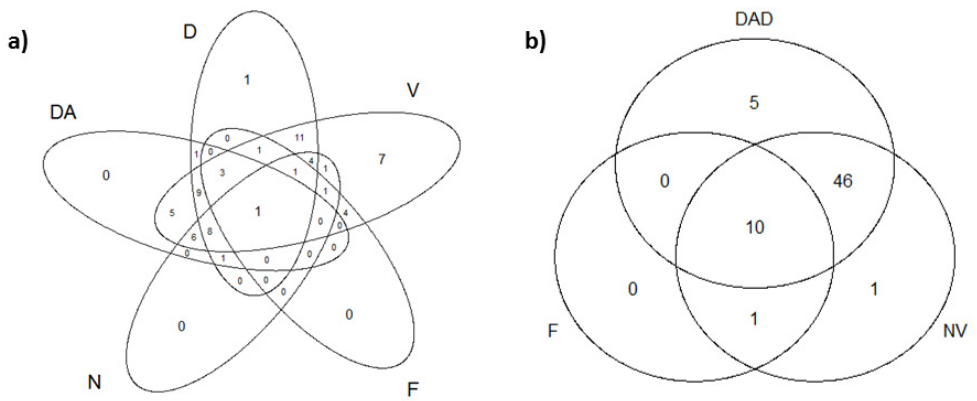

Fig. 1. Repartition of the identified symptoms in the 63 SFP outbreaks. Venn diagram with (a) individual symptoms: diarrhea (D), abdominal pain (DA), vomiting (V), nausea (N) and fever (F); and (b) grouped symptoms: abdominal pain and diarrhea (DAD), nausea and vomiting (NV) .