The Zagreb versus the Essen regimen for the post-exposure prophylaxis of Rabies: A Systematic review and meta-analysis

Introduction

India reports about 18,000 to 20,000 cases of rabies a year and about 36% of the world's deaths from the disease [1]. Despite the availability of many effective vaccines in the country, lack of awareness and poor compliance to post-exposure prophylaxis (PEP) regimens hinder successful PEP in animal bite victims[2]. The World Health Organization (WHO) recommendations for intra-muscular PEP include the 5-dose Essen regimen (1-1-1-1-1) and the 4-dose Zagreb regimen (2-1-1). It has been postulated that a simple and effective immunization procedure is likely to increase patient compliance and rabies coverage[3].

Comment [NM1]: I have not added the new F data since they are recommending an altogether different regimen (1-1-1-1-1).

Also, haven't included the exact incidence of rabi in the world since WHO only reports nationwide data and makes an approximate contribution of each country to the case burden.

Aim

In this systematic review and meta-analysis, we aim to compare he Zagreb to the Essen regimen for PEP in animal bite victims and simulated PEP IN healthy volunteers, for immunogenicity on day 14 post-exposure.

Materials and methods:

- Search strategy: The PubMed, EMBASE, CENTRAL and google scholar databases will be searched for English language literature until March 2015 using the keywords 'Rabies vaccine', 'Zagreb', 'Essen'. The following specific searches will also be run: Rabies AND Zagreb AND Essen.
  Relevant articles in reference lists of published articles will be searched. The search will be performed in March 2015.

- Inclusion criteria and exclusion criteria
  All studies in our review will be selected according to the following criteria:
  1. Study participants: Animal bite victims who received PEP for rabies and healthy human volunteers who received simulated PEP
  2. Vaccine subtype and administration: trials on any subtype of the rabies vaccine administered intra-muscularly
  3. Endpoint: rabies virus neutralizing antibody (RVNA) titres on Day 14 post-exposure have been reported as a measure of immunogenicity
  4. Trial design: Controlled clinical trials will be included

- Data extraction and quality assessment

  The Cochrane collaboration's data extraction sheet and the published protocol[4] by Kannan S et al. will be used as a guideline and will be piloted on a sample study. The Cochrane risk and bias assessment tool will be used for methodological integrity. It will be integrated into the data extraction sheet.

- Outcome measurement

  The primary outcome will be RVNA titres on day 14 post exposure as a measure of immunogenicity. Safety as measured by the occurrence of local and systemic adverse events will be a secondary outcome.

- Statistical analysis

  Pooled data from the trials will be analysed using the Review Manager 5.3™

  A Forest plot will be used to summarize the results and statistical significance will be set at a P value of < 0.05. Descriptive statistics will be used where appropriate.

References:

1. Kole AK, Roy R, Kole DC. Human rabies in India: A problem needing more attention. Bull World Health Organ. 2014;92:230.
2. Mahendra BJ, Narayana DHA, Agarkhedkar S, Ravish HS, Harish BR, Agarkhedkar S, et al. Comparative study on the immunogenicity and safety of a purified chick embryo cell rabies vaccine (PCECV) administered according to two different simulated post exposure intramuscular regimens (Zagreb versus Essen). Hum Vaccin Immunother. 2015 Feb;0.
3. Liu H, Huang G, Tang Q, Li J, Cao S, Fu C, et al. The immunogenicity and safety of vaccination with purified Vero cell rabies vaccine (PVRV) in China under a 2-1-1 regimen. Hum Vaccin. 2011;7(March 2015):220–4.
4. Kannan S, Gogtay N, Um T. Interaction of calcium channel blockers and grapefruit juice in healthy adults (Protocol). 2014;(12).