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Review

Variation in the reporting of outcomes among pregnant women with epilepsy: a systematic review

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ABSTRACT

Studies on pregnant women with epilepsy should evaluate both neurological and pregnancy outcomes. We undertook a systematic review of the literature of studies on pregnant women with epilepsy to collate the outcomes reported, and the quality of outcomes report in these studies.

We searched major electronic databases (from 1999 until January 2015). Two independent reviewers selected studies and extracted data on study design, the risk of bias of the studies, journal impact factor and the quality of reported outcomes. We assessed the quality outcomes report using a six items standardised tool (score range 0–6).

There were 70 different outcomes reported in 232 studies (maternal neurological (13/70, 19%), fetal and neonatal (28/70, 40%), and obstetric outcomes (29/70, 41%)). Most studies reported on major congenital fetal abnormalities (103/232, 44%), followed by live birth (60/232, 26%). Quality of the reported outcomes was poor (mean 1.54, SD 1.36). It was associated with journal impact factor ($p = 0.007$), but not with study design ($p = 0.60$), or risk of bias ($p = 0.17$).

The outcomes reported in studies on pregnant women with epilepsy varied widely, and the quality of the outcomes report was poor. There is a need to identify a set of core outcome to harmonise reporting in future clinical studies.

Contents

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Introduction

Epilepsy in pregnancy is one of the major contributory factors to maternal morbidity and mortality [1,2]. About a third of women with epilepsy experience seizure deterioration in pregnancy [3]. Often they are exposed to anti-epileptic drugs (AED) before and during pregnancy. Both uncontrolled seizures, and exposure to AEDs contribute to maternal complications [4], and adverse offspring outcomes [5].

Existing studies on epilepsy in pregnancy tend to focus on evaluation of fetal and childhood outcomes related to AED exposure [6]. The proportion of studies that report on important and clinically relevant outcome such as seizure control in pregnancy, and obstetric complications is not known. The estimated incidence of epilepsy in pregnancy is 3–4 per 1000 [7]. Given its relative rarity as a pre-existing medical condition in pregnancy, we can ill afford heterogeneity in reported outcomes. Standardised and consistent reporting leads to meaningful evidence synthesis. Identifying gaps in outcome reporting is crucial to adequately plan future studies.

Before standardising core outcome sets for studies on pregnant women with epilepsy, there is a need to map the various outcomes reported in primary studies. We undertook a systematic review to assess the range and the quality of the outcomes reported in clinical studies on pregnant women with epilepsy.

Material and methods

We undertook a systematic review in line with current recommendations using a prospective protocol [8], and reported to comply with PRISMA guidelines (Appendix 1).

Literature search

We searched major electronic databases MEDLINE, Embase, CINAHL, AMED and Cochrane Library (1999–January 2015) for studies on women with epilepsy. We combined the Mesh terms for "pregnancy", "anti-epileptic drugs", and "epilepsy" using the Boolean operators AND or OR as appropriate (Appendix 2). There were no language restrictions. We manually searched the bibliographies of relevant articles to identify papers that were not captured by electronic searches. We contacted the authors for additional data where required.

Study selection

Two independent reviewers (BHA and JT) selected the studies. We screened the abstracts and obtained the full copies of all relevant articles. Then, we evaluated the retrieved manuscripts in detail to identify studies that may be eligible for inclusion. Any discrepancies were resolved by discussion with a third reviewer (ST). We excluded studies on non-pregnant population, only on pharmacodynamics of AEDs, surveys, case series, case reports, and animal studies.

Quality assessment of the included studies

Two independent reviewers (BHA and JT) assessed the risk of bias in the included studies using the Newcastle–Ottawa Scale [9] for study selection, comparability and outcome assessment. The studies were allocated stars according to the rating. A study was awarded a maximum of four stars for selection, two for comparability, and three for ascertainment of exposure. Studies were considered to have a low risk of bias if they scored 4 stars for selection, 2 stars for comparability, and 3 stars for assessment of outcomes [9]. Studies with only 1 or no stars for selection, comparability, or outcome assessment were considered to have high risk of bias. The risk of bias was considered to be medium in studies with 2 or 3 stars for selection, 2 or 1 for comparability, and 2 stars for outcome assessment. For randomised studies we planned to assess the risk of bias using the Cochrane risk of bias assessment tool [10].

Quality assessment of reported outcomes

We assessed the quality of the outcomes reported using a standardised six items tool [11]. One point was awarded if each of the following items were met: primary outcome stated; clearly defined primary outcome; authors stated whether there were any secondary outcomes; clearly defined secondary outcomes; authors stated the rationale for choosing the reported outcomes; methods were used to enhance the quality of outcomes measurement such as the repeating measures or training in the use of measurement tools. A maximum score of 6 could be awarded for a study. We considered a score above 4 to be of high quality, 2–4 as moderate quality, and less than 2 as low quality.

Data extraction and analysis

Two independent reviewers (BHA, JT) extracted data on study design (cohort studies, case control studies, and randomised controlled trials), the outcomes reported, country of the study, type of journal (general vs. specialist), impact factor of the journal, and year of publication using pre-designed forms. Journals with an impact factor above the 95th percentile of all included studies were considered to have high impact.

We categorised the reported outcomes into three main domains: Maternal neurological, obstetric, and fetal and neonatal outcomes. We grouped similar outcomes together, and estimated the proportion of these grouped outcomes that were reported in each domain. In the maternal neurological domain, outcomes related to AED such frequency of AED use in pregnancy, AED serum levels, and AED maternal toxicity were categorised as AED related outcomes; and postnatal depression and psychosis were grouped as mental health related outcomes. In the fetal and neonatal domain, outcomes such as birth weight, neonatal height, and head circumference were categorised as anthropometric outcomes; and neonatal conditions such as acute respiratory distress syndrome, hypotonia, feeding problems, and hypoglycemia as neonatal clinical complications. In the obstetric domain, pregnancy viability outcomes included live birth, miscarriage, ectopic pregnancy, and