Annals of Epidemiology xxx (2016) 1–5

Contents lists available at ScienceDirect

Annals of Epidemiology

journal homepage: www.annalsofepidemiology.org

Brief communication

Validation of maternal recall of early pregnancy medication exposure using prospective diary data

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ARTICLE INFO

Article history:
Received 3 August 2016
Accepted 30 November 2016
Available online xxx

Keywords:
Validation studies
Mental recall
Pregnancy
Diary
Nonsteroidal anti-inflammatory agents
Serotonin and noradrenaline reuptake inhibitors

ABSTRACT

Purpose: Data about maternal recall accuracy for classifying early pregnancy medication exposure are meager. Nonetheless, studies often rely on recall to evaluate potential impact of pharmaceuticals on the developing fetus.

Methods: Right from the Start is a community-based pregnancy cohort that enrolled women from North Carolina, Tennessee, and Texas. A subset of 318 women participated in daily medication diaries initiated before conception (2006–2012). We examined nonsteroidal anti-inflammatory drugs (NSAIDs) as an example of a drug type that is difficult to study due to its intermittent and primarily over-the-counter use as well as its incomplete documentation in medical and pharmaceutical records. Selective serotonin reuptake inhibitors (SSRI) were assessed as a prescription medication comparator. Maternal recall of NSAID and SSRI use in early pregnancy was examined by comparing diary data (gold standard) to first-trimester interview.

Results: Sensitivity and specificity for recall of NSAID exposure were 78.6% and 62.3%, respectively (kappa statistic: 0.41), with 72.3% agreement for exposure classification. Sensitivity and specificity for recall of SSRI exposure were 77.8% and 99.0%, respectively (kappa statistic: 0.79), with 97.8% agreement.

Conclusions: Our findings suggest the validity of maternal recall varies with medication type and prospective data collection should be prioritized when studying early pregnancy drug exposures.

Introduction

Over 80% of women report medication exposure during the first trimester [1], yet the impact of the majority of medications on fetal development and pregnancy outcomes remains unknown [2,3]. Epidemiologic studies evaluating the safety of medication use in pregnancy frequently rely on maternal recall to assign drug exposure status. Past studies have investigated the validity of medication exposure recall through comparison of maternal self-report with pharmaceutical or medical records [4–7]. However, these sources of exposure status often overestimate prescribed medication use and fail to capture information about over-the-counter (OTC) medications [8–10].

The impact of nonsteroidal anti-inflammatory drugs (NSAIDs) on pregnancy is an area of research interest because these medications decrease prostaglandin production, which has potential to modify embryo transport, implantation, placental development, and maintenance of pregnancy [11–16]. NSAIDs are generally purchased OTC, taken intermittently, and not well documented in the medical record resulting in maternal report serving as the predominant source of exposure for related research.

Therefore, we sought to assess the validity of maternal recall of early pregnancy medication exposures by comparing self-reported exposures at the end of first trimester with diary data. Because maternal recall is influenced by drug type and pattern of use [4,5,17,18], we compare the accuracy of reporting NSAID use and selective serotonin reuptake inhibitor (SSRI) use, a prescribed medication expected to be taken daily over an extended period. We evaluated the extent of agreement in diary and interview reporting for early medication exposure status among women intending to conceive to quantify the accuracy of maternal recall in an optimized population.

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http://dx.doi.org/10.1016/j.annepidem.2016.11.015
1047-2797/

Materials and methods

Study population

Right from the Start (RFTS) is a community-based pregnancy cohort that recruited study participants in North Carolina, Tennessee, and Texas between 2000 and 2012 [19,20]. To be enrolled, participants had to speak English or Spanish, be at least 18 years old, and conceive without using assisted reproductive technologies. A subset of women enrolled between 2006 and 2012 participated in Web-based daily and weekly diaries initiated before conception. These diaries collected information about medication use, lifestyle behaviors, and a variety of symptoms. Diary participants contacted the study after first positive pregnancy test, answered baseline questions, and reported date of last menstrual period (LMP). At approximately 13 weeks of gestation, a computer-assisted telephone interview (CATI) collected information about medication exposure in the first trimester and periconception period. An analogous interview with modified language was conducted among women who had already experienced a loss by this time. To be eligible for this analysis, participants had to be enrolled before conception, become pregnant during diary participation, provide consent, and complete the first-trimester interview. This substudy was approved by the Vanderbilt University Institutional Review Board.

Medication exposure data

Retrospective data collection

Women were questioned about medications when pregnancy was confirmed and during the first-trimester CATI. Interviews targeted NSAID exposure during the periconception window and women were classified as exposed or unexposed based on report (see Appendix for questionnaire) [21]. NSAIDs were grouped by drug class, generic name, and brand name based on the Food and Drug Administration database [22]. In the same manner, women were queried about SSRI use and categorized as exposed or unexposed. The exposure window considered in this analysis was defined as 7 days before to 42 days after LMP.

Prospective data collection

In the daily diary entries, women recorded the name and dosages of the medications that they used each day. Daily diaries prompted women to record NSAID use through questions analogous to those used in the first-trimester CATI (see Appendix). Women also completed weekly diaries concerning prescribed medications. Instructions for diary participation were given over the phone and the study contact guided the participant through an electronic diary entry at this time to confirm understanding. Daily diaries were made available online at 8 PM nightly, and participants were encouraged to complete diaries promptly. To be included in the analysis, women had to be adherent to daily diary participation defined as record of an entry for 5 of 7 days a week for the daily diaries and at least 6 of the 7 weeks in the exposure window for the weekly diaries. Women were considered exposed if SSRI or NSAID use was reported at least once in either daily or weekly diaries regardless of duration or dosage of exposure.

Maternal characteristics

Maternal demographics (age, race/ethnicity, education attainment, marital status, household income), health (diabetes diagnosis, smoking status, alcohol use), and obstetric history (parity, history of spontaneous or induced abortion, and pregnancy intention) were collected at baseline or the first-trimester CATI. Pregnancy outcome was collected through maternal report and verified with medical or vital records.

Statistical analysis

Participant characteristics are presented as proportions for the entire substudy cohort and stratified by NSAID exposure status based on prospective report. Prospective and retrospective reports of early pregnancy exposure were compared for both NSAIDs and SSRIs. Sensitivity, specificity, kappa statistics, and percent agreement were calculated for both NSAID and SSRI recall using diary data as gold standard.

Recall sensitivity was calculated for different frequencies of NSAID use reported prospectively in the daily diaries. NSAID use frequency was categorized as single exposure (one record of use in the diaries), low exposure (less than one exposure for every 2 weeks on average), moderate exposure (at least one exposure every 2 weeks to one exposure a week on average), and high (at least one exposure a week on average). Recall sensitivity for NSAID use was also evaluated in terms of timing of pregnancy detection (NSAID use only before positive pregnancy test vs. any exposure after positive pregnancy test; $n = 4$ missing date of positive pregnancy test). We further evaluated recall performance stratifying subjects by maternal age, ethnicity, education attainment, annual income, parity, and history of spontaneous abortion (SAB) because these factors have been associated with reporting accuracy [4,23,24]. Analyses were conducted with STATA statistical software version 13.0 (StataCorp LP, College Station, TX).

Results

Five hundred and thirty women who participated in daily and weekly diaries became pregnant during diary participation and completed the first-trimester interview (Fig. 1). Women who were excluded for insufficient diary adherence ($n = 212$) did not differ in baseline characteristics when compared to women with complete diary data (*P*-values ranging 0.11–0.99, χ^2 test). Six of the eligible study participants had a SAB before the end of the exposure window. All six had complete diary data and were included in the final

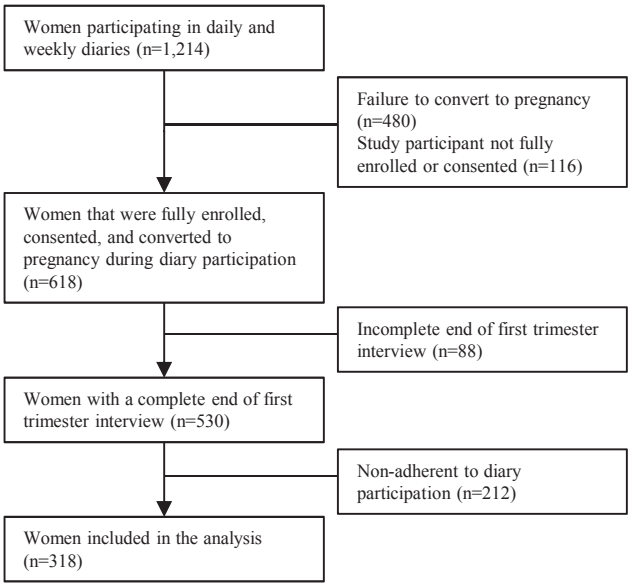

Fig. 1. Inclusion criteria for analysis, *Right from the Start* cohort, 2006–2012.