MONSTER PHASE OF ACETAMINOPHEN USE IN PREGNANCY: CURRENT VISION OF AN OLD DRUG

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ABSTRACT

In various countries, Acetaminophen [APAP] is the frequently used painkiller found in hundreds of medications during pregnancy. It has been broadly used for eras and health care professionals prefer acetaminophen as a choice during pregnancy for relieving pain and fever. Current research reports bothersome inclinations in the rate of acetaminophen exposure and related pregnancy outcome. The exposure of pregnant women to acetaminophen is of great concern. Existing literature evidence shows that acetaminophen exposure during pregnancy may lead to preterm birth, attention deficit hyperactivity disorder (ADHD), autism, male infertility, asthma in pediatrics. Therefore, the prophylactic anticipation of acetaminophen exposure can be a far-sighted approach in order to safeguard humans and wildlife from enduring dangerous effects. This article reviews the epidemiological findings and aims to shed awareness into the second generation outcome of an old drug in pregnant women.

Keywords: Acetaminophen, Neonatal exposure, Pregnancy outcome

INTRODUCTION

In the United States, more than 50% of mothers use Acetaminophen [APAP] during their pregnancy [1]. This could be due to APAP safety reports and favorable maternal-fetal safety profile (pregnancy category C). In effective doses, APAP is predominantly metabolized hepatically, swiftly forming nontoxic sulfates and glucuronides which are eliminated through urine [2]. Innon-pregnant and pregnant women, APAP metabolism, remains the same [3]. One study has demonstrated that apparent oral clearance of APAP was 58% greater and elimination half-life was 28% lesser in the pregnant women than non-pregnant women. Enhanced glucuronide conjugation and oxidation (clearance to the glutathione-derived conjugates) may contribute to greater clearance in the pregnant women. Pregnancy has no role on APAP sulphation and clearance of unchanged drug through renal means. APAP is the first analgesic of choice during pregnancy due to rapid elimination [3]. But recently, few investigational studies reported that APAP exposure during gestational period lie between 46% to 65%. APAP has become the most common drug involved in suicidal overdose and fulminant hepatic failure. It is the most common drug overdose in pregnancy. It has been proposed that APAP crosses the placenta and in toxic doses may harm the fetal and maternal hepatocytes. In fetus, it may cause hepatic necrosis. There is no association with the woman’s use of APAP after giving birth or a partner’s use. Alcohol abuse and intake of other drugs may be the causes of increased possibility to APAP toxicity. If the fetal circulation becomes saturated with APAP as a result of a maternal overdose, oxidation of APAP through cytochromeP450 enzyme system may produce toxic intermediates to cause hepatic injury in the neonate. Neonates appear to be less susceptible to hepatic injury possibly because of differences in metabolism and pharmacokinetics of the drug. The outcome of mother will generally reflect the outcome of the fetus. APAP toxicity in pregnancy is not rare and can result in significant morbidity and mortality in both the mother and the fetus. Over many years, use of acetaminophen, questions about its safety in pregnancy have been addressed by studies in different populations using different designs, but because of universal use of this medication and limitations of earlier studies, new studies continue to address the question [4]. APAP may influence the oxidative stress via disturbing inflammatory and immunological mechanisms. This effect is hypothesized to have the potential to cause an evil role in pregnancy outcome [5, 6].

Methods

The PubMed database was used to search for articles issued from 1986 to 2016, by means of the following MeSH keywords: Acetaminophen, pregnancy outcome, asthma, autism, brain development and infertility. Only studies using the English language were considered. The leading review measure was human epidemiological studies in which a bond between Acetaminophen exposure and pregnancy was appraised. Moreover, as the analysis of the limited epidemiological data could be inclined by many confounding factors, sustaining experimental research in animal models was also considered. The full texts of 47 selected articles were deemed significant and included in this review.

Acetaminophen and preterm birth

There are limited studies which suggest a possible link between APAP usage and potential teratogenic effects, other pregnancy effects and outcomes after birth and most of these studies were based on very small numbers of exposed women [7]. One of the suggested explanation for this association is inhibition of Prostacyclin (PGI2) synthesis and inequality between PGI2 (a vasodilator) and Thromboxane A2 (TXA2, a vasoconstrictor) [8, 9]. Similarly, a reduction in PGI2 synthesis could also be coupled with an augmented risk of pre-eclampsia leading to an amplified risk induced preterm birth that could not be detected in a study using only spontaneous preterm births as endpoints [10]. About 15% to 25% of preterm infants are delivered because of maternal or fetal complications of pregnancy. The principal causes are hypertensive disorders of pregnancy and severe intrauterine growth restriction which is often associated with hypertensive disorders [11]. Another study reported that mothers who took APAP at the third trimester of pregnancy were at greater risk of preterm birth following pre-eclampsia [7]. This could be a real end product of APAP through pathways such as oxidative stress.

Maternal acetaminophen administration and ADHD

APAP has the ability to cross the placenta, and lately, some studies reported that revelation to APAP consumption at the time of pregnancy may negatively affect fetal brain growth by disrupting endocrine function and snooping with maternal hormone [1, 12]. Another study found that children exposed to APAP prenatally for more than one trimester were at hyperkinetic behavior risk, particularly if the exposure was during the second and third...
outcomes of psychomotor and behavioral changes by almost 70% exposure during the gestational period to APAP increases adverse receptor effects may also predispose to autism [1, 24].

pregnant women. Large analyses of databanks and case–control blood in asthma patients [31-33].

decreased glutathione peroxidase activity in platelets and whole glutathione, a key airway antioxidant [27-30]. More than 95% to be allied with Reyes syndrome [26]. Induction of asthma by APAP cause for the current asthma outbreak [25]. From 1990s onwards during pregnancy. APAP has recently been identified as a possible APAP has lost the glamour of being well tolerated and harmless to pregnant women to OTC medications including APAP. The study reported that APAP and with offspring whose mothers had taken mild analgesics, primarily reproduction evaluated the incidence of inherited cryptorchidism

Conclusions and clinical implications

The occurrence of the different aspects of the autistic spectrum by the offspring of pregnant women who took APAP frequently leads to the believe that APAP is the etiological agent of autism [8]. However, the evidence is not conclusive.opathological effects of acute APAP intoxication in the rat fetus are associated with microcephaly and behavioral alterations [6, 8]. The data suggest that the use of APAP during pregnancy may contribute to the occurrence of autism spectrum disorder in offspring.

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