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Pregnancy outcomes following the use of thiocolchicoside

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ABSTRACT

Thiocolchicoside is a commonly used muscle relaxant in orthopedic, rheumatologic or musculoskeletal disorders to treat painful muscle spasms. It is contraindicated in pregnancy and lactation. There is no previously published experience with thiocolchicoside exposure during pregnancy. In this observational study, we collected and evaluated 18 pregnancy outcomes of the women referred to our prenatal consultation service for thiocolchicoside exposure between 2007–2012, and offspring were followed up until 2 years of age. There were 16 live births, 1 spontaneous abortion and 1 elective termination of pregnancy. No major birth defect was observed. The mothers and their babies were free of perinatal complications. No growth or developmental abnormalities were found during follow-up period. Our findings add information on inadvertent use of thiocolchicoside in pregnancy. Further large prospective cohort studies are required to investigate this issue.

1. Introduction

Biomechanical and hormonal changes during pregnancy impact the musculoskeletal system that can lead to pain. Approximately half of all pregnant women suffer from low back pain. There are many nonpharmacologic interventions for management of musculoskeletal pain during pregnancy, such as manual therapy, water therapy, stabilization belts [1]. Regular exercise, postural modifications, dietary changes, relaxation and stress reduction may help reduce pregnancy-related muscle soreness. The benefits and potential fetal risks of pharmacological options should be considered if drug therapy is required [2].

Thiocolchicoside, a semi-synthetic sulfur derivative of colchicoside, is a muscle relaxant drug with anti-inflammatory and analgesic properties. It is indicated for the treatment of painful muscle spasms in patients with orthopedic, rheumatologic or musculoskeletal disorders. Its effectiveness for muscle pain and contractures, particularly for low-back pain, has been shown by some clinical studies [3–5]. Thiocolchicoside and other formulations containing the drug are contraindicated in pregnancy and lactation, as well as in children or for long-term conditions.

As illustrated in Fig. 1, thiocolchicoside is marketed outside the United States and some countries in European Union under different trade names. It is available for use by mouth, by injection into the muscles and by application to the skin. In recent years, there have been various case reports of thiocolchicoside-induced adverse events, such as epileptic seizures [6] and hepatic injury [7], and preclinical animal studies suggesting convulsant activity of the drug [8]. In 2013, the recent safety alert of European Medicine Agency (EMA) has recommended restriction on the long term and systemic use of thiocolchicoside based on the potential aneugenic properties of the drug [9]. This report reviewed unpublished experimental data, and there have been no cases of cancer, congenital abnormalities, spontaneous abortion and impaired male fertility in the literature.

To our knowledge, there are no data regarding thiocolchicoside use in pregnancy. Therefore, the risk assessment of the prenatal drug exposure is difficult. Here we report the first case series describing the obstetric and neonatal outcome following thiocolchicoside use during pregnancy.

2. Methods

We collected and evaluated pregnancy outcomes of the women referred to our prenatal consultation service for thiocolchicoside exposure between 2007–2012. All contacts to our service were initiated via gynaecologists. At the first contact, a detailed patient history form was used to record the following information: maternal demographic data and obstetric history, consanguineous marriage, smoking and alcohol consumption, X-ray and all drug exposures (dose, duration and timing in pregnancy). After

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0890-6238/

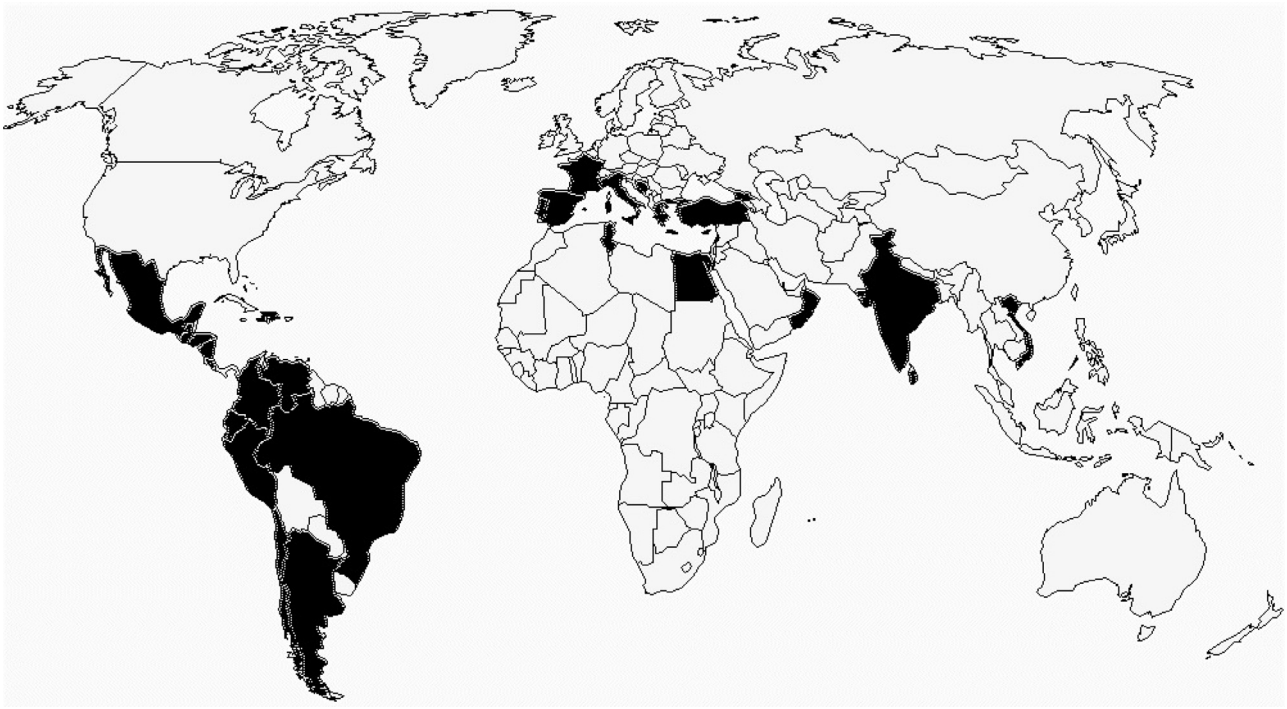

Fig. 1. Thiocolchicoside use by country. The dark areas represent the countries in which thiocolchicoside is marketed.

counseling about thiocolchicoside exposure, we followed up the women and their babies. Each newborn baby was checked at birth for signs of problems or complications. All patients were informed that their medical information will be used for scientific research. Informed consent was obtained from all participants.

Follow-up controls after birth were monthly performed by the family physicians or pediatricians during a 2-year period. Weight, supine length and head circumference measurements were recorded at the periodic visits, plotted and analyzed on the growth chart for turkish children. Additionally, cognitive, fine-gross motor, social- emotional and language development were assessed at each visit. After the expected day of delivery, data on pregnancy outcomes were obtained by telephone interview with the women and their family physicians. In this study, we investigated major congenital and structural abnormalities in infants which were described by Merks and colleagues [10]. In addition, we evaluated other adverse pregnancy outcomes including preterm birth, low birth weight and miscarriage among women exposed to thiocolchicoside in pregnancy.

3. Results

During the 5-year period, a total of 18 pregnancies with maternal thiocolchicoside exposure were identified. There were no patients lost to follow up. The median daily thiocolchicoside dose was 8 mg (range 4–16 mg). Except for four women who received intramuscular thiocolchicoside (case 4, case 8, case 13, case 16), all women used thiocolchicoside orally.

Treatment indications were myalgia ($n = 6$), lumbago ($n = 4$), fibromyalgia ($n = 3$), lumbar hernia ($n = 2$), soft tissue injury ($n = 1$), arthralgia ($n = 1$) and ankylosing spondylitis ($n = 1$). Except for one woman treated with misoprostol (case 6), there were no patients who received another teratogenic drugs. Two women treated for depression (case 12, case 15), and there was one woman with type 2 diabetes (case 14). Except for the diabetic mother and one mother treated with etofenamate at week 25 (case 4), all patients took one or more nonsteroidal anti-inflammatory drugs at the same time. Further data on maternal characteristics and obstetrical history of thiocolchicoside exposed women are shown in Table 1.

Of the 18 pregnancies, there were 16 live births, 1 spontaneous abortion and 1 elective termination of pregnancy. A patient (case 6), who took misoprostol and diclofenac with thiocolchicoside, underwent induced abortion. One spontaneous abortion was observed in a patient (case 12) receiving sertraline and etodolac at the same time. One preterm birth occured in a woman (case 13) who had consanguineous marriage.

Table 2 presents the pregnancy outcomes and newborn characteristics. Neither a congenital defect nor low birth weight was observed. Each newborn baby was checked at birth for signs of problems or complications. The physical examinations revealed normal findings with no birth defects. Except for one preterm baby, all babies and mothers were free of perinatal complication. No congenital or developmental abnormalities were found during a 2-year follow-up period. The physical growth and neurological development were uneventful for the babies at 2 years of age.

4. Discussion

At present, this is the first prospective case series investigating pregnancy outcomes following maternal use of thiocolchicoside. We found only 18 women, who were treated with thiocolchicoside and referred for medical consultation on prenatal drug exposure. Except for one preterm baby, 15 healthy babies were delivered at term. Of the other two pregnancies, there was one spontaneous abortion, and one woman decided to terminate the pregnancy.

Thiocolchicoside is one of the most commonly used muscle relaxant and marketed under twenty different brand names in our country. Despite the widespread use of this drug, the sample size of this study, also the number of teratology consultations, remained small maybe because the clinicians used the pregnancy risk classifications to evaluate the risk of drug exposure in pregnancy and had low risk perception of thiocolchicoside exposure in years 2007–2012. In terms of pregnancy risk evaluation, thiocolchicoside has an interesting history, from “unknown” to “contraindicated”.