Perinatal Outcomes with Tamsulosin Therapy for Symptomatic Urolithiasis

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Purpose: Medical expulsive therapy represents an effective adjunctive treatment for nonpregnant patients with symptomatic urolithiasis. Tamsulosin is classified by the FDA (Food and Drug Administration) as a category B medication. However, to our knowledge no published data exist for human pregnancy. We explored the safety and efficacy of tamsulosin therapy for symptomatic urolithiasis occurring during pregnancy.

Materials and Methods: We retrospectively identified patients treated with tamsulosin for stone disease during pregnancy at the Mayo Clinic during 2000 to 2014. This medical expulsive therapy cohort was matched 2:1 to pregnant women with symptomatic urolithiasis during pregnancy who did not receive medical expulsive therapy. Groups were compared using linear mixed models for continuous variables and exact conditional logistic regression models for nominal variables to take into account correlation due to matching.

Results: A total of 27 patients receiving medical expulsive therapy comprised the study cohort. Median duration of antepartum tamsulosin exposure was 3 days (range 1 to 110), occurring during the first, second and third trimester in 3 (11%), 11 (40.7%) and 18 (67%) patients, respectively. Mean gestational age at delivery was 38.1 weeks (SD 2.4) and 6 (22%) infants were born preterm. All infant birthweights were considered appropriate for gestational age, and no cases of spontaneous abortion, intrauterine demise or neonatal congenital anomalies were encountered. Comparison between the medical expulsive therapy and control groups demonstrated no significant differences in maternal or infant outcomes for any of the examined variables.

Conclusions: Tamsulosin medical expulsive therapy does not appear to be associated with adverse maternal or fetal outcomes and may be considered as adjunctive therapy for urolithiasis during pregnancy.

Key Words: tamsulosin, pregnancy, urolithiasis, drug therapy

Abbreviation and Acronyms

MET = medical expulsive therapy

SIDS = sudden infant death syndrome

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ALTHOUGH pregnancy does not intrinsically increase the risk of symptomatic episodes, the management of urolithiasis during pregnancy can be challenging.[1–3] In an effort to mitigate anesthetic and radiation exposure during gestation, initial management of clinically stable pregnant cases typically consists of a period of observation. Several studies have reported the spontaneous stone passage rate in pregnant women to be as high as 70% to 80%.[4–8] However, a more recent analysis has suggested that over diagnosis and suboptimal followup may contribute to artificially

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inflated passage rates, with the true rate of spontaneous passage being as low as 48%.[9] Conservative management will fail in a significant number of patients who will consequently require procedural interventions with accompanying surgical and anesthetic risks. The addition of medical expulsive therapy could potentially increase the incidence of and decrease the time to spontaneous stone passage in pregnant patients. However, the safety of antepartum off label use of tamsulosin, the most common alpha blocker medication, remains unstudied to date.

MET using tamsulosin or nifedipine has been assessed in the nonpregnant population. A 2007 meta-analysis revealed a significantly higher rate and shorter time to spontaneous passage with tamsulosin therapy compared to narcotic therapy alone.[10] The FDA currently defines tamsulosin as a category B medication for pregnant patients. Animal reproduction studies have failed to demonstrate risk to the fetus and there are no adequate, well controlled studies in pregnant women. A PubMed® search using the terms "tamsulosin" and "pregnancy" revealed no reports of use during pregnancy. Therefore, we evaluated the safety of antepartum tamsulosin use and effects on neonatal outcomes.

MATERIALS AND METHODS

After obtaining internal review board approval we retrospectively identified patients 18 years old or older treated with tamsulosin for stone disease during pregnancy (MET group) between January 1, 2000 and January 1, 2014 with a minimum of 90 days postpartum followup. Potential patients were identified by searching for hospital discharge ICD-9 codes V22, V23, 591, 592 and 788. Individual medical records were then abstracted for demographic information, presenting symptomatology and urological intervention, and previous medical, obstetric, family and social histories. In addition, we reviewed the timing, dose and duration of tamsulosin use. Compliance with outpatient therapy was presumed. All patients were counseled before treatment regarding the risks and benefits of off label use of tamsulosin for MET. Outcome variables included medication side effects, rates of spontaneous abortion and intrauterine fetal demise, and mode of delivery. Head circumference, congenital malformations, Apgar scores, intensive care unit admission and mortality were also recorded.

The MET cohort was matched 2:1 with a group of pregnant patients with symptomatic urolithiasis during pregnancy who did not receive MET (control group) based on the variables of antepartum surgical stone procedure, maternal age less than 20 years, tobacco use during pregnancy, small for gestational age infant and premature birth (gestational age less than 37 weeks). All selected variables, excluding postpartum surgical intervention, are identified risk factors for adverse neonatal outcomes.[11,12]

Score tests derived from exact conditional logistic regression models were used to compare dichotomous variables. F tests derived from linear mixed models were used to compare continuous variables.

RESULTS

A total of 27 women were treated with tamsulosin MET during the study interval. Maternal demographics and perinatal outcomes for the MET and control groups are displayed in table 1. Onset of symptoms occurred in the first, second and third trimesters in 5 (19%), 10 (37%) and 12 (44%) patients in the MET group compared to 7 (13%), 26 (48%) and 21 (39%) control patients, respectively. Gestational age at symptom onset did not differ significantly between the groups. All pregnancies were singleton.

Presenting symptom (pain, nausea/emesis, sepsis, fever, urinary tract infection, dysuria, gross hematuria, urinary urgency or urinary frequency) did not differ between the groups. One patient presented with a urinary tract infection without flank pain, but all other patients exhibited pain as their presenting symptom. Additional patient symptoms and testing are summarized in table 2. In the MET group the median duration of tamsulosin use was 3 days (range 1 to 110), with exposure in the first, second and third trimester in 3 (11%), 11 (40%) and 18 (67%) patients, respectively. Four women had tamsulosin exposure during multiple trimesters. Further details on the timing and duration of tamsulosin exposure for each patient can be seen in table 3. None of the patients treated with tamsulosin reported any medication related side effects.

Table 1. *Maternal demographics and outcomes*

	MET Group		Control Group		p Value
No. pts	27		54		
Mean maternal age at delivery (SD)*	28.42 (4.15)		29.42 (4.67)		0.35
Mean BMI (SD)	29.14 (7.33)		26.22 (6.16)		0.60
Mean Charlson comorbidity index (SD)	0.04 (0.19)		0.09 (0.35)		0.46
Median gravidity (IQR)	3	(2–5)	3	(2–4)	0.69
Median parity (IQR)	1	(0–3)	1	(0–2)	0.11
No. spontaneous abortion	0		0		Not applicable
No. alcohol use during pregnancy (%)	2	(7.4)	5	(9.3)	1.00
No. smoking during pregnancy (%)*	5	(18.5)	10	(18.5)	1.00
No. illegal drug use during pregnancy (%)	0		2	(3.7)	0.56
No. family history of urolithiasis (%)	11	(42.3)	1	(1.9)	<0.0001
No. prior episode of urolithiasis (%)	16	(59.3)	16	(29.6)	0.029
No. gestational hyperemesis (%)	0	(0)	2	(3.7)	0.56
No. gestational diabetes (%)	3	(11.1)	4	(7.4)	0.67
No. placenta previa (%)	1	(3.7)	0	(0)	0.33
No. preeclampsia (%)	0	(0)	1	(1.9)	1.00
No. gestational hypertension (%)	2	(7.4)	0	(0)	0.11
No. pyelonephritis (%)	0	(0)	2	(3.7)	0.56
No. cesarean delivery (%)	11	(40.7)	16	(29.6)	0.48
Median days postpartum hospitalization (IQR)	2	(2–3)	2	(2–3)	0.43

*Variable used for matching.