Use of the Levonorgestrel Intrauterine Device in Women With Type 2 Diabetes

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IN BRIEF Women with type 2 diabetes are less likely to receive prescriptions for contraceptives despite the fact that diabetes is associated with an increased risk of maternal and fetal complications. In the largest case series to date examining use of the levonorgestrel-releasing intrauterine device (LNG-IUD) in women with type 2 diabetes, we demonstrate that the LNG-IUD is safe and effective and does not affect glycemic control in women with type 2 diabetes. In this study of 115 women under the age of 55 years with type 2 diabetes who had an LNG-IUD placed between 2007 and 2012, we found low rates of pregnancies, expulsions, and other complications in every age category and disease stratification. Thirty-nine patients had A1C data before and up to 2 years after placement, and there was no significant change in A1C (mean A1C decrease of 0.17, 95% CI –0.76 to 0.43). This study will enable evidence-based contraceptive counseling for women with type 2 diabetes.

Type 2 diabetes in women of reproductive age increases the risk of maternal perinatal mortality and complications in pregnancy (1) and may lead to fetal and neonatal complications, including major congenital malformations, spontaneous abortion, and macrosomia (2–4). Given the significant risks of type 2 diabetes to both maternal and neonatal health, it is particularly important that women with type 2 diabetes have access to safe and effective contraception. The purpose of this study was to assess the safety and effectiveness of the levonorgestrel-releasing intrauterine device (LNG-IUD) in women with type 2 diabetes.

The Medical Eligibility Criteria for Contraceptive Use from the World Health Organization (5) and the Centers for Disease Control and Prevention (CDC) (6) assign four possible safety categories for the use of contraceptives among women with various complex or chronic medical conditions (summary available at www.cdc.gov/reproductivehealth/contraception/mmwr/mec/summary.html). These categories are *1*) no restriction for the use of the contraceptive method for a woman with that condition, *2*) advantages of using the method generally outweigh theoretical or proven risks, *3*) theoretical or proven risks of the method usually outweigh the advantages, and *4*) risks are unacceptably high if this contraceptive method is used by a woman with that condition. The LNG-IUD receives a category 2 rating for use among women with type 2 diabetes. A systematic review in 2013 concluded that there was limited evidence for the safety and effectiveness of the LNG-IUD in women with type 2 diabetes (7). However, some experts have suggested that the category 2 rating for the LNG-IUD in women with diabetes may be overly cautious (8). To our knowledge, there has been no new research on the topic since that time.

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The lack of data on the LNG-IUD for patients with type 2 diabetes may contribute to differences in clinical care. Women with diabetes are less likely to be offered highly effective reversible contraception and more likely to undergo sterilization procedures than women who do not have diabetes (9). In conversations about contraception, providers may recommend less effective nonhormonal methods (10–12) or methods with lower user satisfaction (13), putting these patients at higher risk of unintended pregnancies. Finally, women with diabetes may particularly benefit from the noncontraceptive effects of the LNG-IUD, such as treatment for heavy menstrual bleeding, the prevention and treatment of endometrial hyperplasia, and prevention of endometrial cancer (14), conditions for which women with diabetes are at increased risk (15).

Studying the safety and effectiveness of the LNG-IUD among women with type 2 diabetes is especially important given the limited contraceptive options available to these women. Estrogen-containing hormonal contraceptives (including the oral contraceptive pill, transdermal patch, and vaginal ring) have been found to increase the risk of thrombosis and cardiovascular disease among women with certain medical conditions (16). These estrogen-containing contraceptives have been assigned a category 3/4 rating by the Medical Eligibility Criteria for Contraception Use for women with longstanding diabetes or diabetic vascular complications, indicating that they should generally not be used in this population (17). Depot medroxyprogesterone acetate (DMPA), a progestin-based contraceptive, has also been assigned a category 3 by the CDC for women with diabetes and vascular disease because of the evidence that it may negatively disrupt cholesterol, lead to weight gain, and increase the risk of thrombosis (6).

In healthy women, the LNG-IUD is highly effective and very safe (18). We expect the same to be true for women with type 2 diabetes due to low systemic absorption of the progestin hormone in the LNG-IUD (19). Although DMPA has been associated with negative effects on cholesterol, weight gain, and thrombosis, the same has not been found for other progestin-based contraceptives, including the LNG-IUD (20,21). Furthermore, a small case series of 11 women with type 2 diabetes using the LNG-IUD found little or no influence on glycemic control in their 12 months of follow-up (22). Our hypothesis is that the LNG-IUD is safe and effective in women with type 2 diabetes and does not affect glycemic control.

Methods

We conducted a retrospective chart review of all women previously diagnosed with type 2 diabetes who had an LNG-IUD placed at the University of Washington in Seattle between 1 January 2007 and 1 March 2012. Our data came from a retrospective database created in March 2012 that included all women who had a long-acting reversible contraceptive placed at the University of Washington or its affiliated clinics as early as 2007, the year in which the University of Washington instituted electronic medical records. We used similar methods as in the study by Vu et al. (23) on long-acting reversible contraceptive use among patients with cardiovascular conditions at the University of Washington during the same time period. The University of Washington institutional review board approved this study (IRB application no. 42808). Microsoft Amalga Unified Intelligence System was used to extract data from the electronic medical records from the University of Washington Medical Center, Harborview Medical Center, and other University of Washington–affiliated clinics. Study data were collected and managed using REDCap electronic data capture tools hosted at the University of Washington (24). We identified subjects using ICD-9 codes for type 2 diabetes and related complications, as well as procedure and pharmacy codes for LNG-IUD placement. At the time of this study, the University of Washington was still using ICD-9 codes for primary billing. All charts were individually reviewed to confirm accuracy of the electronic extraction. Two researchers independently reviewed a subset of charts in duplicate and compared results to confirm congruence between reviewers.

Subjects were excluded if they were over 55 years of age or using the LNG-IUD for postmenopausal indications. A1C laboratory data were included in the analysis if a patient had an A1C value within 3 months before to 10 days after LNG-IUD placement and had an A1C value 3–24 months after placement while the device was still present. These time constraints were chosen because the A1C value demonstrates glycemic control over the prior 3-month period, and these criteria adequately reflect blood glucose levels before and after LNG-IUD placement. We excluded A1C data for individuals who were having an LNG-IUD replacement or switching from another form of hormonal birth control to remove the possibility of effects on glycemic control related to exogenous sex hormones before IUD placement. We compared mean values of A1C before and after IUD placement to determine whether there was a significant change in glycemic control using a two-sample, two-tailed *t* test and used this to determine 95% CIs. To determine whether patients with recorded A1C values adequately represented individuals without data recorded, we compared the two groups using two-sample, two-tailed *t* tests for polynomial data (e.g., weight and age) and used χ^2 tests for data of proportions (e.g., medication use). We analyzed patient characteristics, indications, and complications after LNG-IUD placement and compared these data to population means using one-sample *t* tests for proportions. All

analyses were performed in Stata 14 (StataCorp, College Station, Tex.).

Results

We identified 115 women under the age of 55 years with type 2 diabetes who had an LNG-IUD placed during the study period. The characteristics of this patient group are outlined in Table 1. Patient characteristics are presented by age-group, since circumstances for IUD placement, contraceptive indication, medications, and diabetes control may vary by age. We included patients in our results whose primary indication was not contraception, since women use contraceptives for a complex variety of reasons, and we did not expect key results such as complications or glycemic control to vary based on indication. The majority of women in this study had multiple medical comorbidities, and many were prescribed insulin, statins, and other medications, as described in Table 1.

The IUD placements that occurred in the operating room were primarily in the context of dilation and curettage or hysteroscopy procedures. A total of 5% of the LNG-IUD devices were placed within 1 week of an elective abortion, and 20% were placed within 6 weeks postpartum. Of the 23 patients who had postpartum IUD insertions, 3 of the 8 women who had an immediate postpartum IUD placed (at the time of delivery) discontinued the LNG-IUD, whereas 2 of the 15 women who had a delayed postpartum IUD placed (within 6 weeks of delivery) discontinued the IUD.

Four subjects (3.5%) experienced IUD expulsion, 16 (13.9%) had a subsequent clinic visit in which they reported abdominal or pelvic pain, and 2 (1.7%) were diagnosed with pelvic inflammatory disease. Of the IUDs that were expelled, one had been placed at a 6-week postpartum visit, whereas the other three had been interval placements.

No patient became pregnant with an IUD in place; however, one patient had a presumed luteal-phase IUD insertion, with negative urine pregnancy test at the time of IUD placement. Ten weeks after IUD placement, she was found to be pregnant at an estimated gestational age of 12 weeks. This subject underwent a surgical abortion and replacement of the IUD. One subject became pregnant after spontaneous IUD expulsion, and three subjects became pregnant after their IUD was removed because of pain or bleeding.

A total of 39 patients had A1C laboratory data both before and after IUD placement per criteria, described in Methods. With a mean A1C at the time of placement of 8.5% (range 4.3–14.6%) and a mean A1C after placement of 8.48% (range 4.3–14.6%), these patients exhibited no significant change in A1C after LNG-IUD placement during the mean follow-up time of 287 days (mean decrease of 0.17%, 95% CI −0.76 to 0.43%). As outlined in Table 2, the demographics and characteristics of the 39 patients who had A1C data both before and after IUD placement were all statistically similar

TABLE 1. Patient Characteristics by Age-Group

	Age ≤35 Years	Age >35 Years	All Patients
Patients, *n*	49	66	115
Weight at IUD placement, mean ± SD, lb	225.0 ± 55.5	271.5 ± 92.1	252.2 ± 82.0
BMI at IUD placement, mean ± SD, kg/m^2	45.9 ± 14.2	38.1 ± 8.1	42.8 ± 12.7
Nulligravid	7 (14.3)	11 (16.7)	18 (15.6)
Nulliparous	9 (18.4)	18 (27.3)	27 (23.4)
Insurance status			
Private	15 (30.1)	28 (42.4)	43 (37.4)
Public	26 (53.1)	28 (42.4)	54 (46.9)
Self-pay	2 (4.1)	5 (7.6)	7 (6.1)
Unknown	6 (12.2)	5 (7.6)	11 (9.6)
Time of placement			
Interval clinic visit	19 (38.8)	32 (48.4)	51 (44.4)
Operating room	6 (12.2)	24 (36.3)	30 (26.1)
Postpartum	17 (34.7)	6 (9.1)	23 (20)
Vaginal delivery	6 (12.2)	3 (4.5)	9 (7.8)
Caesarean section	11 (22.4)	3 (4.5)	14 (12.2)
Post-abortion	6 (12.2)	0 (0)	6 (5.2)
Replacement	1 (2.0)	4 (6.1)	5 (4.3)

TABLE CONTINUED ON P. 254 →

TABLE 1. Patient Characteristics by Age-Group, *continued from p. 253*

	Age ≤35 Years	Age >35 Years	All Patients
Diabetes control pre-IUD placement			
Diabetic eye disease	2 (4.3)	4 (6.1)	6 (6.9)
Renal complications	3 (7.7)	3 (0.45)	6 (4.3)
Vascular insufficiency	0 (0)	3 (0.05)	3 (2.6)
Neuropathy	0 (0)	3 (0.05)	3 (3.4)
Indication			
Contraception	42 (85.7)	23 (34.8)	65 (56.5)
Menorrhagia	6 (12.2)	41 (62.1)	47 (40.9)
Pain treatment	1 (2.0)	1 (1.5)	2 (1.7)
Cancer prophylaxis	0 (0)	1 (1.5)	1 (0.9)
Medications at IUD placement			
ACE inhibitors	4 (8.2)	24 (36.4)	28 (24.3)
Angiotensin receptor blockers	2 (4.1)	13 (19.6)	15 (13.0)
β-Blockers	6 (12.2)	11 (16.6)	17 (14.8)
Calcium channel blockers	4 (8.1)	7 (10.6)	11 (9.6)
Diuretics	7 (14.2)	28 (42.4)	35 (30.4)
Insulin	18 (36.7)	28 (42.4)	46 (40.0)
Statins	5 (10.2)	30 (45.5)	35 (30.4)
Steroids	1 (2.0)	3 (4.5)	4 (3.5)
Thyroid replacement	3 (6.1)	7 (10.6)	10 (8.7)

Data are n *(%) unless otherwise indicated.*

to those patients who did not have A1C checks before and after IUD placement.

The 10 patients who had their IUD placed postpartum had a nonsignificant increase in A1C of 1.35% (95% CI −0.02 to 2.7%). The 29 patients with interval placement had a mean decrease of 0.24% (95% CI −1.06 to 0.57%). The nine patients using insulin at the time of placement in this group also had no significant difference, with a mean increase of 0.87% (95% CI −1.19 to 2.95%).

After IUD placement, 6% of patients had new diagnoses of kidney disease (presumed to be related to diabetes), 2.6% had new diagnoses of neuropathy, 2.6% had new diagnoses of retinopathy, 2.6% had new diagnoses of vascular disease, and one patient began using insulin. Most women (77.5%) were still using the IUD at the end of the study period, with a mean follow-up time of 754 days.

Discussion

This case series provides evidence that the LNG-IUD is safe and effective and does not affect glycemic control in women with type 2 diabetes. Women with type 2 diabetes using the LNG-IUD experience low rates of side effects and complications that appear to be on par with those noted in published data in women without diabetes (20). The rates of diabetes complications seen in this population are similar to those noted in other studies of patients with type 2 diabetes (25).

There were several limitations of the study. This is a retrospective case series without a comparison group of individuals without diabetes. Additionally, our subjects were all from one academic medical center, tended to be older, and had more medical comorbidities than the average patient using the LNG-IUD for contraception, all of which could limit generalizability. However, this population represents a diverse group of patients with type 2 diabetes using the LNG-IUD, and the study demonstrated safety and effectiveness that is in line with population data.

Furthermore, the size of our study was limited, particularly for the group in which we examined A1C data from before and after IUD placement. Only 39 patients met our criteria of having an A1C value within 3 months before to 10 days after LNG-IUD placement and an A1C value 3 months to 24 months after placement while the device was still in place. Our inclusion criteria for A1C data excluded a large number of laboratory values but allowed us to more reliably measure the temporal effect of the LNG-IUD on glycemic control, thereby assessing diabetes control. Because individuals with longitudinal A1C measurements and those without did not statistically differ in their characteristics, we believe that those patients with A1C values are an adequate representation of the entire sample of patients.

TABLE 2. Patient Characteristics for Patients With and Without Longitudinal A1C Data

	With A1C	Without A1C	All Patients	Difference of Means, 95% CI	*P*
Patients, *n*	39	76	115	NA	NA
Age, mean ± SD, years	36.4 ± 9.3	37.6 ± 9.3	37.1 ± 9.3	1.2 (–2.4 to 4.8)	0.51
Weight at IUD placement, mean ± SD, lb	239.7 ± 70.9	259.0 ± 87.6	252.2 ± 82.0	19.3 (–12.8 to 51.4) 2.0	0.24
BMI at IUD placement, mean ± SD, kg/m^2	41.5 ± 11.1	43.5 ± 13.5	42.8 ± 12.7	(–3.0 to 7.0)	0.43
Nulligravid	7 (17.9)	11 (14.5)	18 (15.7)	3.4 (–11.0 to 20.5)	0.64
Nulliparous	10 (25.6)	17 (22.3)	27 (23.5)	3.3 (–13.4 to 22.0)	0.69
Insurance status					
Private	12 (30.8)	31 (40.8)	43 (37.4)	10.0 (–10.2 to 28.2)	0.30
Public	21 (53.8)	33 (43.4)	54 (46.9)	10.4 (–10.1 to 30.1)	0.29
Self-pay	2 (5.1)	5 (6.6)	7 (6.1)	1.5 (–11.5 to 10.8)	0.75
Unknown	4 (10.3)	7 (9.2)	11 (9.6)	1.1 (–10.4 to 16.1)	0.85
Time of placement					
Interval clinic visit	18 (46.1)	33 (43.4)	51 (44.4)	2.7 (–17.3 to 22.9)	0.78
Operating room	10 (25.6)	20 (26.3)	30 (26.1)	0.8 (–18.3 to 17.7)	0.94
Postpartum	9 (23.1)	14 (18.4)	23 (20)	4.7 (–11.2 to 22.8)	0.55
Vaginal delivery	3 (7.7)	6 (7.9)	9 (7.8)	0.2 (–13.9 to 10.7)	0.97
Caesarean section	6 (15.4)	8 (10.5)	14 (12.2)	4.9 (–8.3 to 21.1)	0.45
Post-abortion	1 (2.6)	5 (6.6)	6 (5.2)	4.0 (–7.8 to 12.5)	0.36
Replacement	1 (2.6)	4 (5.3)	5 (4.3)	2.7 (–8.9 to 10.7)	0.51
Diabetes control pre-IUD placement					
Diabetic eye disease	5 (12.8)	3 (3.9)	8 (6.9)	8.9 (–2.2 to 23.8)	0.08
Renal complications	3 (7.7)	2 (2.6)	5 (4.3)	5.1 (–3.8 to 18.5)	0.21
Vascular insufficiency	1 (2.6)	2 (2.6)	3 (2.6)	(–11.2 to 7.0)	1.00
Neuropathy	3 (7.7)	0 (0.0)	3 (7.7)	7.7 (–0.24 to 19.48)	0.02
Indication					
Contraception	20 (51.3)	45 (59.2)	65 (56.5)	0.6 (–19.5 to 20.8)	0.95
Menorrhagia	18 (46.1)	29 (38.2)	47 (40.9)	7.9 (–12.1 to 27.8)	0.42
Pain treatment	1 (2.6)	1 (1.3)	2 (1.7)	1.3 (–5.0 to 12.3)	0.61
Cancer prophylaxis	0 (0.0)	1 (1.3)	1 (0.9)	1.3 (–7.8 to 7.1)	0.48
Medications at IUD placement					
ACE inhibitors	12 (30.8)	16 (21.1)	28 (24.3)	9.7 (–7.8 to 28.5)	0.25
Angiotensin receptor blockers	4 (10.3)	11 (14.5)	15 (13.0)	4.2 (–11.4 to 16.6)	0.52
β-Blockers	6 (15.4)	11 (14.5)	17 (14.8)	0.9 (–12.9 to 17.6)	0.90
Calcium channel blockers	5 (12.8)	6 (7.9)	11 (9.6)	4.9 (–7.1 to 20.3)	0.40
Diuretics	13 (33.3)	22 (28.9)	35 (30.4)	4.4 (–13.9 to 23.9)	0.63
Insulin	20 (51.3)	26 (34.2)	46 (40.0)	17.1 (–3.2 to 36.5)	0.08
Statins	16 (41.0)	19 (25.0)	35 (30.4)	16.0 (–3.1 to 35.2)	0.08
Steroids	2 (5.1)	2 (2.6)	4 (3.5)	2.5 (–5.3 to 14.9)	0.49
Thyroid replacement	3 (7.7)	7 (9.2)	10 (8.7)	1.5 (–12.8 to 12.2)	0.79

Data are n *(%) unless otherwise indicated.*

The only statistically valid difference between the groups was that the group with A1C data had a higher proportion of neuropathy ($P = 0.02$), but it was unclear to us how this possible confounder would influence glycemic control, especially at such a low prevalence.

Finally, because this was a case series, we cannot determine whether patients were lost to follow-up or seen for complications at other health care facilities, and we cannot determine how patients' glycemic control may have been influenced by factors such as changes to medication or lifestyle. Because the University of Washington medical system is a large network that includes inpatient and outpatient care throughout the area, it is unlikely that many patients were lost to follow-up, and we believe that their medical care was adequately captured during this study's time period.

Despite these potential limitations in generalizability and available data, our study represents the largest retrospective case series to date examining type 2 diabetes patients and the LNG-IUD. This study helps to fill a gap in the literature and demonstrates that the LNG-IUD appears to be safe and effective in the type 2 diabetes population. Several studies have shown that women with diabetes are less likely to receive prescriptions for contraceptives (9) even though pregnancy among these women carries an increased risk of maternal and fetal complications (1). Given the high satisfaction and continuation rates of the LNG-IUD among the general population (13) and the evidence provided in this study that the LNG-IUD is safe and effective in women with type 2 diabetes, the LNG-IUD should be considered a first-line contraceptive option for women with type 2 diabetes.

Duality of Interest

E.M. is a Nexplanon trainer (Merck). No other potential conflicts of interest relevant to this article were reported.

Author Contributions

B.L., T.J., and E. Micks contributed to discussion, researched data, wrote the manuscript, and reviewed/edited the manuscript. E. McCoy and S.P. contributed to discussion, researched data, and reviewed/edited the manuscript. B.L. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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