Tropical Journal of Pharmaceutical Research December 2022; 21 (12): 2707-2713
ISSN: 1596-5996 (print); 1596-9827 (electronic)

Available online at http://www.tjpr.org
http://dx.doi.org/10.4314/tjpr.v21i12.28

Original Research Article

Clinical benefit of dexmedetomidine in combination with dezocine as epidural anesthesia during cesarean delivery for pregnant women with gestational diabetes mellitus

Luxin Wei, Xiaojing Li, Kun He*
Department of Anesthesiology, The Fourth Hospital of Shijiazhuang (Obstetrics and Gynecology Hospital Affiliated to Hebei Medical University), Shijiazhuang City 050011, Hebei Province, China

For correspondence:* ***Email:* *hk20210413sci@163.com*

Sent for review: 14 June 2022 *Revised accepted: 14 November 2022*

Abstract

Purpose: *To investigate the clinical benefit of dexmedetomidine (DEX) when used in combination with dezocine as epidural anesthesia during cesarean delivery for puerperae with gestational diabetes mellitus (GDM).*
Methods: *A total of 120 puerperae with GDM admitted to The Fourth Hospital of Shijiazhuang (Obstetrics and Gynecology Hospital Affiliated to Hebei Medical University, Shijiazhuang City, China) who underwent cesarean delivery from January 2019 to January 2020 were randomly assigned to groups A and B, with 60 patients per group. Epidural anesthesia with dezocine was used on patients in both groups, while DEX was added for patients in group A. Comparison was made between the 2 groups with regard to pregnancy outcomes, pain scores, maternal and infant blood glucose levels, hemodynamic indices, hormonal levels and adverse reaction rates (ARR).*
Results: *Patients in group A had significantly better maternal and infant outcomes ($p < 0.05$), lower maternal postoperative pain scores ($p < 0.05$), lower maternal postoperative blood glucose levels ($p < 0.001$), higher infant postoperative blood glucose levels ($p < 0.001$). Furthermore, maternal incidence of adverse reactions in group A was lower than in group B ($p <0.05$). At the time point of 0.5 h after anesthesia and operation, the hemodynamic indices of puerperae in group A were significantly more stable, and levels of estradiol and prolactin were higher, relative to those in group B ($p < 0.05$). However, group A had a lower chemotaxin levels at immediate postoperative period and 1 day after operation than group B ($p < 0.05$).*
Conclusion: *The combination of DEX and dezocine for epidural anesthesia stabilizes hemodynamics, improves hormone levels and lowers the incidence of adverse reactions in puerperae with GDM, thereby potentially ensuring better pregnancy outcomes and well-controlled blood glucose levels. Therefore, this strategy for epidural anesthesia has potentials for use in clinical practice.*

Keywords: *Dexmedetomidine (DEX), Dezocine, Gestational diabetes mellitus, Adverse reactions, Puerperae, Pain score, Epidural anesthesia, Pregnancy outcomes*

Tropical Journal of Pharmaceutical Research is indexed by Science Citation Index (SciSearch), Scopus, Web of Science, Chemical Abstracts, Embase, Index Copernicus, EBSCO, African Index Medicus, JournalSeek, Journal Citation Reports/Science Edition, Directory of Open Access Journals (DOAJ), African Journal Online, Bioline International, Open-J-Gate and Pharmacy Abstracts

INTRODUCTION

Diabetes mellitus, a common complication during the gestation period, may increase the possibility of poor pregnancy outcomes and lead to organ failure in puerperae, thereby seriously affecting maternal and infant health [1-3]. In order to optimize the conditions of the health of mother

and the baby, many pregnant women with gestational diabetes mellitus (GDM) choose cesarean delivery. However, while alleviating the pain during delivery to a certain extent, cesarean delivery intensifies hemodynamic fluctuations and disturbs hormonal secretion of puerperae. In addition, the mandatory fasting before operation increases the possibility of abnormal maternal and infant blood glucose levels after parturition [4-7].

In recent years, studies have shown that epidural anesthesia, the preferred anesthesia method for cesarean section, has minimal impact on infants: it reduces postoperative pain of puerperae, and increases the level of prolactin, indicating its high suitability for puerperae with GDM [8-10]. Dezocine is a common analgesic drug in clinical practice, and dexmedetomidine (DEX) is a drug used to relieve intraoperative stress, and for preventing drastic changes in pulse and BP in puerperae. Thus, a combination of the two improves the perioperative indices of puerperae.

Therefore, the present research was carried out to study the effect of application of DEX in combination with dezocine in epidural anesthesia during cesarean delivery for puerperae with GDM, and the effect of the anesthesia on hemodynamics, hormone levels and adverse reaction rates (ARR).

METHODS

Enrollment and grouping of patients

A total of 120 puerperae with GDM who were admitted to The Fourth Hospital of Shijiazhuang (Obstetrics and Gynecology Hospital Affiliated to Hebei Medical University, Shijiazhuang City, China) were enrolled in this study. They were equally assigned to 2 groups, based on their order of admission, with 60 patients in each group.

Ethical approval

The study received approval from the Ethical Authority of The Fourth Hospital of Shijiazhuang (O & G Hospital Affiliated to Hebei Medical University (approval no. 20181114), and followed the guidelines of the Declaration of Helsinki, as revised in 2013 [11]. All puerperae or family members submitted written informed permission to participate in the study.

Inclusion criteria

Puerperae who were diagnosed with GDM after examination [12], and those who met the conditions of cesarean delivery [13] were included in the study.

Exclusion criteria

Puerperae in the following categories were excluded: those with mental challenges or communication problems, those having diseases in major organs, puerperae with low BMI, those who were allergic to medications applied in the research, and those with coagulation disorders.

Treatments

Puerperae in both groups received epidural anesthesia with dezocine. However, DEX was added in group A, but other anesthesia drugs used were similar in both groups. The specific procedures used were as follows: when the puerperae entered the operation room, their peripheral veins were opened and vital signs were monitored. Oxygen inhalation was carried out through a nasal catheter, and lactated ringer solution (Anhui Shuanghe Pharmaceutical Limited by Share Limited; NMPA no. H20023235) was given through *i.v.* infusion at a dose of 5 mL/kg. Epidural catheter was inserted after performing puncture at L_{3-4} which resulted in discharge of spinal fluid. Then, ropivacaine (manufacturer: Hebei Yipin Pharmaceutical Company Limited) was infused through the epidural catheter.

Thereafter, 2 % of lidocaine (Fujian Jinshan Biological Pharmaceutical Limited by Share Ltd; NMPA approval no. H35020528) was infused into the puerperae in the supine position. The drug was used based on the actual conditions of the puerperae. For anesthesia, puerperae in group B received 5 mL of dezocine diluted with 1 mL of physiological saline, while 80 μg of DEX in combination with 5 mg of dezocine was administered to the puerperae in group A (for anesthesia). Cesarean delivery was conducted after successful anesthesia.

Assessment of parameters/indices

Pregnancy outcomes

The pregnancy outcomes for the infants were mild asphyxia, severe asphyxia, large-for-gestational-age (LGA) newborn and hypoglycemia, while pregnancy outcomes for the mother were postpartum hemorrhage, infection of incision site, polyhydramnios, hypertension and hyperglycemia. The numbers of mothers and babies with different pregnancy outcomes were recorded.

Pain score

At 1, 4, 8 and 16 h after operation, pain in the puerperae was evaluated using the Numeric Rating Scale (NRS) on a scale of 0-10 points, with higher scores indicating more severe pain.

Maternal and infant blood glucose levels

At 1, 4, 8 and 16 h post-operation, the blood glucose levels of the puerperae were measured. Moreover, at the time of birth, the blood glucose levels of the infants were measured.

Hemodynamic indices

Before operation, 0.5 h after anesthesia, and at the immediate postoperative period, mean arterial pressure (MAP), heart rate, systolic blood pressure, and diastolic blood pressure of the puerperae were determined.

Hormonal levels

Before operation, at immediate postoperative period, and 1 day after operation, the levels of estradiol, chemotaxin and prolactin in the puerperae were determined.

Incidence of adverse drug reactions

The adverse reactions included respiratory depression, slow heart rate, gastrointestinal reactions, dizziness, somnolence, and shiver. The population of puerperae showing each of these toxic effects was recorded.

Statistical analysis

The SPSS20.0 software was used for processing of results, while graphs were produced with GraphPad Prism 7. Counted data were compared using chi squared (χ^2) test, while measured data were compared with *t*-test. Values of $p < 0.05$ were taken as indicative of statistical significance.

RESULTS

Patients' baseline information

As shown in Table 2, there were no significant differences between the two groups with respect to general information on puerperae ($p > 0.05$).

Pregnancy outcomes

There were markedly better pregnancy outcomes with respect to the mothers and babies in group A than in group B ($p < 0.05$, Table 2).

Pain scores in puerperae

Figure 1 shows that the NRS scores of groups A and B were 4.12 ± 0.56 and 4.56 ± 0.77 at 1 h after operation, 3.10 ± 0.45 and 3.52 ± 0.56 at 4 h after operation, 2.21 ± 0.35 and 2.87 ± 0.34 at 8 h after operation, and 1.67 ± 0.69 and 2.00 ± 0.65 at 16 h after operation, respectively.

Table 1: Comparison of general information (n = 60)

Group	Age (years)	BMI (kg/m^2)	Gestational age (weeks)	Cervical diameter before anesthesia (cm)	Operation time (min)
A	28.98±2.31	22.98±1.58	38.65±1.51	3.10±0.21	53.98±5.12
B	29.10±2.58	22.48±1.77	38.98±1.57	3.09±0.22	54.95±5.10
χ^2	0.268	1.632	1.173	0.255	1.040
P-value	0.789	0.105	0.243	0.799	0.301

Table 2: Pregnancy outcomes [n (%)]

Group	A (n=60)	B (n=60)	χ^2	*P*-value
Infant				
Mild asphyxia	2 (3.3)	10 (16.7)	5.926	0.015
Severe asphyxia	1 (1.7)	4 (6.7)	1.878	0.171
LGA newborn	1 (1.7)	4 (6.7)	1.878	0.171
Hypoglycemia	2 (3.3)	8 (13.3)	3.927	0.048
Total	6 (10.0)	26 (43.3)	17.046	< 0.001
Puerpera				
Postpartum hemorrhage	2 (3.3)	6 (10.0)	2.143	0.143
Incision infection	0 (0.0)	3 (5.0)	3.077	0.079
Polyhydramnios	1 (1.7)	6 (10.0)	3.793	0.051
Hypertension	0 (0.0)	4 (6.7)	4.138	0.042
Hyperglycemia	4 (6.7)	8 (13.3)	1.482	0.224
Total	7 (11.7)	27 (45.0)	16.416	< 0.001

Thus, the postoperative pain scores of puerperae in group A were markedly lower than those of group B.

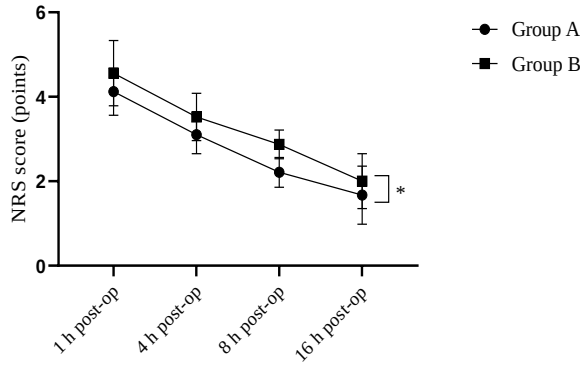

Figure 1: Pain scores of puerperae (mean ± SD). *P < 0.05

Maternal and infant blood glucose levels

After operation, group A showed significantly lower maternal blood glucose levels (p < 0.001) and higher infant blood glucose levels (p < 0.001) than group B (Table 3).

Hemodynamic indices of puerperae

At the time points of 0.5 h after anesthesia and after operation, the hemodynamic indices of puerperae in group A were significantly more stable than those of group B (p < 0.05, Table 4).

Hormonal levels in puerperae

Group A had significantly higher levels of estradiol and prolactin, and a lower chemotaxin level at immediate postoperative period, and at day after operation than group B (p < 0.05). These results are presented in Table 5.

Incidence of adverse reactions

In group A, the numbers of puerperae with respiratory depression, slow heart rate, gastrointestinal reactions, dizziness and drowsiness, and shiver were 1, 1, 5, 2, and 2, respectively, while the corresponding numbers in group B were 7, 8, 13, 10 and 12, respectively. Thus, as shown in Figure 2, there was higher incidence of unwanted reactions in group B than in group A.

Table 3: Comparison of maternal and infant blood glucose levels of the 2 groups (mmol/L)

Group	Puerpera blood glucose levels				
	1 h post-operation	***4 h post-operation***	***8 h post-operation***	***16 h post-operation***	***Infant Time of birth***
A	5.14±0.58	5.98±0.65	6.24±0.58	7.12±0.74	4.65±1.10
B	6.15±0.68	6.54±0.58	7.98±1.10	9.10±0.68	3.76±0.98
χ^2	8.753	4.979	10.838	15.261	4.679
P-value	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001

Values are presented as mean± SD

Table 4: Comparison of hemodynamics indices of puerperae in both groups (mean ± SD)

Parameter	Group A	Group B	*t*	*P*-value
MAP (mmHg)				
Pre-op	81.65±8.14	82.11±8.54	0.302	0.763
0.5h post-anesthesia	82.15±8.54	71.65±7.58	7.123	< 0.001
Post-op	81.58±8.00	77.84±8.15	2.537	0.013
Heart rate (bpm)				
Pre-op	78.65±9.54	77.45±8.59	0.724	0.471
0.5h after anesthesia	85.12±7.45	95.68±7.41	7.785	< 0.001
Post-op	83.54±7.11	89.65±9.87	3.891	< 0.001
Systolic blood pressure (mmHg)				
Pre-op	115.65±8.98	116.65±8.74	0.618	0.538
0.5h after anesthesia	108.15±5.10	99.15±5.20	9.571	< 0.001
Post-op	112.98±8.52	96.15±5.21	13.054	< 0.001
Diastolic blood pressure (mmHg)				
Pre-op	74.11±7.54	75.98±7.65	1.349	0.180
0.5h after anesthesia	69.15±7.41	64.22±8.57	3.371	0.001
Post-op	72.15±7.22	58.65±8.15	9.604	< 0.001

Data are presented as mean ± SD

Table 5: Comparison of hormonal levels in puerperae in both groups

Parameter	Group A	Group B	χ^2	*P*-value
Estradiol (pmol/L)				
Pre-op	268.98±9.11	270.12±8.15	0.722	0.472
Immediate post-op	245.15±8.87	230.65±7.98	9.414	< 0.001
1day post-op	240.59±8.57	215.68±8.51	15.976	0.013
Chemotaxin (mg/L)				
Pre-op	42.51±2.62	41.98±2.41	1.153	0.251
Immediate post-op	55.51±3.54	72.98±3.68	26.501	< 0.001
1day post-op	64.11±5.95	85.68±5.98	19.806	< 0.001
Prolactin (μg/L)				
Pre-op	30.68±2.11	31.45±2.41	1.862	0.065
Immediate post-op	26.58±1.98	22.68±1.90	11.009	< 0.001
1day post-op	25.98±2.14	20.57±2.00	14.307	< 0.001

Data are presented as mean ± SD

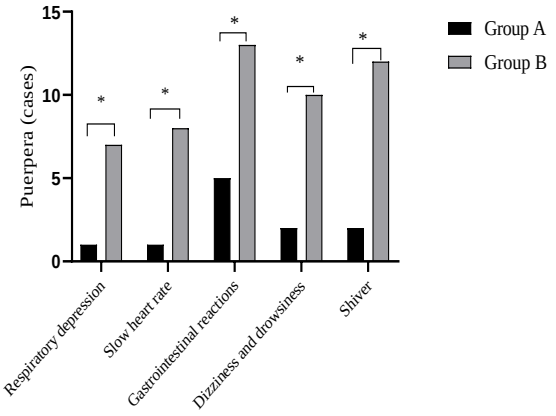

Figure 2: Comparison of incidence of adverse reactions. *P* < 0.05

DISCUSSION

Due to advances in techniques used in medical practice, the number of GDM puerperae who opt for cesarean delivery has continued to increase year by year. However, this delivery mode readily causes incision pain and visceral pain, such that most puerperae with GDM experience strong postoperative discomfort. Besides, intense pain may increase the possibility of postpartum hemorrhage and inhibit the secretion of prolactin, which is unfavorable for neonatal feeding [14].

In this study, the puerperae in group A had significantly lower postoperative pain scores than those in group B. This was due to the fact that dezocine, which exerts strong analgesic effects, acted on the spinal cord K-opiate receptor, thereby alleviating visceral pain and reducing negative emotions in puerperae. In addition, DEX lowered the rate of release of harmful substances by the peripheral nerves, and exerted analgesic effects on the central and peripheral nerves. The combination of dezocine and DEX reduced the effect of pain on prolactin. Therefore the level of prolactin was markedly raised in puerperae of group A, relative to puerperae of group B.

In addition, cesarean section elevates the rate of release of catecholamines. Large amounts of catecholamines not only exacerbate maternal hemodynamic changes but also impair the frequency of insulin production. Therefore, pregnant women with GDM have extremely high probability of developing blood glucose fluctuations during operation due to stress, with serious effect on maternal and fetal outcomes.

Epidural anesthesia blocks sympathetic nerve impulses and decreases maternal perioperative stress response, which in turn stabilize maternal hemodynamic indices [15,16]. Moreover, DEX weakens the secretion of catecholamines and reduces influence on maternal blood vessels. Therefore, the levels of MAP and blood pressure of puerperae in group A were more stable, and the magnitude of the change in heart rate was also relatively lower, when compared to group B. Moreover, DEX slowed down the secretion rate of glucagon when the stress response was diminished, leading to lower maternal glucose levels in the group that received the combined anesthesia, with a concomitant reduction in the possibility of hypoglycemia in the newborns. This study showed that the use of DEX in combination with dezocine for epidural anesthesia produced good glycemic control and attenuated maternal stress response.

The study also showed that the combined anesthesia produced significantly higher levels of estradiol and prolactin, and a lower chemotaxin level at immediate postoperative period and at 1 day after operation, when compared with group B, which might be related to the more stable hemodynamic indices in the puerperae of group A. It is worth noting that there is an important link between chemotaxins and grade of inflammation. Puerperae with GDM usually have low levels of inflammatory factors, which is an indication of

insulin resistance. Therefore, chemotaxins reflect the disease progression in puerperae [17]. There were markedly lower levels of chemotaxins in group A, indicating better maternal body condition in this group and a lower possibility of unwanted events due to diabetes. Therefore, maternal and neonatal pregnancy outcomes were much better in group A than in group B. This is in agreement with previous findings of Biesty *et al*. in their work in which one group of puerperae received epidural anesthesia of DEX in combination with dezocine, while control puerperae were given epidural anesthesia with dezocine. The results revealed markedly lower possibility of poor pregnancy outcomes in the combination group [11.0 % (11/100)] than in control group [18]. This suggests that the combined anesthesia optimizes maternal-infant outcomes. In addition, in the present study, the significantly lower frequency of unwanted events in group A puerperae suggest that it would be safe to combine the two drugs in epidural anesthesia.

CONCLUSION

The combined use of DEX and dezocine in epidural anesthesia stabilized hemodynamics, improved hormonal levels and lowered the incidence of adverse reactions in puerperae with GDM, thereby ensuring better pregnancy outcomes and well-controlled blood glucose levels. However, further clinical trials are required prior to the application of this strategy in clinical practice.

DECLARATIONS

Acknowledgements

None provided.

Funding

None provided.

Ethical approval

The study received approval from the Ethical Authority of The Fourth Hospital of Shijiazhuang (O & G Hospital Affiliated to Hebei Medical University (approval no. 20181114),

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

We declare that this work was done by the authors named in this article, and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. Luxin Wei and Xiaojing Li conceived and designed the study; and drafted the manuscript. Xiaojing Li and Kun He collected, analyzed and interpreted the experimental data. Luxin Wei and Kun He revised the manuscript for important intellectual contents. All authors read and approved the final manuscript. Luxin Wei and Xiaojing Li contributed equally as first authors.

REFERENCES

1. *Helal KF, Badr MS, Rafeek ME, Elnagar WM, Lashin ME. Can glyburide be advocated over subcutaneous insulin for perinatal outcomes of women with gestational diabetes? A systematic review and meta-analysis. Arch Gynecol Obstet 2020; 301(1): 19-32.*
2. *Moll U, Landin-Olsson M, Nilsson C, Ursing D, Strevens H. Pregnancy outcome in women with gestational diabetes –A longitudinal study of changes in demography and treatment modalities. Acta Obstet Gynecol Scand 2020; 99(3): 333-340.*
3. *Kwon H, Lee J, Lee BW, Kwon JY, Kim YH. The association between low 50g glucose challenge test values and adverse pregnancy outcomes. J Womens Health (Larchmt) 2018; 27(6): 801-807.*
4. *Gohier H, Guyard-Boileau B, Tuyeras G, Bertrand M, Coustols M, Guerby P, Parant O, Ritz P, Hanaire H. Glucose Abnormalities and Inappropriate Weight Gain Predict Negative Pregnancy Outcomes After Gastric Bypass Surgery. Obes Surg 2021; 31(7):3123-3129.*
5. *Usami T, Yokoyama M, Ueno M, Iwama N, Sagawa N, Kawano R, Waguri M, Sameshima H, Hiramatsu Y, Sugiyama T, et al. Comparison of pregnancy outcomes between women with early-onset and late-onset*

gestational diabetes in a retrospective multi-institutional study in Japan. Diabetes Investig 2020; 11(1): 216-222.

6. *Hosseini E, Janghorbani M, Shahshahan Z. Comparison of risk factors and pregnancy outcomes of gestational diabetes mellitus diagnosed during early and late pregnancy. Midwifery 2018; 66: 64-69.*
7. *Ducarme G, Desroys Du Roure F, Le Thuaut A, Grange J, Dimet J, Crepin-Delcourt I. Efficacy of maternal and biological parameters at the time of diagnosis of gestational diabetes mellitus in predicting neonatal morbidity. Eur J Obstet Gynecol Reprod Biol 2018; 221: 113-118.*
8. *Osuagwu UL, Fuka F, Agho K, Khan A, Simmons D. adverse maternal outcomes of fijian women with gestational diabetes mellitus and the associated risk factors. Reprod Sci 2020; 27(11): 2029-2037.*
9. *Allehdan SS, Basha AS, Asali FF, Tayyem RF. Dietary and exercise interventions and glycemic control and maternal and newborn outcomes in women diagnosed with gestational diabetes: Systematic review. Diabetes Metab Syndr 2019; 13(4): 2775-2784.*
10. *Doughty KN, Taylor SN. Barriers and benefits to breastfeeding with gestational diabetes. Semin Perinatol 2021; 45(2): 151385.*
11. *World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA 2013; 310(20): 2191-2194.*
12. *Rowan JA, Rush EC, Plank LD, Lu J, Obolonkin V, Coat S, Hague WM. Metformin in gestational diabetes: the offspring follow-up (MiG TOFU): body composition and metabolic outcomes at 7-9 years of age. BMJ Open Diabetes Res Care 2018; 6(1): e000456.*
13. *Dehmer EW, Phadnis MA, Gunderson EP, Lewis CE, Bibbins-Domingo K, Engel SM, Jonsson Funk M, Kramer H, Kshirsagar AV, Heiss G. association between gestational diabetes and incident maternal CKD: The coronary artery risk development in young adults (CARDIA) Study. Am J Kidney Dis 2018; 71(1): 112-122.*
14. *Huvinen E, Eriksson JG, Koivusalo SB, Grotenfelt N, Tiitinen A, Stach-Lempinen B, Rönö K. Heterogeneity of gestational diabetes (GDM) and long-term risk of diabetes and metabolic syndrome: findings from the RADIEL study follow-up. Acta Diabetol 2018; 55(5): 493-501.*
15. *Petry CJ, Fisher BG, Ong KK, Hughes IA, Acerini CL, Dunger DB. Temporal trends without seasonal effects on gestational diabetes incidence relate to reductions in indices of insulin secretion: The Cambridge Baby Growth Study. Acta Diabetol 2019; 56(10): 1133-1140.*
16. *McManus R, Miller D, Mottola M, Giroux I, Donovan L. Translating healthy living messages to postpartum women and their partners after gestational diabetes (GDM): Body habitus, A1C, lifestyle habits, and program engagement results from the families defeating diabetes (FDD) randomized trial. Am J Health Promot 2018; 32(6): 1438-1446.*
17. *Daly B, Toulis KA, Thomas N, Gokhale K, Martin J, Webber J, Keerthy D, Jolly K, Saravanan P, Nirantharakumar K. Increased risk of ischemic heart disease, hypertension, and type 2 diabetes in women with previous gestational diabetes mellitus, a target group in general practice for preventive interventions: A population-based cohort study. PLoS Med 2018; 15(1): e1002488.*
18. *Biesty LM, Egan AM, Dunne F, Smith V, Meskell P, Dempsey E, Ni Bhuinneain GM, Devane D. Planned birth at or near term for improving health outcomes for pregnant women with pre-existing diabetes and their infants (Review). Cochrane Database Syst Rev 2018; 2(2): CD012948.*