实验研究案例

Probiotics for the Prevention of Gestational Diabetes Mellitus in Overweight and Obese Women: Findings From the SPRING Double-blind Randomized Controlled Trial

研究案例目录

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研究背景

肠道菌群与宿主的代谢密切相关。因此，在妊娠期期间服用益生菌可能会预防妊娠糖尿病(GDM)。然而目前还没有在超重和肥胖孕妇中进行过相关研究。

研究目的

确定超重和肥胖孕妇在孕中期口服益生菌(鼠李糖乳杆菌和动物双歧杆菌亚种乳酸菌[BB-12])能否预防GDM的发生，为GDM的防治提供流行病学依据。

研究设计

◆随机双盲对照试验（RCT）

◆研究对象及干预方法：在澳大利亚布里斯班对超重和肥胖孕妇进行的益生菌　VS.　安慰剂的双盲随机对照试验。

◆主要结局变量：GDM

◆次要结局变量：包括产妇和新生儿并发症、产妇血压和BMI，以及婴儿身体状况

研究方案

在孕20周前，采用随机数方法将411名超重/肥胖孕妇随机分为2组，分别服用益生菌（鼠李糖乳杆菌+动物双歧杆菌乳亚种BB-12）或安慰剂，每天服用一次，一直干预至分娩。

在孕28周时进行口服葡萄糖耐量试验进行GDM诊断，并收集孕妇其他妊娠结局（孕期体重增长、子痫前期、妊娠期高血压、剖宫产等）及新生儿结局资料（早产儿、新生儿黄疸、新生儿低血糖、出生体重、小于胎龄儿、大于胎龄儿、死产、出生缺陷等）。分析口服益生菌干预对孕妇血糖、GDM及其他结局的影响。

技术路线

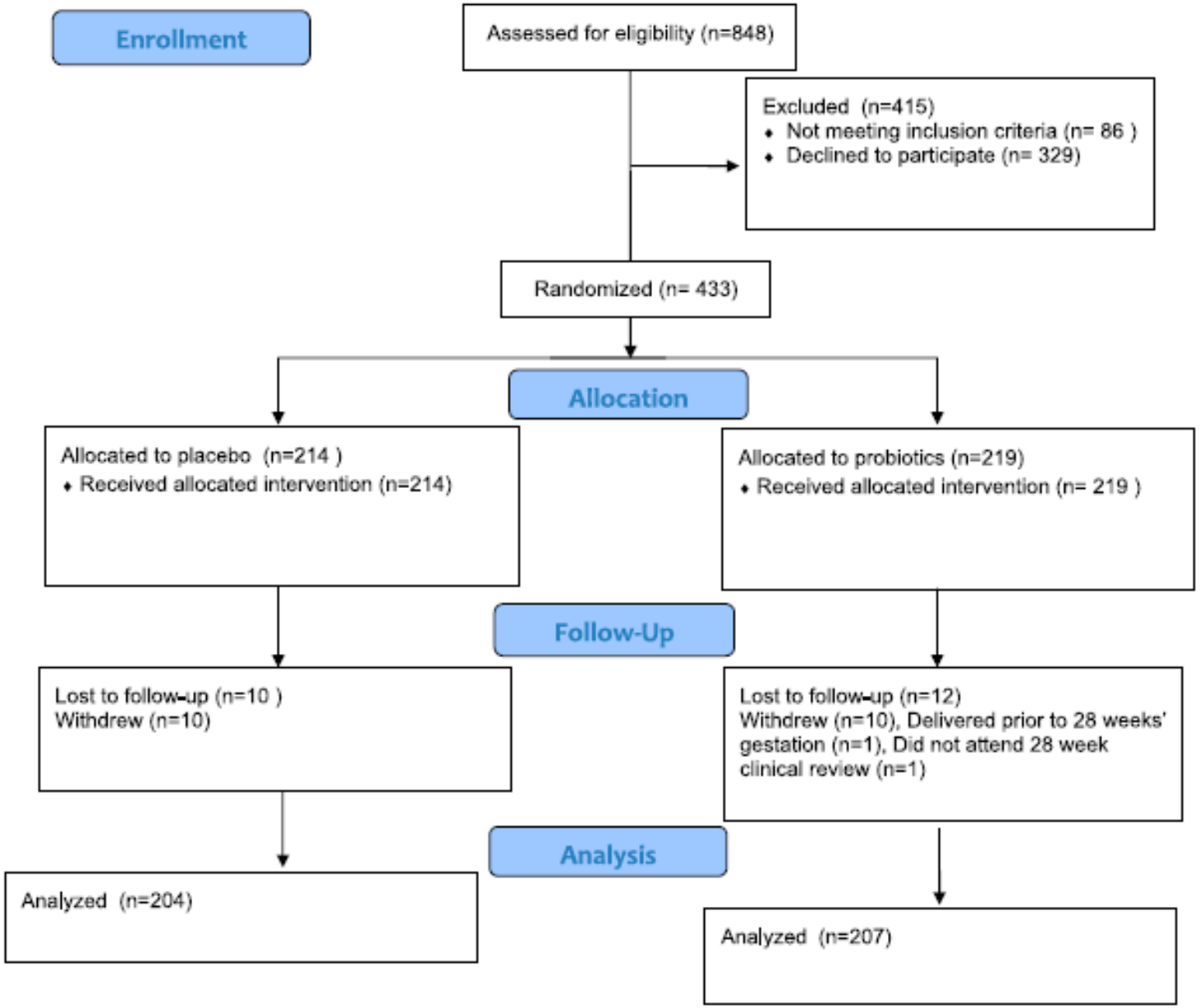

Figure 1—Eligibility, randomization, and follow-up. (A high-quality color representation of this figure is available in the online issue.)

研究结果

安慰剂组孕妇GDM的发病率为12.3%，而益生菌组GDM发病率为18.4%，两组间无显著差异。

在口服葡萄糖耐量试验中，益生菌组孕妇的平均空腹血糖显著高于安慰剂组；

研究结果

益生菌组子痫前期的发病率为9.2%，安慰剂组的为4.9%，两组无显著差异；

益生菌组孕妇体重过度增长的比例为32.5%，显著低于安慰剂组的（46%）；

益生菌组孕妇子代小于胎龄儿的发生率为2.4%，显著低于安慰剂组的（6.5%）。

Primary outcome: GDM at 28 weeks' gestation

	Summary			
	Placebo (n = 204)	Probiotics (n = 207)	Effect (95% CI)‡	P‡
GDM*	25 (12.3)	38 (18.4)	1.62 (0.91–2.89)	0.10
Fasting glucose, mmol/L [mg/dL]†§	4.3 (0.45) [77.5 (8.1)]	4.4 (0.5) [79.3 (9.0)]	0.085 (0.00053–0.17) [1.53 (0.0095–3.06)]	0.049
1-h glucose, mmol/L [mg/dL]†§	7.5 (1.6) [135.1 (28.8)]	7.6 (1.8) [136.9 (32.4)]	0.052 (−0.27 to 0.37) [0.94 (−4.86 to 6.66)]	0.75
2-h glucose, mmol/L [mg/dL]†§	6.3 (1.4) [113.5 (25.2)]	6.4 (1.5) [115.3 (27.0)]	0.13 (−0.15 to 0.40) [2.34 (−2.70 to 7.20)]	0.37

*Summary: n (%). Effect: odds ratio with placebo as referent. †Summary: mean (SD). ‡Effect: difference of means. Adjusted for BMI (25–29, 30–39, and 40+ kg/m^2) and patient center (RBWH, Redcliffe, Mater). §$n_{placebo}$ = 202; $n_{probiotics}$ = 205.

Secondary outcomes

Secondary outcomes	n		Summary		Effect (95% CI)‡	*P*
	Placebo	Probiotic	Placebo	Probiotic		
Mother						
Preeclampsia*	203	206	10 (4.9)	19 (9.2)	2.00 (0.89–4.50)	0.09
Gestational hypertension*	203	206	11 (5.4)	10 (4.9)	0.86 (0.35–2.09)	0.74
Hypertensive disorders of pregnancy*	203	206	26 (12.8)	34 (16.5)	1.35 (0.76–2.37)	0.30
Caesarean*	204	207	80 (39.2)	73 (35.3)	0.85 (0.56–1.27)	0.41
In labor/intrapartum/emergency caesarean*	78	73	36 (46.2)	33 (45.2)	1.00 (0.52–1.93)	1.00
Induced labor*	202	206	62 (30.7)	74 (35.9)	1.23 (0.81–1.87)	0.34
28 weeks systolic BP (mmHg)†	196	197	110.3 (10.6)	110.4 (9.9)	0.003 (−1.90 to 1.91)	1.00
28 weeks diastolic BP (mmHg)†	196	197	65.0 (7.6)	66.4 (7.8)	1.36 (−0.11 to 2.84)	0.070
36 weeks systolic BP (mmHg)†	177	169	114.0 (10.6)	115.7 (11.3)	1.62 (−0.66 to 3.90)	0.16
36 weeks diastolic BP (mmHg)†	177	169	70.5 (8.3)	70.9 (9.8)	0.51 (−1.35 to 2.37)	0.59
36 weeks weight gain from baseline (kg)†	176	169	9.5 (4.3)	8.9 (5.3	−0.55 (−1.55 to 0.45)	0.28
Excess weight gain*	176	169	81 (46)	55 (32.5)	0.56 (0.36–0.87)	0.01
Inadequate weight gain			28 (15.9)	34 (20.1)		
Weight gain per week from baseline to 36 weeks (kg/week)	176	169	0.40 (0.19)	0.37 (0.23)	−0.03 (−0.08 to 0.01)	0.17
Infant						
Gestational age at delivery (weeks)	180	193	39.32 (1.75)	39.14 (1.88)	−0.18 (−0.55 to 0.19)	0.34
Very preterm (<34 weeks)*	180	193	3 (1.7)	5 (2.6)	1.59 (0.37–6.85)	0.53
Preterm (<37 weeks)*	180	193	12 (6.7)	17 (8.8)	1.36 (0.63–2.96)	0.43
Special care unit admission*	199	207	43 (21.6)	42 (20.3)	0.92 (0.57–1.50)	0.75
Jaundice*	201	205	40 (19.9)	35 (17.1)	0.82 (0.50–1.36)	0.45
Birth injury*	198	203	1 (0.5)	1 (0.5)	—	—
Hypoglycemia*	200	202	27 (13.5)	25 (12.4)	0.90 (0.50–1.63)	0.73
Stillbirth*	204	207	1 (0.5)	0 (0.0)	—	—
Congenital abnormality*	201	204	6 (3.0)	10 (4.9)	1.70 (0.60–4.80)	0.32
Macrosomia (>4,000 g)*	203	206	35 (17.2)	31 (15.0)	0.85 (0.50–1.45)	0.56
Macrosomia (>4,500 g)*	203	206	2 (1.0)	7 (3.4)	—	—
Large for gestational age (>90th percentile)*	180	193	30 (16.7)	35 (18.1)	1.09 (0.64–1.88)	0.75
SGA (<2,500 g)*	203	206	6 (3.0)	7 (3.4)	1.15 (0.38–3.50)	0.81
SGA (<10th percentile)*	199	205	13 (6.5)	5 (2.4)	0.33 (0.12–0.96)	0.042
Birth weight (g)†	203	206	3,541 (514)	3,524 (540)	−15.55 (−118.24 to 87.15)	0.77
Fat-free mass (g)†	105	103	3,011 (357)	3,033 (356)	21.27 (−76.66 to 119.20)	0.67
Percentage fat†	105	105	12.3 (3.6)	12.2 (4.4)	−0.13 (−1.23 to 0.97)	0.82

*Summary columns: *n* (%). Effect: odds ratio. †Summary columns: mean (SD). Effect: difference of means. ‡Adjusted for BMI (25–29, 30–39, and 40+ kg/m^2) and patient center (RBWH, Redcliffe, Mater).

研究结论

◆在这项研究中使用的益生菌未见有预防超重和肥胖孕妇发生GDM的作用。

◆益生菌可显著减少孕妇体重过度增长的比例，但显著增加了小于胎龄儿的比例。