doi: 10.13241/j.cnki.pmb.2020.12.031

# 门冬胰岛素联合甘精胰岛素对新诊断2型糖尿病患者炎性因子、血糖及血脂水平的影响*

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**摘要 目的:**探讨门冬胰岛素联合甘精胰岛素对新诊断2型糖尿病患者血清炎性因子、血糖及血脂水平的影响。**方法:**选取我院2017年3月~2019年3月收治的100例新诊断2型糖尿病患者,将其随机分为研究组和对照组,每组50例患者。对照组患者给予门冬胰岛素治疗,研究组患者给予门冬胰岛素联合甘精胰岛素治疗,对比两组患者治疗前后血清炎性因子、血糖及血脂水平的变化。**结果:**治疗后,两组患者糖化血红蛋白(hemoglobin A1c,HbA1c)、空腹血糖(fasting plasma glucose,FPG)、餐后2h血糖(2h postprandial blod glucose,2hPBG)、血清肿瘤坏死因子(Tumor necrosis factor,TNF-α)、高敏C反应蛋白(high-sensitive C-reactive protein,hs-CRP)水平均较治疗前明显降低($P<0.05$),且研究组患者以上指标均显著低于对照组($P<0.05$);两组患者治疗后总胆固醇(Total Cholesterol,TC)、甘油三酯(Triglyceride,TG)、低密度脂蛋白胆固醇(Low-density lipoprotein cholesterol,LDL-C)水平均较治疗前明显降低,高密度脂蛋白胆固醇(High-density lipoprotein cholesterol,HDL-C)明显升高($P<0.05$),且研究组以上指标的改善程度均优于对照组($P<0.05$)。研究组患者的胰岛素用量明显少于对照组($P<0.05$),患者血糖首次达标时间明显短于对照组($P<0.05$)。**结论:**门冬胰岛素联合甘精胰岛素适用于新诊断2型糖尿病患者,可有效降低血糖、血脂、血清TNF-α和hs-CRP水平。

**关键词:**门冬胰岛素;甘精胰岛素;新诊断2型糖尿病;炎性因子;血糖;血脂

**中图分类号:**R587.1 **文献标识码:**A **文章编号:**1673-6273(2020)12-2342-04

# Effect of Insulin Aspart and Insulin Glargine on the Inflammatory Factor, Blood Lipid and Glucose Levels in the Newly Diagnosed Type 2 Diabetic Patients*

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**ABSTRACT Objective:** To investigate the effects of insulin aspart and insulin glargine on the serum inflammatory factor, blood glucose and blood lipid levels in the newly diagnosed type 2 diabetic patients. **Methods:** One hundred patients with newly diagnosed type 2 diabetes admitted from March 2017 to March 2019 in our hospital were randomly divided into study group and control group, with 50 patients in each group. The control group received insulin aspart and the study group received insulin aspart and insulin glargine. The changes of serum inflammatory factors, blood glucose and blood lipid levels before and after treatment were compared between the two groups. **Results:** After treatment, the HbA1c, FPG, 2hPBG, TNF-α, and hs-CRP of both groups of patients were significantly lower than those before treatment ($P<0.05$), and the above indexes of study group were significantly lower than those of the control group ($P<0.05$). The levels of TC, TG and LDL-C in both groups were significantly lower than those before treatment, and HDL-C was significantly increased ($P<0.05$), and the improvement of the above indexes in the study group was better than that in the control group ($P<0.05$). The insulin dosage of the study group was significantly lower than that in the control group ($P<0.05$). The first time of blood glucose compliance in the study group was significantly shorter than that in the control group ($P<0.05$). **Conclusion:** Insulin aspart and insulin glargine are suitable for patients with newly diagnosed type 2 diabetes, which can effectively lower the blood glucose, blood lipids, serum TNF-α and hs-CRP levels.

**Key words:** Insulin aspart; Insulin glargine; Newly diagnosed type 2 diabetes; Inflammatory factor; Blood glucose; Blood lipid

**Chinese Library Classification(CLC): R587.1 Document code: A**

**Article ID: 1673-6273(2020)12-2342-04**

* 基金项目:陕西省科技厅科研基金项目(2017SF-093)

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(收稿日期:2019-12-02 接受日期:2019-12-27)

## 前言

2 型糖尿病是内分泌系统常见慢性疾病。近年来，随着人们生活水平的提高[1]，饮食结构及生活习惯的改变，每年新诊断 2 型糖尿病患者越来越多，但是治疗方案一直没有新的突破[2,3]。对于新诊断的 2 型糖尿病患者，临床上常常采取迅速降糖措施，使其血糖控制在平稳状态，但其胰岛素处于正常分泌状态[4-6]。一味追求降低血糖，忽略糖尿病患者部分胰岛素正常作用，可能导致胰岛细胞进一步萎缩和退化，造成整体胰岛功能彻底丧失[7,8]。但是胰岛素用药费用较高，如何在保证患者降糖效果的同时，减轻用药经济负担是糖尿病患者治疗的重点[9]。本研究选择近 3 年在我院新诊断并治疗的 100 例 2 型糖尿病患者病历资料，现将结果报道如下。

## 1 资料与方法

### 1.1 一般资料

选取我院 2017 年 3 月 ~2019 年 3 月收治的 100 例新诊断 2 型糖尿病患者，将其随机分为研究组和对照组，每组患者 50 例。入选标准：新诊断为 2 型糖尿病；未使用降糖药物或胰岛素；近 1 个月无任何感染性疾病；意识清楚，自愿参与本研究，并签署知情同意书。排除标准：合并严重并发症患者；妊娠、哺乳期患者。两组患者性别、年龄、病程、体质指数(Body mass index，BMI) 等一般资料如表 1 所示，组间对比无统计学差异($P>0.05$)，具有可比性。

**表 1 两组患者一般资料的对比**

Table 1 Comparison of the general data between the two groups of patients

| Groups | Case | Gender (Male/ Female) | Age (years) | Disease duration (months) | BMI(kg/m$^2$) |
|---|---|---|---|---|---|
| Research group | 50 | 27/23 | 49.3±17.9 | 6.8±1.5 | 24.5±2.73 |
| Control group | 50 | 28/22 | 49.5±18.1 | 6.9±1.3 | 24.6±2.52 |

### 1.2 治疗方法

对照组患者给予门冬胰岛素，生产企业：诺和诺德(中国)制药有限公司，批准文号：国药准字 J20050097，于早晚餐前注射治疗，注射剂量按照产品说明书进行。初始剂量 12 U/d，每 3~4 d，根据患者血糖调整剂量，直至将血糖控制在合理范围内。研究组患者给予门冬胰岛素联合甘精胰岛素，于三餐前皮下注射门冬胰岛素注射液，晚上皮下注射甘精胰岛素注射液(生产企业：长春天诚药业有限公司，注册证号 S20030078)。采取艾科全血糖仪监测空腹、餐后 2 h 及睡前指末血糖值。针对血糖值，调整胰岛素注射剂量，将血糖控制在正常水平。两组患者连续治疗 3 个月，然后对比疗效。

### 1.3 评价标准

分别在治疗前及治疗后 12 周抽取患者静脉血，检测两组患者治疗前后炎症因子、血糖及血脂水平[10]。① 采取电发光法检测两组患者的治疗前后血清 TNF-α、hs-CRP 水平。② 血糖水平包括 FPG(空腹血糖)、2hPBG(餐后 2h 血糖)、HbA1c(糖化血红蛋白)。③ 血脂水平包括 TG (三酰甘油)、TC (总胆固醇)、HDL-C(高密度脂蛋白胆固醇)、LDL-C(低密度脂蛋白胆固醇)。④ 胰岛素用量、血糖首次达标时间。

### 1.4 统计学方法

采取统计学软件对两组患者的一般资料及临床效果数据进行统计学分析，炎性因子水平、血糖水平、胰岛素用量及血糖首次达标时间等计量资料采取平均数±标准差($\bar{x}\pm s$)描述，组间对比采取 t 检验；计数资料采取百分数来描述，组间对比采取 $\chi^2$ 检验。以 $P<0.05$ 表示差异具有统计学意义。

## 2 结果

### 2.1 两组患者治疗前后血糖水平的对比

两组患者治疗前血糖水平(FPG、2hPBG 、HbA1c)对比差异无统计学意义($P>0.05$)。治疗后，两组患者各项血糖指标均较治疗前明显降低($P<0.05$)，且研究组患者以上指标均显著低于对照组($P<0.05$)。如表 2 所示。

**表 2 两组患者治疗前后血糖水平的对比**

Table 2 Comparison of the blood glucose levels before and after treatment between two groups of patients

| Groups | n | FPG (mmol/L) | | 2hPBG (mmol/L) | | HbA1c (%) | |
|---|---|---|---|---|---|---|---|
| | | Before treatment | After treatment | Before treatment | After treatment | Before treatment | After treatment |
| Research group | 50 | 10.54±1.35 | 6.32±1.09*# | 14.42±1.41 | 7.85±1.39*# | 9.53±1.38 | 6.11±1.03*# |
| Control group | 50 | 10.56±1.32 | 7.54±1.13* | 14.48±1.40 | 8.95±1.45* | 9.51±1.40 | 7.97±1.12* |

Note: Compared with the same group before treatment, *$P<0.05$, compared with the control group after treatment, #$P<0.05$.

### 2.2 两组患者治疗前后血脂水平的对比

两组患者治疗前血脂水平(TG、TC、HDL-C、LDL-C)对比无统计学差异($P>0.05$)，治疗后，两组患者 TG、TC 和 LDL-C 均显著降低，HDL-C 均显著升高($P<0.05$)，而研究组患者上述指标的改善程度优于对照组($P<0.05$)。如表 3 所示。

### 2.3 两组患者治疗前后血清炎性因子水平的对比

两组患者治疗前血清 TNF-α、hs-CRP 对比无统计学差异($P>0.05$)；治疗后，两组患者以上指标均明显低于对照组($P<0.05$)，且研究组患者以上指标均显著低于对照组($P<0.05$)。如表 4 所示。

### 2.4 两组患者胰岛素用量及血糖首次达标时间的对比

研究组患者的胰岛素用量明显少于对照组，且研究组患者

血糖首次达标时间明显短于对照组($P<0.05$)。如表 5 所示。

**表 3 两组患者治疗前后血脂水平的对比($\bar{x}\pm s$,mmol/L)**

Table 3 Comparison of the blood lipid levels before and after treatment betwen two groups of patients($\bar{x}\pm s$,mmol/L)

| Groups | n | TG | | TC | | HDL-C | | LDL-C | |
|---|---|---|---|---|---|---|---|---|---|
| | | Before treatment | After treatment | Before treatment | After treatment | Before treatment | After treatment | Before treatment | After treatment |
| Research group | 50 | 2.54±0.76 | 1.78±0.67*# | 5.43±0.80 | 4.31±0.69*# | 1.85±0.35 | 2.41±0.53*# | 3.21±0.75 | 2.73±0.78*# |
| Control group | 50 | 2.53±0.75 | 2.13±0.78* | 5.41±0.79 | 4.80±0.76* | 1.86±0.34 | 1.99±0.43* | 3.22±0.78 | 3.10±0.53* |

Note: Compared with before treatent, *$P<0.05$; compared with the control group, #$P<0.05$.

**表 4 两组患者治疗前后血清炎性因子水平的对比($\bar{x}\pm s$)**

Table 4 Comparison of the serum inflammatory factor levels before and after treatment betwen two groups($\bar{x}\pm s$)

| Groups | n | TNF-α(μg/L) | | hs-CRP (mg/L) | |
|---|---|---|---|---|---|
| | | Before treatment | After treatment | Before treatment | After treatment |
| Research group | 50 | 2.25±0.50 | 1.80±0.21*# | 4.80±2.37 | 1.75±1.18*# |
| Control group | 50 | 2.23±0.48 | 2.03±0.59* | 4.78±2.34 | 2.98±1.09* |

Note: Compared with before treatent, *$P<0.05$; compared with the control group, #$P<0.05$.

**表 5 两组患者胰岛素用量及血糖首次达标时间对比**

Table 5 Comparison of the insulin dosage and blood glucose first time between two groups

| Group | n | Insulin dosage (IU) | Blood glucose first time (d) |
|---|---|---|---|
| Research group | 50 | 35.87±1.43* | 7.02±1.45* |
| Control group | 50 | 48.41±1.90 | 8.92±1.73 |

Note: Compared with the control group after treatment, *$P<0.05$.

## 3 讨论

糖尿病是一种慢性代谢性疾病，因机体胰岛 β 细胞受损，胰岛素分泌减少，血糖升高[11]。2 型糖尿病是糖尿病常见类型，随着近年来我国人民生活水平的不断提高，我国糖尿病发病率一直居高不下，同时呈年轻化趋势[12-14]。如果血糖未及时有效控制，易发生多种并发症，严重影响患者的身体健康[15]。

糖尿病患者通过改变生活方式、饮食习惯或者是服用药物后，血糖仍然未有效控制，则需采取胰岛素注射治疗[16]。门冬胰岛素和甘精胰岛素是临床上使用较多的胰岛素，门冬胰岛素是一种速效胰岛素类似物，主要兼顾降低餐后血糖，调整基础血糖水平，能够满足患者的基础胰岛素及餐时胰岛素需求[17]，皮下注射 10-20 min 内见效，可被人体迅速吸收，作用持续 3-5 h，需多次注射[18,19]。甘精胰岛素是一种长效胰岛素，经过皮下注射后，可在局部形成沉淀，缓慢释放胰岛素，多在 2 h 后见效，作用持续 24 h，可平稳降低血糖。虽然这两种药物单个均可有效降低患者的血糖值[20,21]，但临床研究表明两种药物联合应用对治疗糖尿病的效果更佳，本研究则应用两种药物治疗新诊断 2 型糖尿病患者[22,23]。

研究显示炎性因子水平的异常升高影响胰岛素信号传导通路，可加重患者对胰岛素的抵抗[24,25]。相关报道显示糖尿病属于低度炎性疾病，TNF-α、hs-CRP 是影响较大的血清炎症因子。其中 TNF-α 可抑制酪氨酸磷酸化，减少葡糖糖转运子表达，增加肝糖原分解，促进血糖升高[26]；hs-CRP 可预测病情严重程度的指标因子之一，其越高则代表代表患糖尿病风险越高[27,28]。本研究结果显示对新诊断 2 型糖尿病患者给予门冬胰岛素联合甘精胰岛素治疗可降低血清 TNF-α 因子水平，增加胰岛素分泌，提高血管敏感性，控制血糖[29,30]。

本研究结果显示研究组患者治疗后的血糖血脂水平改善程度明显优于对照组，分析原因主要是联合治疗可为患者补充外源性胰岛素，对患者进行持续性降糖，释放内源性胰岛素，并可改善患者内分泌紊乱，降低机体外周组织对胰岛素的抵抗，进而提升降糖降脂效果。且研究组患者的胰岛素用量及血糖首次达标时间明显低于对照组。因此，联合治疗可加快患者血糖恢复至达标速度，减少胰岛素用量，减轻患者用药经济负担。

总而言之，门冬胰岛素联合甘精胰岛素适用于新诊断 2 型糖尿病患者，可有效降低血糖、血脂、血清 TNF-α 和 hs-CRP 水平。

### 参 考 文 献(References)

[1] Cemeroglu A, Kleis L, Wood A, et al. Comparison of the Effect of Insulin Glulisine to Insulin Aspart on Breakfast Postprandial Blood Glucose Levels in Children with Type 1 Diabetes Mellitus on Multiple Daily Injections[J]. Endocr Pract, 2013, 19(4): 614-619

[2] Janukonyté J, Parkner T, Bruun NH, et al. Interaction Between Exogenous Insulin, Endogenous Insulin, and Glucose in Type 2 Diabetes Patients[J]. Diabetes Technol Ther, 2015, 17(5): 335-342

[3] Luo P, Cheng Q, Chen B, et al. Hypoglycemia and Blood Glucose Fluctuations in the Application of a Sensor-Augmented Insulin Pump [J]. Diabetes Technol Ther, 2013, 15(12): 984-989

[4] Tennagels N, Welte S, Hofmann M, et al. Differences in metabolic and mitogenic signalling of insulin glargine and insulin aspart B10 in rats

[J]. Diabetologia, 2013, 56(8): 1826-1834

[5] Freemantle N, Meneghini L, Christensen T, et al. Insulin degludec improves health related quality of life (SF-36® ) compared with insulin glargine in people with Type 2 diabetes starting on basal insulin: a meta analysis of phase 3a trials[J]. Diabet Med, 2013, 30(2): 226-232

[6] Yang W, Xu X, Liu X, et al. Treat-to-target comparison between once daily biphasic insulin aspart 30;and insulin glargine in Chinese and Japanese insulin-naive subjects with type 2 diabetes[J]. Curr Med Res Opin, 2013, 29(12): 1599-1608

[7] Liebl A, Davidson J, Mersebach H, et al. A Novel Insulin Combination of Insulin Degludec and Insulin Aspart Achieves a More Stable Overnight Glucose Profile Than Insulin Glargine: Results from Continuous Glucose Monitoring in a Proof-of-Concept Trial [J]. J Diabetes Sci Technol, 2013, 7(5): 1328-1336

[8] Shao N, Kuang HY, Hao M, et al. Benefits of exenatide on obesity and non-alcoholic fatty liver disease with elevated liver enzymes in patients with type 2 diabetes [J]. Diabetes Metab Res Rev, 2015, 30 (6): 521-529

[9] Xu Z, Han P, Wei Y, et al. Cost-effectiveness analysis of biphasic insulin aspart versus insulin glargine in people with type 2 diabetes in China[J]. Value in Health, 2014, 17(3): A247

[10] Nambala N, Mweemba P, Labib M. Women's Intention to Prevent Vesico Vaginal Fistula Recurrence in Two Repair Centres in Zambia [J]. Annales De Biologie Clinique, 2015, 70(70): 335-340

[11] Grams MK, Dinsmore S, Goldman-Levine J, et al. An Overview of Glycemic Goals and Medications Used to Manage Type 2 Diabetes [J]. Nutrition Today, 2015, 50(1): 40-48

[12] Okuroglu N, Sertbas M, Ozdemir A. Treatment of Chronic Hepatitis C Can Improve Glycemic Control in Patients with Type 2 Diabetes[J]. Case Reports in Hepatology, 2018, 2018: 1-2

[13] Gao GQ, Heng XY, Wang YL, et al. Comparison of continuous subcutaneous insulin infusion and insulin glargine-based multiple daily insulin aspart injections with preferential adjustment of basal insulin in patients with type 2 diabetes[J]. Exp Ther Med, 2014, 8(4): 1191-1196

[14] Lv WS, Li L, Wen JP, et al. Comparison of a Multiple Daily Insulin Injection Regimen (Glargine or Detemir Once Daily Plus Prandial Insulin Aspart) and Continuous Subcutaneous Insulin Infusion (Aspart) in Short-Term Intensive Insulin Therapy for Poorly Controlled Type 2 Diabetes Patients[J]. Int J Endocrinol, 2013, 13(1): e614242

[15] Rys P, Wojciechowski P, Siejka S, et al. A comparison of biphasic insulin aspart and insulin glargine administered with oral antidiabetic drugs in type 2 diabetes mellitus - a systematic review and meta-analysis[J]. Int J Clin Pract, 2014, 68(3): 304-313

[16] Kumar S, Jang HC, Demirağ NG, et al. Efficacy and safety of once daily insulin degludec/insulin aspart compared with once daily insulin glargine in participants with Type 2 diabetes: a randomized, treat to target study[J]. Diabet Med, 2017, 34(2): 180-188

[17] Ishii H, Terauchi Y, Jinnouchi H, et al. Effects of insulin changes on quality of life and glycemic control in Japanese patients with type 2 diabetes mellitus: The insulin-changing study intending to gain patients' insights into insulin treatment with patient-reported health outcomes in actual clinical treatments (INSIGHTs) study [J]. J Diabetes Investig, 2013, 4(6): 560-570

[18] Kumar A, Franek E, Wise J, et al. Efficacy and Safety of Once-Daily Insulin Degludec/Insulin Aspart versus Insulin Glargine (U100) for 52 Weeks in Insulin-Naïve Patients with Type 2 Diabetes: A Randomized Controlled Trial[J]. PLoS ONE, 2016, 11(10): e0163350

[19] Yoneda C, Tashima-Horie K, Fukushima S, et al. Association of morning fasting blood glucose variability with insulin antibodies and clinical factors in type 1 diabetes[J]. Endocr J, 2016, 63(7): 603-609

[20] Murakami T, Nambu T, Kato T, et al. Add-on Treatment with Mitiglinide Improves Residual Postprandial Hyperglycemia in Type 2 Diabetic Patients Receiving the Combination Therapy with Insulin Glargine and Sitagliptin[J]. Tohoku J Exp Med, 2015, 235(4): 255-260

[21] Kumar A, Kesavadev J, Sethi B, et al. Intensifying Insulin Therapy in Type 2 Diabetes: Choices & Challenges [J]. J Assoc Physicians India, 2015, 63(5): 8-14

[22] Farshchi A, Aghili R, Oskuee M, et al. Biphasic insulin Aspart 30 vs. NPH plus regular human insulin in type 2 diabetes patients; a cost-effectiveness study[J]. BMC Endocr Disord, 2016, 16(1): 35-47

[23] Onishi Y, Ono Y, RabL R, et al. Superior glycaemic control with once-daily insulin degludec/insulin aspart versus insulin glargine in Japanese adults with type 2 diabetes inadequately controlled with oral drugs: a randomized, controlled phase 3 trial [J]. Diabetes?Obes Metab, 2013, 15(9): 826-832

[24] Tennagels N, Welte S, Hofmann M, et al. Differences in metabolic and mitogenic signallingof insulin glargine and AspB10 human insulin in rats [corrected][J]. Diabetologia, 2013, 56(8): 1826-1834

[25] Shao N, Kuang HY, Hao M, et al. Effects of exenatide on obesity and NAFLD with elevated liver enzymes in patients with type 2 diabetes [J]. Diabetes Metab Res Rev, 2014, 30(6): 521-529

[26] Dieuzeide G, Chuang LM, Almaghamsi A, et al. Safety and effectiveness of biphasic insulin aspart 30 in people with type 2 diabetes switching from basal-bolus insulin regimens in the A1chieve study[J]. Prim Care Diabetes, 2014, 8(2): 111-117

[27] Mohammadian S, Fatahi N, Zaeri H, et al. Effect of Vitamin D3 Supplement in Glycemic Control of Pediatrics with Type 1 Diabetes Mellitus and Vitamin D Deficiency [J]. J Clin Diagn Res, 2015, 9(3): SC05-SC07

[28] Wu P, Ji C, Wang M, et al. Desensitization of allergy to human insulin and its analogs by administering insulin aspart and insulin glargine[J]. Ann Endocrinol (Paris), 2013, 74(1): 56-58

[29] Vionnet N, Hani EH, Dupont S, et al. Genomewide search for type 2 diabetes-susceptibility genes in French whites: evidence for a novel susceptibility locus for early-onset diabetes on chromosome 3q27-qter and independent replication of a type 2-diabetes locus on chromosome 1q21-q24[J]. Am J Hum Genet, 2017, 67(6): 1470-1480

[30] Forslund K, Hildebrand F, Nielsen T, et al. Corrigendum: Disentangling type 2 diabetes and metformin treatment signatures in the human gut microbiota[J]. Nature, 2017, 545(7652): 262-266