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吡格列酮联合阿卡波糖对2型糖尿病患者血清RBP4、Leptin、Visfatin水平的影响*

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摘要 目的：探讨吡格列酮联合阿卡波糖治疗2型糖尿病的临床效果及对患者血清视黄醇结合蛋白4(RBP4)、瘦素(Leptin)、内脂素(Visfatin)表达的影响。**方法：**选择2015年10月至2017年10月我院接诊的90例2型糖尿病患者为本研究对象，通过随机数表法将其分为观察组(n=46)和对照组(n=44)。对照组在常规治疗基础上给予阿卡波糖治疗，观察组在对照组基础上联合吡格列酮治疗，两组均连续治疗12周。比较两组治疗前后血糖、动态血糖、胰岛细胞功能、血清RBP4、Leptin和Visfatin水平的变化和不良反应的发生情况。**结果：**治疗后，观察组空腹血糖(FBG)、餐后2 h血糖(2hPBG)、糖化血红蛋白(HbA1c)均明显低于对照组[(6.58± 1.30)mmol/L vs. (7.47± 1.44)mmol/L，(9.20± 1.22)mmol/L vs. (10.36± 1.31)mmol/L，(5.23± 0.46)% vs. (5.88± 0.62)%](P＜0.05)；观察组最大血糖波动幅度(LAGS)、平均血糖波动幅度(MAGE)均明显低于对照组低，日平均达标率明显高于对照组[(7.43± 1.26)mmol/L vs. (8.58± 1.59)mmol/L，(3.39± 0.42)mmol/L vs. (5.21± 0.69)mmol/L，(90.34± 2.40)% vs. (82.01± 2.15)%](P＜0.05)；观察组胰岛素β细胞(HOMA-β)明显高于对照组，胰岛素抵抗指数(HOMA-IR)明显低于对照组[(53.84± 6.20) vs. (41.85± 5.03)，(2.84± 0.40) vs. (3.72± 0.72)](P＜0.05)；观察组血清RBP4、Leptin、Visfatin水平均明显低于对照组[(8.30± 1.20)mg/L vs. (10.57± 1.65)mg/L，(8.23± 1.42)μg/L vs. (10.84± 1.79)μg/L，(17.40± 2.42)μg/L vs. (24.03± 3.06)μg/L](P＜0.05)。两组治疗期间均未发生头晕、低血糖等药物不良反应。**结论：**吡格列酮联合阿卡波糖治疗2型糖尿病患者的临床效果显著由于单用阿卡波糖的患者，其可显著患者降低血糖水平和改善IR，其内在机制可能和降低血清RBP4、Leptin、Visfatin的表达相关。

关键词：2型糖尿病；吡格列酮；阿卡波糖；视黄醇结合蛋白4；瘦素；内脂素

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Effects of Pioglitazone Combined with Acarbose on the Serum RBP4, Leptin and Visfatin Levels of Patients with Type 2 Diabetes Mellitus*

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ABSTRACT Objective: To study the effect of pioglitazone combined with acarbose on the serum RBP4, leptin and visfatin levels of patients with type 2 diabetes mellitus. **Methods:** 80 patients of type 2 diabetes mellitus who admitted in our hospital from October 2015 to October 2017 were selected and divided into the observation group (n=46) and the control group (n=44) according to random number table. The control group was treated by acarbose on the basis of routine treatment, while the observation group was combined with pioglitazone on the basis of control group, all the patients were treated continuously for 12 weeks. The changes of blood glucose, dynamic blood glucose, islet cell function, serum RBP4, leptin and visfatin levels before and after treatment and incidence of adverse reactions were compared between the two groups. **Results:** After treatment, the fasting blood glucose (FBG), postprandial 2h blood glucose (2hPBG) and glycosylated hemoglobin (HbA1c) of observation group were significantly lower than those of the control group [(6.58± 1.30)mmol/L vs. (7.47± 1.44)mmol/L，(9.20± 1.22)mmol/L vs. (10.36± 1.31)mmol/L，(5.23± 0.46)% vs. (5.88± 0.62)%](P＜0.05); the maximal blood glucose fluctuation range (LAGS) and the average blood glucose fluctuation range (MAGE) of observation group were significantly lower than those of the control group, and the average daily rate of compliance was significantly higher than that of the control group [(7.43± 1.26)mmol/L vs. (8.58± 1.59)mmol/L, (3.39± 0.42)mmol/L vs. (5.21± 0.69)mmol/L, (90.34± 2.40)% vs. (82.01± 2.15)%](P＜0.05); the insulin beta cells (HOMA-β) of observation group were significantly higher than that of the control group, and the insulin resistance index (HOMA-IR) was significantly lower than that of the control group [(53.84± 6.20) vs. (41.85± 5.03), (2.84± 0.40) vs. (3.72± 0.72)](P＜0.05); the serum RBP4, leptin and visfatin levels of observation group were significantly lower than those of

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the control group [(8.30± 1.20)mg/L vs. (10.57± 1.65)mg/L, (8.23± 1.42)μg/L vs. (10.84± 1.79)μg/L, (17.40± 2.42)μg/L vs. (24.03± 3.06)μg/L](P＜0.05). There was no adverse reactions such as dizziness and hypoglycemia occurred in the two groups during treatment. **Conclusion:** Pioglitazone combined with acarbose is more effective in treatment of type 2 diabetes mellitus than acarbose alone, it can significantly reduce the blood glucose level and improve the IR, which may be related to the decrease of serum RBP4, leptin and visfatin levels.

Key words: Type 2 diabetes mellitus; Pioglitazone; Acarbose; Retinol-binding protein 4; Leptin; Visfatin

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前言

随着人们饮食习惯、生活方式的不断改变,我国 2 型糖尿病的患病率日趋升高[3]。长期的高血糖容易对机体各组织造成损伤,尤其是肾脏、心脏、神经、血管、眼,影响患者预后[1,2]。2 型糖尿病的发生和多种因素之间均存在着密切关系,近年来有大量报道显示各类脂肪因子的异常表达在该病的发生中发挥着重要作用,例如血清视黄醇结合蛋白 4(RBP4)、瘦素(Leptin)、内脂素(Visfatin)等[4,5]。

目前,2 型糖尿病的治疗包括饮食、运动及降糖治疗。阿卡波糖属α 葡萄糖苷酶抑制剂,对餐后高血糖具有明显的降低作用[6]。吡格列酮是一种噻唑烷二酮类抗糖尿病药物,属于胰岛素增敏剂,可增加依赖胰岛素对葡萄糖的处理,减少肝糖输出,发挥降糖效果[7,8]。目前,关于吡格列酮联合阿卡波糖用于 2 型糖尿病的治疗报道仍较少。因此,本研究主要探讨了吡格列酮联合阿卡波糖治疗 2 型糖尿病的临床效果,结果报道如下。

1 资料与方法

1.1 一般资料

选择 2015 年 10 月至 2017 年 10 月我院接诊的 2 型糖尿病患者 90 例进行研究,且研究已经我院伦理委员会批准。病例纳入标准:① 符合《中国 2 型糖尿病防治指南(2013 年版)》[9]中 2 型糖尿病诊断标准,空腹血糖(FBG)≥ 7.00 mmol/L,餐后 2 h 血糖(2hPBG)≥ 11.10 mmol/L;② 签署研究知情同意书。病例排除标准:① 合并肝、肾、心功能等严重障碍;② 合并糖尿病相关急性并发症;③ 合并严重急慢性感染、自身免疫性疾病、恶性肿瘤等;④ 近 6 个月内实施过重大手术;⑤ 对研究药物过敏。通过随机数表法将所有患者随机分为观察组和对照组(n=44),两组一般资料比较差异均无统计学意义(P＞0.05),具体见表 1。

表 1 两组一般资料的比较[$\bar{x}$± s]

Table 1 Comparison of the general information between two groups[$\bar{x}$± s]

Groups	Sex(M/F)	Age(year)	Waistline(cm)	BMI(kg/m²)	Course of disease(year)
Observation group(n=46)	26/20	47.84± 7.45	88.45± 7.24	24.76± 2.61	6.49± 1.36
Control group(n=44)	23/21	48.10± 7.19	88.10± 7.35	24.53± 2.70	6.63± 1.35
P value	0.686	0.867	0.821	0.682	0.625

1.2 治疗方法

两组均进行糖尿病常规处理,包括疾病相关知识普及、指导运动及饮食等。对照组于三餐餐前口服阿卡波糖片(规格 50 mg/ 片,厂家:杭州中美华东制药有限公司,国药准字 H20020202),50 mg/ 次,3 次 /d;观察组于早餐前联合吡格列酮片(规格 15 mg/ 片,厂家:大连石药集团远大制药有限公司,国药准字 H20052682)的口服,15 mg/ 次,1 次 /d。两组均连续治疗 12 周。

1.3 观察指标

1.3.1 血糖相关指标 于治疗前后采集 5 mL 空腹静脉血,离心速度为 3000 r/min,时间 10 min,离心完毕后,提取上层血清液,储存于冷冻箱内待检测,使用德国罗氏 ACCU-CHEK 罗康全血糖仪器检测 FBG、2hPBG 的变化;糖化血红蛋白(HbA1c)所使用的全自动生化分析仪 AU5421 由 Olympusa 提供,试剂盒为武汉明德生物科技股份有限公司生产的酶联免疫吸附法(ELISA)试剂盒。

1.3.2 动态血糖指标 于治疗前后为患者佩戴美国美敦力公司生产的血糖检测仪进行 72 h 的动态血糖监测,监测指标包括最大血糖波动幅度(LAGS)、平均血糖波动幅度(MAGE)以及日平均达标率。

1.3.3 胰岛细胞功能 使用稳态模型对胰岛素 β 细胞(HOMA-β)、胰岛素抵抗指数 (HOMA-IR) 进行评价,其中 HOMA-β 计算方式:20× 空腹胰岛素 (FINS)/ (FPG-3.5);HOMA-IR 计算方式:FPG× FINS/22.5。

1.3.4 血清 RBP4、Leptin、Visfatin 血清 RBP4、Leptin、Visfatin 的检测均使用 ELISA 法进行,试剂盒均购于上海联硕生物科技有限公司。

1.4 统计学分析

以 SPSS18.0 软件包处理实验数据,计量资料用均数± 标准差($\bar{x}$± s)表示,组间比较采用 t 检验,计数资料组间比较采用 x^2 检验,以 P<0.05 表示差异具有统计学意义。

2 结果

2.1 两组治疗前后血糖指标的比较

治疗前,两组 FBG、2hPBG、HbA1c 比较差异无统计学意义(P＞0.05);治疗后,两组 FBG、2hPBG、HbA1 均较治疗前显著降低 (P＜0.05),且观察组以上指标指标均明显低于对照组(P＜0.05),见表 2。

表 2 两组治疗前后血糖指标的比较($\bar{x}\pm s$)

Table 2 Comparison of the blood glucose index between two groups before and after treatment($\bar{x}\pm s$)

Groups		FBG(mmol/L)	2hPBG(mmol/L)	HbA1c(%)
Observation group(n=46)	Before treatment	8.55± 1.62	15.78± 1.40	6.47± 0.79
	After treatment	6.58± 1.30*#	9.20± 1.22*#	5.23± 0.46*#
Control group(n=44)	Before treatment	8.52± 1.67	15.59± 1.47	6.52± 0.78
	After treatment	7.47± 1.44*	10.36± 1.31*	5.88± 0.62*

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

2.2 两组治疗前后动态血糖指标的比较

治疗前，两组 LAGS、MAGE 和血糖日平均达标率比较差异无统计学意义(P＞0.05)，治疗后，两组 LAGS、MAGE 均较治疗前显著降低，而日平均达标率明显提高 (P＜0.05)，观察组 LAGS、MAGE 均明显低于对照组低，日平均达标率明显比对照组高(P＜0.05)，见表 3。

表 3 两组治疗前后动态血糖指标的比较($\bar{x}\pm s$)

Table 3 Comparison of the dynamic glycemic index between two groups before and after treatment ($\bar{x}\pm s$)

Groups		LAGS(mmol/L)	MAGE(mmol/L)	Average daily standard rate (%)
Observation group(n=46)	Before treatment	12.02± 2.30	7.47± 1.50	49.65± 7.42
	After treatment	7.43± 1.26*#	3.39± 0.42*#	90.34± 2.40*#
Control group(n=44)	Before treatment	12.15± 2.24	7.53± 1.47	49.27± 7.59
	After treatment	8.58± 1.59*	5.21± 0.69*	82.01± 2.15*

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

2.3 两组治疗前后胰岛细胞功能的比较

治疗前，两组 HOMA-β 和 HOMA-IR 比较差异无统计学意义 (P＞0.05)，两组治疗后 HOMA-β 较治疗前显著升高，而 HOMA-IR 较治疗前显著降低(P＜0.05)，观察组 HOMA-β 明显高于对照组，HOMA-IR 明显低于对照组(P＜0.05)，见表 4。

表 4 两组治疗前后胰岛细胞功能的比较($\bar{x}\pm s$)

Table 4 Comparison of the islet cell function between two groups before and after treatment($\bar{x}\pm s$)

Groups		HOMA-β	HOMA-IR
Observation group(n=46)	Before treatment	24.34± 2.41	4.75± 1.24
	After treatment	53.84± 6.20*#	2.84± 0.40*#
Control group(n=44)	Before treatment	24.17± 2.49	4.83± 1.21
	After treatment	41.85± 5.03*	3.72± 0.72*

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

2.4 两组治疗前后血清 RBP4、Leptin、Visfatin 水平的比较

治疗前，两组血清 RBP4、Leptin、Visfatin 水平比较差异无统计学意义(P＞0.05)。治疗后，两组血清 RBP4、Leptin、Visfatin 水平均明显低于治疗前(P＜0.05)，且观察组以上指标均明显低于对照组(P＜0.05)，见表 5。

表 5 两组治疗前后血清 RBP4、Leptin、Visfatin 水平的比较($\bar{x}\pm s$)

Table 5 Comparison of the serum RBP4, Leptin, Visfatin levels between two groups before and after treatment($\bar{x}\pm s$)

Groups		RBP4(mg/L)	Leptin(μg/L)	Visfatin(μg/L)
Observation group(n=46)	Before treatment	14.04± 1.75	13.30± 2.17	32.40± 4.76
	After treatment	8.30± 1.20*#	8.23± 1.42*#	17.40± 2.42*#
Control group(n=44)	Before treatment	13.95± 1.82	13.19± 2.35	32.72± 4.50
	After treatment	10.57± 1.65*	10.84± 1.79*	24.03± 3.06*

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

2.5 两组不良反应发生情况的比较

两组治疗期间均未发生头晕、低血糖等药物不良反应。

3 讨论

近 30 年来,我国糖尿病的发生率呈现着不断增长的趋势。1980 年，我国糖尿病的患病率为 0.70%左右,1994~1995 年增加至 2.50%,近 10 年的调查数据中显示我国 20 岁以上人群患糖尿病的概率高达 9.00%,且呈现着增长趋势[10,11]。目前,对于糖尿病的治疗尚无根治手段，主要以积极控制血糖水平为主。阿卡波糖的降糖作用主要是通过对各种 α- 葡萄糖苷酶如麦芽糖酶、葡萄糖淀粉酶、异麦芽糖酶等活性产生抑制作用,令淀粉分解,减缓肠道对葡萄糖的吸收能力,继而达到降低餐后血糖的作用。但有研究显示需长期使用阿卡波糖才可达到有效的降低 FBG、HbA1c 作用,但其在一定程度上可导致患者出现胃肠道功能紊乱[12,13]。吡格列酮主要是通过对过氧化物酶增殖物受体产生激活作用,继而对葡萄糖和脂肪酸相关代谢的转录进行调节,改善胰岛素性敏感基因[14]。Niu SW 等[15]基础实验也证实吡格列酮还具有抗炎作用，并对 IR 相关的代谢指标具有改善作用。

本研究结果显示联合用药的患者在血糖指标、动态血糖指标、胰岛素细胞功能指标的改善程度上均明显优于单用阿卡波糖治疗的患者。黄凯程等[16]报道也得出与本研究相似结论。考虑和联合使用吡格列酮可加强机体细胞对葡萄糖的利用度,提高周围组织和肝脏对胰岛素的敏感性,减少肝糖输出,并联合阿卡波糖的降糖作用,两药发挥相互协调效果,进一步发挥更好的降糖、改善 IR 效果。本研究中,两组均未发生头晕、低血糖等药物不良反应,也提示该方式用于 2 型糖尿病是安全有效的。

RBP4 的分泌主要来自于肝脏,Meex RCR 等[17]动物实验显示血清 RBP4 的增加可降低胰岛素敏感性,使小鼠葡萄糖的内环境稳态发生改变。Codoñer-Franch P 等[18]报道也指出 RBP4 对磷酸烯醇、丙酮酸激酶基因的表达均具有直接诱导作用,可使肝糖输出增加,限制肌肉的糖摄取量,继而引发全身心的胰岛素抵抗(IR)。Leptin 在机体摄食、能量代谢、体质量调节等方面发挥着重要的作用,且其可直接作用于下丘脑,影响中枢调节系统,并通过向中枢系统提供机体营养状况和脂肪组织的信息。已有较多报道指出 2 型糖尿病患者血清 Leptin 的表达明显高于健康人群,且和远期心血管疾病的发生、发展之间存在着密切的关系 [19,20]。Visfatin 是一种由脂肪组织所分泌的脂肪因子,参与着机体的炎症反应和免疫调节等,其可通过和胰岛素受体的非胰岛素结位点的相互结合，促进脂肪细胞的分化、成熟及蓄积,并通过旁分泌的形式促使脂肪合成,导致血糖升高[21]。Berezin AE 等[22]研究显示 Visfatin 可作为 2 型糖尿病发病的独立危险因素。

本研究结果显示联合吡格列酮的患者血清 RBP4、Leptin、Visfatin 的降低程度明显优于单独使用阿卡波糖的患者，通过分析可能是由于吡格列酮对游离脂肪酸具有抑制作用,可进一步降低体内脂肪因子的表达。Yandrapalli S 等[23]研究将吡格列酮用于糖尿病合并高血压的患者,也发现吡格列酮不仅具有降糖作用,且可调节脂肪代谢紊乱。这也可能是联合用药的患者疗效更令人满意的内在机制之一。但由于本研究的时间较短,而糖尿病的治疗是一个漫长的过程,对其用于治疗糖尿病的远期疗效及安全性仍需深入研究。

综上所述,吡格列酮联合阿卡波糖治疗 2 型糖尿病患者的临床效果显著由于单用阿卡波糖的患者,其可显著患者降低血糖水平和改善 IR，其内在机制可能和降低血清 RBP4、Leptin、Visfatin 的表达相关。

参 考 文 献(References)

[1] Qiu QY, Zhang BL, Zhang MZ, et al. Combined Influence of Insulin Resistance and Inflammatory Biomarkers on Type 2 Diabetes: A Population-based Prospective Cohort Study of Inner Mongolians in China [J]. Biomed Environ Sci, 2018, 31(4): 300-305

[2] Ding C, Yang Z, Wang S, et al. The associations of metabolic syndrome with incident hypertension, type 2 diabetes mellitus and chronic kidney disease: a cohort study[J]. Endocrine, 2018, 60(2): 282-291

[3] Hu C, Jia W. Diabetes in China: Epidemiology and Genetic Risk Factors and Their Clinical Utility in Personalized Medication [J]. Diabetes, 2018, 67(1): 3-11

[4] Huang N, Zhou J, Wang W, et al. Retinol-binding protein 4 is positively associated with bone mineral density in patients with type 2 diabetes and osteopenia or osteoporosis [J]. Clin Endocrinol (Oxf), 2018, 88 (5): 659-664

[5] Tan S, Du P, Zhao W, et al. Exercise Training at Maximal Fat Oxidation Intensity for Older Women with Type 2 Diabetes [J]. Int J Sports Med, 2018, 39(5): 374-381

[6] Proença C, Freitas M, Ribeiro D, et al. α-Glucosidase inhibition by flavonoids: an in vitro and in silico structure-activity relationship study[J]. J Enzyme Inhib Med Chem, 2017, 32(1): 1216-1228

[7] Qian X, Wang H, Yang G, et al. Pioglitazone Improved Insulin Sensitivity and First Phase Insulin Secretion Among Obese and Lean People with Diabetes: A Multicenter Clamp Study [J]. Diabetes Ther, 2018, 9(2): 815-826

[8] Goyal A, Singh H, Sehgal VK, et al. Impact of regulatory spin of pioglitazone on prescription of antidiabetic drugs among physicians in India: A multicentre questionnaire-based observational study[J]. Indian J Med Res, 2017, 146(4): 468-475

[9] Chinese Diabetes Society. Guidelines for the prevention and control of type 2 diabetes in China (2013 Edition)[J]. Chinese Journal of medical Frontiers (Electronic Edition), 2015, 7(03): 26-89

[10] Tang H, Li G, Zhao Y, et al. Comparisons of diabetic retinopathy events associated with glucose-lowering drugs in patients with type 2 diabetes mellitus: A network meta-analysis [J]. Diabetes Obes Metab, 2018, 20(5): 1262-1279

[11] Zhao HY, Yang J, Sun F, et al. Risk and related factors on metabolic syndrome among people who had received screening on physical check-up programs, in China [J]. Chin J of Epidemiology, 2017, 38 (12): 1591-1597

[12] Nauck MA, Meier JJ. Break point instead of ACE: acarbose, postload glycaemic excursions, and cardiovascular events [J]. Lancet Diabetes Endocrinol, 2017, 5(11): 843-845

[13] Du J, Liang L, Fang H, et al. Efficacy and safety of saxagliptin compared with acarbose in Chinese patients with type 2 diabetes mellitus uncontrolled on metformin monotherapy: Results of a Phase IV open-label randomized controlled study (the SMART study)[J]. Diabetes Obes Metab, 2017, 19(11): 1513-1520

(下转第 4121 页)

(12): 3028-3033

[6] Kahwati LC, Feltner C, Halpern M, et al. Primary Care Screening and Treatment for Latent Tuberculosis Infection in Adults: Evidence Report and Systematic Review for the US Preventive Services Task Force[J]. JAMA, 2016, 316(9): 970-983

[7] Moro RN, Borisov AS, Saukkonen J, et al. Factors Associated With Noncompletion of Latent Tuberculosis Infection Treatment: Experience From the PREVENT TB Trial in the United States and Canada [J]. Clin Infect Dis, 2016, 62(11): 1390-400

[8] Cruz AT, Starke JR. Safety and Adherence for 12 Weekly Doses of Isoniazid and Rifapentine for Pediatric Tuberculosis Infection [J]. Pediatr Infect Dis J, 2016, 35(7): 811-813

[9] Hatzenbuehler LA, Starke JR, Graviss EA, et al. School-based Study to Identify and Treat Adolescent Students at Risk for Tuberculosis Infection[J]. Pediatr Infect Dis J, 2016, 35(7): 733-738

[10] Zurlinden TJ, Eppers GJ, Reisfeld B. Physiologically Based Pharmacokinetic Model of Rifapentine and 25-Desacetyl Rifapentine Disposition in Humans [J]. Antimicrob Agents Chemother, 2016, 60(8): 4860-4868

[11] Lines G, Hunter P, Bleything S. Improving Treatment Completion Rates for Latent Tuberculosis Infection: A Review of Two Treatment Regimens at a Community Health Center [J]. J Health Care Poor Underserved, 2015, 26(4): 1428-1439

[12] Vidal JS, Silva MT, Sanchez MN. Rifapentine for latent tuberculosis infection treatment in the general population and human immunodeficiency virus-positive patients: summary of evidence[J]. Rev Soc Bras Med Trop, 2015, 48(5): 507-513

[13] Stennis NL, Burzynski JN, Herbert C, et al. Treatment for Tuberculosis Infection With 3 Months of Isoniazid and Rifapentine in New York City Health Department Clinics[J]. Clin Infect Dis, 2016, 62(1): 53-59

[14] Kowada A. Cost effectiveness of interferon-gamma release assay for tuberculosis screening using three months of rifapentine and isoniazid among long-term expatriates from low to high incidence countries[J]. Travel Med Infect Dis, 2016, 14(5): 489-498

[15] Wyndham-Thomas C, Corbière V, Selis E, et al. Immune Activation by Mycobacterium tuberculosis in HIV-Infected and -Uninfected Subjects[J]. J Acquir Immune Defic Syndr, 2017, 74(1): 103-111

[16] Ravimohan S, Tamuhla N, Nfanyana K, et al. Robust Reconstitution of Tuberculosis-Specific Polyfunctional $CD4^+$ T-Cell Responses and Rising Systemic Interleukin 6 in Paradoxical Tuberculosis-Associated Immune Reconstitution Inflammatory Syndrome [J]. Clin Infect Dis, 2016, 62(6): 795-803

[17] Zhang L, Chen Y, Liu W, et al. Evaluating the clinical significances of serum HE4 with CA125 in peritoneal tuberculosis and epithelial ovarian cancer[J]. Biomarkers, 2016, 21(2): 168-172

[18] Ma J, Xia D, Hu J, et al. Predictive Role of Serum Tumor Markers in Diagnosis of Pulmonary Tuberculosis [J]. Iran J Public Health, 2016, 45(4): 435-440

[19] Podany AT, Bao Y, Swindells S, et al. Efavirenz Pharmacokinetics and Pharmacodynamics in HIV-Infected Persons Receiving Rifapentine and Isoniazid for Tuberculosis Prevention [J]. Clin Infect Dis, 2015, 61(8): 1322-1327

[20] Dawson R, Narunsky K, Carman D, et al. Two-stage activity-safety study of daily rifapentine during intensive phase treatment of pulmonary tuberculosis[J]. Int J Tuberc Lung Dis, 2015, 19(7): 780-786

(上接第 4155 页)

[14] Jameshorani M, Sayari S, Kiahashemi N, et al. Comparative Study on Adding Pioglitazone or Sitagliptin to Patients with Type 2 Diabetes Mellitus Insufficiently Controlled With Metformin [J]. Open Access Maced J Med Sci, 2017, 5(7): 955-962

[15] Niu SW, Chang KT, Lin HY, et al. Decreased incidence of gout in diabetic patients using pioglitazone[J]. Rheumatology (Oxford), 2018, 57(1): 92-99

[16] Huang KC, Chen XM, Wang YF, et al. Clinical trial of pioglitazone and acarbose on type 2 diabetes elderly patients with hypertension[J]. Chin J Clin Pharmacol, 2016, 32(16): 1468-1470+1484

[17] Meex RCR, Watt MJ. Hepatokines: linking nonalcoholic fatty liver disease and insulin resistance [J]. Nat Rev Endocrinol, 2017, 13(9): 509-520

[18] Codoñer-Franch P, Carrasco-Luna J, Allepuz P, et al. Association of RBP4 genetic variants with childhood obesity and cardiovascular risk factors[J]. Pediatr Diabetes, 2016, 17(8): 576-583

[19] Diwan AG, Kuvalekar AA, Dharamsi S, et al. Correlation of Serum Adiponectin and Leptin levels in Obesity and Type 2 Diabetes Mellitus[J]. Indian J Endocrinol Metab, 2018, 22(1): 93-99

[20] Bonfante ILP, Chacon-Mikahil MPT, Brunelli DT, et al. Obese with higher FNDC5/Irisin levels have a better metabolic profile, lower lipopolysaccharide levels and type 2 diabetes risk[J]. Arch Endocrinol Metab, 2017, 61(6): 524-533

[21] Carbone F, Liberale L, Bonaventura A, et al. Regulation and Function of Extracellular Nicotinamide Phosphoribosyltransferase/Visfatin [J]. Compr Physiol, 2017, 7(2): 603-621

[22] Berezin AE, Samura TA, Kremzer AA, et al. An association of serum vistafin level and number of circulating endothelial progenitor cells in type 2 diabetes mellitus patients [J]. Diabetes Metab Syndr, 2016, 10 (4): 205-212

[23] Yandrapalli S, Aronow WS. Cardiovascular benefits of the newer medications for treating type 2 diabetes mellitus [J]. J Thorac Dis, 2017, 9(7): 2124-2134