

doi: 10.13241/j.cnki.pmb.2022.07.037

阿卡波糖辅助治疗糖尿病合并甲状腺功能亢进的效果 及对 T₄、TSH 及脂联素的影响 *

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摘要 目的:探讨阿卡波糖辅助治疗糖尿病合并甲状腺功能亢进的效果及对甲状腺素(T₄)、促甲状腺激素(TSH)及脂联素的影响。**方法:**选择 2019 年 1 月-2021 年 1 月在我院接受治疗的 105 例糖尿病合并甲状腺功能亢进患者,采用随机数表法分为试验组(n=53)和对照组(n=52)。对照组给予甲巯咪唑和甘精胰岛素治疗,试验组在对照组的基础上加用阿卡波糖治疗。比较两组临床疗效、T₄、TSH 及脂联素、空腹血糖(FBG)、餐后 2 h 血糖(PBG)、胰岛素抵抗(Homa-IR)、胰岛 β 细胞指数(Homa-β)水平变化情况及不良反应发生情况。**结果:**治疗后,两组总有效率比较差异显著($P<0.05$);治疗前,试验组和对照组血清 T₄、TSH 及脂联素比较无显著差异;治疗后,试验组和对照组血清 T₄ 及脂联素均随着时间的推移而降低,且试验组均低于对照组,TSH 随着时间的推移而升高,且试验组高于对照组,差异显著($P<0.05$);治疗前,试验组和对照组血清 FBG、PBG 比较无显著差异;治疗后,试验组和对照组血清 FBG、PBG 均随着时间的推移而降低,且试验组均低于对照组,差异显著($P<0.05$);治疗前,试验组和对照组血清 Homa-IR、Homa-β 比较无显著差异;治疗后,试验组和对照组血清 Homa-IR、Homa-β 均随着时间的推移而降低,且试验组均低于对照组,差异显著($P<0.05$);两组不良反应总发生率为 3.77%、9.62%,无显著差异($P>0.05$)。**结论:**在糖尿病合并甲状腺功能亢进中应用阿卡波糖辅助治疗疗效显著,可有效改善患者 T₄、TSH 及脂联素水平。

关键词:阿卡波糖;辅助治疗;糖尿病;甲状腺功能亢进;甲状腺素;促甲状腺激素;脂联素

中图分类号:R587.1;R581 **文献标识码:**A **文章编号:**1673-6273(2022)07-1371-04

Effect of Acarbose in the Adjuvant Treatment of Diabetes Mellitus Complicated with Hyperthyroidism and Its Effect on T₄, TSH and Adiponectin*

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ABSTRACT Objective: To study Effect of acarbose in the adjuvant treatment of diabetes mellitus complicated with hyperthyroidism and its effect on Thyroid hormone (T₄), thyroid stimulating hormone (TSH) and adiponectin. **Methods:** 105 diabetic patients with hyperthyroidism who received treatment in our hospital from January 2019 to January 2021 were selected and divided into experimental group (n=53) and control group (n=52) by random number table method. Methimazole and insulin glargine were given to the control group, and acarbose was added to the control group. Clinical efficacy, T₄, TSH, adiponectin, fasting blood glucose (FBG), 2 h postprandial blood glucose (PBG), insulin resistance (HOMA-IR), islet β-cell index (HOMA-β) and the incidence of ADR were compared between the two groups. **Results:** After treatment, the total effective rate between the two groups was significantly different ($P<0.05$). Before treatment, there were no significant differences in serum T₄, TSH and adiponectin between the experimental group and the control group. After treatment, serum T₄ and adiponectin in experimental group and control group decreased with time, and TSH in experimental group was lower than control group, and the difference was significant ($P<0.05$). Before treatment, there was no significant difference in serum FBG and PBG between the experimental group and the control group. After treatment, serum FBG and PBG in experimental group and control group decreased with the passage of time, and the difference was significant ($P<0.05$). Before treatment, there were no significant differences in serum HOMA-IR and HOMA-β between the experimental group and the control group. After treatment, serum HOMA-IR and HOMA-β in both experimental and control groups decreased with time, and the difference was significant ($P<0.05$). The total incidence of adverse reactions between the two groups was 3.77% and 9.62%, with no significant difference ($P>0.05$). **Conclusion:** The adjuvant treatment of acarbose in diabetic patients with hyperthyroidism has a significant effect,

* 基金项目:河北省科技计划项目(16277135)

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(收稿日期:2021-08-26 接受日期:2021-09-22)

which can effectively improve the levels of T₄, TSH and adiponectin in patients.

Key words: Acarbose; Adjuvant therapy; Diabetes; Hyperthyroidism; Thyroxine; Thyroid stimulating hormone; Adiponectin

Chinese Library Classification(CLC): R587.1; R581 **Document code:** A

Article ID: 1673-6273(2022)07-1371-04

前言

甲状腺功能亢进是内分泌常见疾病,是由于多种致病因素导致甲状腺激素异常分泌过高引起的,可加重患者循环、神经系统负担,对机体的生长、发育造成重要的影响,影响患者日常生活^[1-3]。糖尿病是由胰岛素不足所致的代谢紊乱综合征,而甲状腺功能亢进患者多存在糖代谢异常,有研究显示,糖尿病患者并发甲状腺功能异常的发生率较非糖尿病患者高,二种疾病相互促进,对临床治疗带来较大困难^[4,5]。临床治疗糖尿病合并甲状腺功能亢进主要以甘精胰岛素为主,但部分患者治疗后会出现血糖异常波动,治疗效果不佳^[6]。阿卡波糖是一种 α -葡萄糖苷酶抑制剂,可抑制各种 α -葡萄糖苷酶活性,减缓肠道葡萄糖的吸收,从而控制血糖水平^[7,8]。有研究显示,糖尿病合并甲状腺功能亢进的发生可导致T₄、脂联素升高,促进疾病的进展^[9]。本研究旨在探讨阿卡波糖辅助治疗糖尿病合并甲状腺功能亢进的效果,并分析其对T₄、TSH及脂联素的影响。

1 资料与方法

1.1 一般资料

选择2019年1月-2021年1月在我院接受治疗的105例糖尿病合并甲状腺功能亢进患者,采用随机数表法分为2组,试验组53例,男25例,女28例,年龄36~65岁,平均(52.15±3.16)岁,糖尿病病程1~13年,平均(6.89±1.24)年,甲亢病程1~9月,平均(5.26±1.21)月。对照组52例,男26例,女26例,年龄35~66岁,平均(52.21±3.17)岁,糖尿病病程1~12年,平均(6.81±1.22)年,甲亢病程1~10月,平均(5.31±1.15)月。两组一般资料无显著差异($P>0.05$),可比较。

参照《中国2型糖尿病防治指南》^[10]中的诊断标准;空腹血糖大于5.1 mmol/L。甲状腺亢进:代谢性亢进;皮肤潮湿、多汗;

甲状腺多呈弥漫性肿大,质地软或坚韧。

纳入标准:(1)符合相关标准;(2)肝肾功能正常;(3)无胰岛素治疗史;(4)相关指标数据完整;(5)知情同意。排除标准:(1)出血性疾病者;(2)心功能异常者;(3)近3个月有抗生素治疗者;(4)严重自身免疫性疾病;(5)妊娠、哺乳期者;(6)对本研究药物过敏者。

1.2 方法

对照组给予甲巯咪唑(规格20 mg,厂家:Merck KGaA, Darmstadt, 国药准字J20171078)20 mg口服治疗,1d1次;甘精胰岛素(规格3.64 mg,厂家:Aventis Pharma Deutschland GmbH, 国药准字S20140005)10U睡前注射。试验组在对照组的基础上给予阿卡波糖:(规格:50 mg;生产厂家:拜耳医药保健有限公司;国药准字:H19990205)50 mg,餐前口服,每日3次。

1.3 观察指标

采集肘静脉血4 mL,采用酶联免疫吸附试验测定T₄、TSH、脂联素、FBG、PBG水平;记录治疗前后Homa-IR、Homa- β ;记录不良反应。

疗效评定标准:显效:血糖、血压各项恢复正常,症状消失;有效:症状消失,血红蛋白小于6.2%;无效:无明显改善或加重。

1.4 统计学分析

以spss22.0软件包处理,符合正态分布计量资料用均数±标准差($\bar{x}\pm s$)表示,组间比较使用独立样本t检验,计数资料以率表示, χ^2 检验, $P<0.05$ 表示差异具有统计学意义。

2 结果

2.1 治疗后两组临床治疗效果评价

治疗后,两组总有效率比较差异显著($P<0.05$)见表1。

表1 治疗后两组临床治疗效果评价[n(%)]

Table 1 Clinical efficacy evaluation of the two groups after treatment[n(%)]

Groups	n	Excellent	valid	Invalid	Total effective rate
Experimental group	53	24(45.28)	25(47.17)	4(7.55)	49(92.45)
Control group	52	29(55.77)	11(21.15)	12(23.08)	40(76.92)
χ^2 value					4.901
P value					0.027

2.2 治疗前后T₄、TSH及脂联素水平比较

治疗前,试验组和对照组血清T₄、TSH及脂联素比较无显著差异;治疗后,试验组和对照组血清T₄及脂联素均随着时间的推移而降低,且试验组均低于对照组,TSH随着时间的推移而升高,且试验组高于对照组,差异显著($P<0.05$),见表2。

2.3 治疗前后血糖水平比较

治疗前,试验组和对照组血清FBG、PBG比较无显著差

异;治疗后,试验组和对照组血清FBG、PBG均随着时间的推移而降低,且试验组均低于对照组,差异显著($P<0.05$),见表3。

2.4 治疗前后Homa-IR、Homa- β 水平比较

治疗前,试验组和对照组血清Homa-IR、Homa- β 比较无显著差异;治疗后,试验组和对照组血清Homa-IR、Homa- β 均随着时间的推移而降低,且试验组均低于对照组,差异显著($P<0.05$),见表4。

表 2 治疗前后 T₄、TSH 及脂联素水平比较($\bar{x} \pm s$)Table 2 Comparison of T₄, TSH and adiponectin levels before and after treatment($\bar{x} \pm s$)

Groups	n	T ₄ (nmol/L)		TSH(U/L)		adiponectin(mg/dl)	
		Before the intervention	After the intervention	Before the intervention	After the intervention	Before the intervention	After the intervention
Experimental group	53	273.38±31.05	121.78±11.04	0.57±0.15	3.93±1.21	289.48±40.56	214.56±40.15
Control group	52	269.41±30.89	156.51±14.67	0.52±0.16	2.41±1.50	290.15±50.89	256.63±40.78
<i>t</i> value		0.657	13.724	1.652	5.720	0.075	5.327
<i>P</i> value		0.513	0.000	0.102	0.000	0.941	0.000

表 3 治疗前后血糖水平比较($\bar{x} \pm s$, mmol/L)Table 3 Comparison of blood glucose levels before and after treatment($\bar{x} \pm s$, mmol/L)

Groups	n	FBG		PBG	
		Before the intervention	After the intervention	Before the intervention	After the intervention
Experimental group	53	10.18±1.48	6.31±1.04	12.51±2.06	9.51±1.71
Control group	52	10.21±1.51	8.09±1.22	12.47±2.07	10.82±1.67
<i>t</i> value		0.103	8.051	0.099	3.971
<i>P</i> value		0.918	0.000	0.921	0.000

表 4 治疗前后 Homa-IR、Homa-β 水平比较($\bar{x} \pm s$, pmol/L)Table 4 Comparison of thyroid hormone levels before and after treatment($\bar{x} \pm s$, pmol/L)

Groups	n	Homa-IR		Homa-β	
		Before the intervention	After the intervention	Before the intervention	After the intervention
Experimental group	53	4.75±0.86	2.52±0.45	40.93±7.16	66.37±11.13
Control group	52	4.81±0.92	3.45±0.66	41.32±7.24	52.68±9.21
<i>t</i> value		0.314	7.911	0.251	6.095
<i>P</i> value		0.754	0.000	0.802	0.000

2.5 安全性评价

($P>0.05$),见表 5。

两组不良反应总发生率为 3.77%、9.62%，无显著差异

表 5 安全性评价[n(%)]

Table 5 Safety evaluation[n(%)]

Groups	n	Low blood sugar	Nausea	Thyroid disorder	The total incidence of
Experimental group	53	1	1	0	2(3.77)
Control group	52	2	1	2	5(9.62)
χ^2 value					1.439
<i>P</i> value					0.230

3 讨论

糖尿病主要表现为血糖持续升高,致残率和死亡率较高,死亡率仅次于心血管疾病和肿瘤,甲状腺功能亢进是糖尿病常见的并发症,若机体长期处于高血糖会兴奋甲状腺功能,调节胰岛 β 细胞功能,进一步使血糖升高,形成恶性循环^[11,12]。据调查显示,糖尿病和甲状腺功能亢进具有相似的免疫学及遗传学基础,近年来随着人们生活方式的改变,糖尿病合并甲状腺功能亢进发病率逐渐升高,会加重患者机体损伤程度,危及患者

生命^[13]。有学者认为^[14,15],糖尿病合并甲状腺功能亢进的原因可能是:(1) 甲状腺激素具有拮抗胰岛素的作用,可导致血糖增高,而当病情得到控制后血糖水平恢复正常;(2)甲状腺功能亢进与糖尿病遗传缺陷存在于同一染色体上,而甲状腺功能亢进可加重糖尿病病情,因此控制甲亢对缓解糖尿病具有重要意义。甘精胰岛素是一种新的长效胰岛素类似物,是目前治疗糖尿病的常用药物,可调节患者机体糖代谢过程,从患者脂肪、骨骼肌等组织中摄取到葡萄糖,抑制肝葡萄糖的形成,达到控制血糖的效果^[16-18]。但有研究显示,单独使用甘精胰岛素治疗糖尿

病合并甲状腺功能亢进部分患者血糖控制效果欠佳,需联合其他药物辅助治疗提高临床治疗效果^[19]。

阿卡波糖是一种新型口服降糖药,可缓解糖耐量受损,延缓碳水化合物吸收,降低肠道葡萄糖水平,控制餐后血糖,可降低空腹血糖和糖化血红蛋白的浓度,具有平稳降糖效果^[20,21]。有研究显示,阿卡波糖具有较高的安全性,可促进分泌胆囊收缩素,减少糖类摄入,发挥降血糖作用^[22]。本研究结果显示,阿卡波糖辅助治疗的患者总有效率高于对照组,且两组患者不良反应总发生率为3.77%、9.62%,无明显差异,结果提示,阿卡波糖辅助治疗糖尿病合并甲状腺功能亢进效果显著,能提高临床治疗效果,且不会增加不良反应发生率。Ahmed A M^[23]等研究也显示,阿卡波糖辅助治疗可通过降低患者体内炎症反应,缓解糖尿病合并甲状腺功能亢进的临床症状,与本研究结果相似。

有研究显示,甲状腺功能异常与糖尿病及甲状腺功能亢进均有密切关系,甲状腺激素水平异常是糖尿病的发病原因之一,糖尿病较其他患者更易出现甲状腺异常,从而反过来影响体内脂肪、糖代谢,从而促进糖尿病的发展^[24,25]。T₄、TSH是临床常用的甲状腺激素指标,其中T₄是甲状腺所分泌的唯一直接在细胞水平发挥生理作用的激素;TSH是由腺垂体分泌的激素,受下丘脑分泌的促甲状腺激素释放激素的影响,能控制、调节甲状腺的活动^[26-28]。脂联素是由白色脂肪组织特异性分泌的,主要分布于血液循环中,是脂肪组织分泌的唯一对人体有益的细胞因子,具有调节血糖血脂的作用,改善改善胰岛素抵抗^[29]。有研究显示,甲状腺功能异常与脂肪因子之间也存在着密切联系,可能参与了糖尿病等代谢性疾病的发生^[30]。本研究结果显示,治疗后,患者血清T₄及脂联素均随着时间的推移而降低,且试验组均低于对照组,TSH随着时间的推移而升高,且试验组高于对照组,进一步提示了阿卡波糖辅助治疗糖尿病合并甲状腺功能亢进可改善患者甲状腺激素水平,Hu C^[31]等研究也显示,阿卡波糖可降低机体糖分吸收率,改善甲状腺功能,与本研究结果相似。分析其原因可能是因为阿卡波糖能改善甲状腺功能储备,减少机体对甲状腺激素的需求,从而改善甲状腺功能。本研究还显示,治疗后患者血清FBG、PBG明显降低,且阿卡波糖辅助治疗的患者低于对照组,提示,阿卡波糖治疗糖尿病合并甲状腺功能亢进效果显著,能降低患者体内血糖水平,对促进疾病的恢复具有重要意义,分析其原因可能是因为甲状腺功能亢进可导致患者体内甲状腺激素分泌过多,导致患者体内蛋白质、脂肪利用度高,导致血糖升高,而阿卡波糖联合甘精胰岛素可发挥药物协同作用,通过降低葡萄糖苷水解酶活性,从而降低机体糖分吸收率,从而控制血糖水平。本研究结果还显示,治疗后患者Homa-IR均显著减低,试验组低于对照组,Homa-β显著升高,试验组高于对照组,进一步说明阿卡波糖辅助治疗糖尿病合并甲状腺功能亢进可改善患者胰岛素功能。

综上所述,在糖尿病合并甲状腺功能亢进中应用阿卡波糖辅助治疗疗效显著,可有效改善患者T₄、TSH及脂联素水平。

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