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口服降糖药和胰岛素对不同临床分期糖尿病视网膜病变病情进程的影响*

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摘要 目的:探讨降糖药物和胰岛素控制血糖对不同临床分期糖尿病视网膜病变病情进程的影响。**方法:**收集糖尿病伴有视网膜病变的患者 78 例。采用随机表法,将糖尿病视网膜病变患者分为药物控制血糖组和胰岛素控制组,药物治疗组 38 例,胰岛素治疗组 40 例,使血糖达到控制标准。评价干预前后患者血清 C 肽、糖化血红蛋白、胰岛素抵抗指数,以及糖尿病视网膜病变分级。**结果:**药物控制组治疗前后 2 h CP、以及糖化血红蛋白测定差异无统计学意义($p>0.05$)。胰岛素组治疗前后,血清空腹 C 肽、2 h CP 差异有统计学意义($p<0.05$);而糖化血红蛋白、胰岛素抵抗指数差异无统计学意义($p>0.05$)。药物组治疗前 I 期、II 期、III 期、IV 期、V 期、VI 期病例数和治疗后相比,差异有统计学意义($p<0.05$),视网膜病变分级程度明显增高。胰岛素组治疗前 I 期、II 期、III 期、IV 期、V 期、VI 期病例数和治疗后相比,差异有统计学意义($p<0.05$)。药物组和胰岛素组间视网膜病变分级差异无统计学意义($p>0.05$);治疗后差异有统计学意义($p<0.05$)。**结论:**胰岛素能够提高糖尿病患者血清 C 肽,降低胰岛素抵抗,和药物控制血糖相比,能够延缓糖尿病视网膜病变的进展。

关键词:糖尿病视网膜病变;药物控制;胰岛素控制;病变进展

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Effects of Oral Medications and Insulin on Disease Progress of Different Clinical Stages of Diabetic Retinopathy*

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ABSTRACT Objective: To investigate the influences of hypoglycemic drugs and insulin to keep blood sugar under control on the procession of diabetic retinopathy in different clinical stages. **Methods:** From January 2014 to February 2015, 78 cases of diabetes associated with retinopathy patients were collected. By random table method, the patients with diabetic retinopathy were divided into drug group (38 cases) and insulin group (40 cases), to control their blood sugar levels to standards. Evaluate the levels of serum C peptide, glycosylated hemoglobin, insulin resistance index, and diabetic retinopathy grades of patients before and after the intervention. **Results:** There were no statistically significant differences in CP and glycosylated hemoglobin levels in the drug group at 2 h before and after treatment ($p > 0.05$). In Insulin group, there was statistically significant difference in fasting serum c-peptide and 2h CP before and after treatment ($p < 0.05$), while the glycosylated hemoglobin and insulin resistance index had no statistical difference ($p > 0.05$). In drug group, the numbers of cases in stage I, II, III, IV, V or VI before treatment were statistically different from those after treatment ($p < 0.05$), and retinopathy grade increased significantly. In insulin group, the numbers of cases in stage I, II, III, IV, V or VI before treatment were also statistically different from those after treatment ($p < 0.05$). Before treatment, the retinopathy grade differences between drug group and insulin group had no statistical significance ($p > 0.05$), but the difference was statistically significant after treatment ($p < 0.05$). **Conclusion:** Insulin can improve the serum C peptide and reduce the insulin resistance of diabetic retinopathy patients. Compared with medications to control blood sugar, insulin can delay the progress of diabetic retinopathy.

Key words: Diabetic retinopathy; Drug control; Insulin control; Lesion progress

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前言

糖尿病及糖尿病血管病变给社会发展和人类的健康带来了严重的负担。根据国际糖尿病协会保守预计,到 2025 年将近有 3.5 亿的糖尿病患者^[1]。糖尿病最重要的并发症之一小血管

并发症,导致糖尿病视网膜病变、糖尿病足及糖尿病肾病等^[2]。目前,糖尿病视网膜病变(DR)是导致老年人眼失明的主要原因之一,其发病率随糖尿病患病时间和年龄的增长而升高^[3]。DR 会造成糖尿病患者的视力的快速下降,流行病学调查显示,2 型糖尿病中大概有 20%-40% 办法糖尿病视网膜病变,其中大

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概 8% 最终导致失明^[4]。控制血糖可以采用药物控制,或者胰岛素控制,或者药物联合胰岛素联合控制,研究发现,不同降糖方案,对微血管病变有一定的影响^[5],本研究主要探讨药物、胰岛素对糖尿病视网膜病变进展的影响。

1 材料与方法

1.1 研究对象

自 2014 年 1 月到 2015 年 2 月,收集糖尿病伴有视网膜病变的患者 78 例。采用随机表法,将糖尿病视网膜病变患者分为药物组和胰岛素组,其中药物治疗组 38 例,男 22 例,女 16 例,年龄 56.3 ± 7.9 岁;胰岛素治疗组,其中男 24 例,女 16 例,年龄 57.3 ± 8.7 岁。病例的纳入标准,符合糖尿病诊断标准(1999 年 WHO 标准):糖尿病症状加任意时间血糖 ≥ 11.1 mmol/L;或空腹血糖 ≥ 7.0 mmol/L 或 OGTT 2 小时后血糖 ≥ 11.1 mmol/L,可确诊为糖尿病。糖尿病伴视网膜病变根据视网膜病变程度将其分为背景性视网膜病变和增殖性视网膜病变。

1.2 治疗方案

病例分为胰岛素控制组和药物控制组,胰岛素组采用胰岛素皮下注射控制血糖,药物控制组采用二甲双胍片,或者罗格列酮片,或二甲双胍片联合罗格列酮。血糖控制标准,70 岁以下者 FPG < 6 mmol/L,2hPG 6~8 mmol/L;70 岁以上者 FPG 6~8 mmol/L,2 hPG 8~10 mmol/L。

1.3 糖尿病视网膜病变进展评价

根据糖尿病视网膜分期,其中 I 期:视网膜形成微血管瘤,伴出血;II 期:微血管瘤形成,出血并伴有硬性渗出;III 期:视网

膜出血,并开始出现棉絮状渗出。以上 3 期为背景性视网膜病变。IV 期:在渗出的背景下形成新血管,伴有玻璃体出血;V 期:形成纤维机化物;VI 期:继发性视网膜脱落,失明。以上 IV~VI 3 期为增殖性视网膜病变(PDR)。对所有纳入的病例在干预治疗前性视网膜检查并判定分级,所有病例治疗干预周期为 1 年,干预结束后再次评价视网膜病变程度。

1.4 C 肽、糖化血红蛋白、胰岛素抵抗指数测定

所有患者过夜禁食 8h 以上,于清晨空腹抽取肘静脉血后,空腹血糖(FBG)的检测采用葡萄糖氧化酶法。采用放射免疫法测定空腹血清 C 肽(FCP)及餐后 2 h 血清 C 肽(PCP)。采用免疫抑制比浊法测定糖化血红蛋白(HbA1c)。采用稳态模式评估法(HOMA)评价胰岛素抵抗, $HOMA-IR = \text{空腹血糖(FPG)} \times \text{空腹胰岛素(FNS)} / 22.5$ 。

1.5 统计学方法

计量资料采用均值 $\pm$ 标准差($\bar{x} \pm s$),应用 t 检验;p 值均小于 0.05,认为有统计学意义。

2 结果

2.1 治疗前后 C 肽、糖化血红蛋白、胰岛素抵抗指数水平对比

表 1 看出,药物组治疗前后,血清空腹 C 肽、胰岛素抵抗指数差异有统计学意义($p < 0.05$);治疗前后 2h CP、以及糖化血红蛋白测定差异无统计学意义($p > 0.05$)。胰岛素组治疗前后,血清空腹 C 肽、2h CP 差异有统计学意义 ($p < 0.05$);而糖化血红蛋白、胰岛素抵抗指数差异无统计学意义($p > 0.05$)。

表 1 药物组和胰岛素治疗组干预前后血清 C 肽、糖化血红蛋白、胰岛素抵抗指数对比

Table 1 Comparison of serum C peptide, glycosylated hemoglobin, insulin resistance index between drug group and insulin group before and after intervention

		FCP(ng/mL)	2h CP(ng/mL)	Glycated hemoglobin(%)	Insulin resistance index
Drug group	Before treatment	1.21 $\pm$ 0.34	2.43 $\pm$ 0.47	8.34 $\pm$ 1.47	2.66 $\pm$ 1.41
	After treatment	1.37 $\pm$ 0.42	2.58 $\pm$ 0.45	8.27 $\pm$ 1.24	2.15 $\pm$ 1.23
	t	2.23	0.94	1.23	2.03
Insulin group	Before the treatment	1.26 $\pm$ 0.38	2.38 $\pm$ 0.55	8.42 $\pm$ 1.52	2.62 $\pm$ 1.50
	After treatment	1.42 $\pm$ 0.43	2.92 $\pm$ 0.53 [▲]	8.36 $\pm$ 1.46	1.97 $\pm$ 1.32 [▲]
	t	2.09	2.48	1.23	1.03
	p	0.02	0.00	0.18	0.21

Note: ▲ compared with the drug group, $p < 0.05$.

2.2 两组间视网膜病变对比

表 2 看出,药物组治疗前 I 期、II 期、III 期、IV 期、V 期、VI 期病例数和治疗后相比,差异有统计学意义($p < 0.05$),视网膜病变分级程度明显增高。胰岛素组治疗前 I 期、II 期、III 期、IV 期、V 期、VI 期病例数和治疗后相比,差异有统计学意义($p < 0.05$)。药物组和胰岛素组间视网膜病变分级差异无统计学意义($p > 0.05$);治疗后差异有统计学意义($p < 0.05$)。

3 讨论

糖尿病视网膜病变已经严重影响了我国糖尿病患者的健康及生活质量,造成糖尿病患者视力快速下降甚至失明,已经成为我国社会经济发展的沉重负担,成为了世界性公共卫生问题^[6]。据不完全统计,大约 20% - 40% 2 型糖尿病患者最终出现视网膜病变,其中约 8% 发生失明,完全丧失视力^[7]。中华医学会糖尿病分会对 249,46 例住院糖尿病患者进行了调查分析,最终结果显示,35.7% 的 2 型糖尿病并发糖尿病视网膜病变,糖尿病视网膜病变随着随糖尿病病程和患者的年龄的增长而上升^[8]。稳定并控制好血糖,是治疗并预防糖尿病视网膜病变最

表 2 药物组和胰岛素治疗组干预前后视网膜病变进展对比

Table 2 Comparison of the retinopathy progression before and after intervention in drug group and insulin group

Case number		I	II	III	IV	V	VI	x ²	p
Before treatment	Drug group	9	7	7	6	7	2	2.09	0.34
	Insulin group	11	6	9	5	6	3		
After treatment	Drug group	8	7	5	8	9	3	5.35	0.02
	Insulin group	10	6	9	7	6	2		

根本的治疗措施,对血糖和糖化血红蛋白的检测,糖尿病控制临床应用最为广泛的指标,同样可作为视网膜病变的可信赖指标^[9]。

血清 C 肽一直被研究学者们认为是 β 细胞分泌的一个无生物活性的副产品,但是随着胰岛素一起分泌的,所以一直被看作是判断胰岛细胞功能的重要血清学指标^[10]。近年来,随着对 1 型和 2 型糖尿病基础与临床研究的不断深入,研究者发现 C 肽也具有生物学活性,具有改善血管,促进神经功能恢复的作用^[11]。Pentyala S 等研究发现,C 肽能够显著延长胰岛素降糖作用时效,并增强外源性胰岛素作用效率,同时能够降低葡萄糖诱导的胰岛素水平的升高,C 肽可能具有重要的生物功能^[12]。本研究发现,经过正规的治疗,不管是药物控制,或者是胰岛素控制血糖,治疗后的空腹 C 肽水平均有一定水平的改善。而胰岛素治疗对胰岛素抵抗改善不明显。

有研究发现,双胍类降糖药、胰岛素可以降低胰岛素抵抗的功能,保护小血管病变及肾功能^[13]。研究发现,胰岛素可以改善糖尿病患者的脂代谢状态,促进脂质转化,减少血管脂质的沉积形成血管斑块,并显著改善血管内皮细胞的功能^[14,15]。研究认为,胰岛素可以刺激内皮细胞分泌更多的扩张血管活性因子,包括 NO、NOS 等,分泌的 NO 使内皮细胞衍生的血管收缩剂(内皮素-1、血栓素 A₂、ROS)减少密切相关^[16,17]。Tziomalos K 等对比观察了药物控制血糖组和胰岛素控制血糖组患者 2 年到 5 年不等,发现应用胰岛素治疗的患者,胰岛素抵抗得到一定程度改善,每日使用的胰岛素总量基本控制不变,部分患者胰岛素剂量有所减少,但是药物控制的患者大部分患者最终不能得到有效的控制,微血管病变进展加重^[18-20]。本研究的结果显示,药物组治疗前 I 期、II 期、III 期、IV 期、V 期、VI 期病例数和治疗后相比,差异有统计学意义($p < 0.05$),视网膜病变分级程度明显增高。胰岛素组治疗前 I 期、II 期、III 期、IV 期、V 期、VI 期病例数和治疗后相比,差异有统计学意义($p < 0.05$)。

总的认为,对已经发生微血管病变的糖尿病患者,胰岛素在一定程度上保留了残留胰腺细胞分泌胰岛素的功能,所有血清 C 肽水平有所提高,延缓糖尿病患者视网膜病变的进展速度。

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出胃癌患者随着病情的不断恶化,患者凝血反应时间和凝血形成时间越短,血小板功能越强,纤维蛋白原活性越高,血液高凝状态越明显。通过常规凝血功能检查和 TEG 检验评估胃癌患者治疗前后凝血状况的准确率,结果显示 TEG 动态监测患者凝血状态的准确率更高。

综上所述,胃癌患者的血液处于高凝状态,且病情越严重,高凝状态越显著;同时,TEG 评估胃癌患者围术期的凝血状态较常规凝血检验更准确,可有效预防凝血所引发的不良反应。

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