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七味白术散合补阳还五汤对 2 型糖尿病患者颈动脉内中膜厚度和胰岛素抵抗的影响*

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摘要 目的:评价七味白术散合补阳还五汤对 2 型糖尿病(T2DM)患者颈动脉内中膜厚度(IMTc)和胰岛素抵抗(IR)的影响。**方法:**选入我院 2020 年 9 月~2022 年 9 月收治的 T2DM 患者 80 例,根据治疗方法不同分为常规组(常规基础治疗)和联合组(常规基础治疗+七味白术散合补阳还五汤),各 40 例。检测两组的血糖、血脂指标,计算 IR 指数(HOMA-IR),并通过超声测定 IMTc。**结果:**两组治疗后各血糖(FPG 和 HbA1c)、血脂(TC、TG、LDL-C 和 HDL-C)指标均较治疗前有不同程度的改善,而联合组改善幅度明显大于常规组($P<0.05$);相较于治疗前,两组治疗后 HOMA-IR 明显下降、HOMA- β 显著升高($P<0.05$),而联合组下降/升高幅度更大,与常规组差异显著($P<0.05$);治疗前,两组 IMTc 值无明显差异($P>0.05$),而治疗后,联合组 IMTc 值显著低于常规组($P<0.05$);联合组治疗总有效率较常规组高(92.50% vs. 72.50%, $P<0.05$),不良反应发生率较常规组低(2.50% vs. 15.00%, $P<0.05$)。**结论:**七味白术散合补阳还五汤可有效提升 T2DM 的治疗效果,改善糖脂代谢及 β 细胞功能,减少 IR 及 IMTc 值,且不良反应少。

关键词:2 型糖尿病;七味白术散;补阳还五汤;颈动脉内中膜厚度;胰岛素抵抗;疗效

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Effects of Qiwei Baizhu Powder and Buyang Huanwu Decoction on Carotid Intima-media Thickness and Insulin Resistance in Patients with Type 2 Diabetes*

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ABSTRACT Objective: To evaluate the effect of Qiwei Baizhu Powder and Buyang Huanwu Decoction on carotid intima-media thickness (IMTc) and insulin resistance (IR) in patients with type 2 diabetes mellitus (T2DM). **Methods:** 80 T2DM patients admitted to our hospital from September 2020 to September 2022 were selected and divided into a conventional group (conventional basic treatment) and a combination group (conventional basic treatment+Qiwei Baizhu Powder combined with Buyang Huanwu Tang) based on different treatment methods, with 40 patients in each group. Detect blood glucose and lipid indicators in both groups, calculate IR index (HOMA-IR), and measure IMTc through ultrasound. **Results:** After treatment, the blood glucose (FPG and HbA1c) and blood lipid (TC, TG, LDL-C, and HDL-C) indicators in both groups showed varying degrees of improvement compared to before treatment, while the improvement in the combined group was significantly greater than that in the conventional group ($P<0.05$). Compared with before treatment, the two groups showed a significant decrease in HOMA-IR and a significant increase in HOMA- β after treatment ($P<0.05$), while the decrease/increase amplitude in the combination group was significantly greater than that in the conventional group($P<0.05$). Before treatment, there was no significant difference in IMTc values between the two groups ($P>0.05$), while after treatment, the IMTc values in the combination group were significantly lower than those in the conventional group ($P<0.05$). The total effective rate of the combined group was significantly higher than that of the conventional group (92.50% vs. 72.50%, $P<0.05$), and the incidence of adverse reactions was significantly lower than that of the conventional group (2.50% vs. 15.00%, $P<0.05$). **Conclusion:** Qiwei Baizhu Powder combined with Buyang Huanwu Tang can effectively enhance the therapeutic effect of T2DM, improve glucose and lipid metabolism, enhance β Cell function, reduced IR and IMTc values, and minimal adverse reactions.

Key words: Type 2 diabetes; Qiwei Baizhu Powder; Buyang Huanwu Tang; Carotid artery intima media thickness; Insulin resistance; Curative effect

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前言

2型糖尿病(type 2 diabetes mellitus, T2DM)是最常见的糖尿病(DM)类型,主要病理特征为胰岛素分泌不足以及肝脏、脂肪组织和骨骼肌等胰岛素靶器官对胰岛素的敏感性降低,即胰岛素抵抗(insulin resistance, IR)^[1-3]。T2DM患者面临的威胁不仅是疾病本身,更是长期高血糖及血糖波动带来的大血管、微血管、神经病变的并发症^[4],特别是大血管并发症是T2DM患者出现心脑血管合并症及致残、致死的主要因素^[5,6],而动脉粥样硬化(atherosclerosis, AS)斑块形成是大血管并发症的病理基础^[7]。因此,早期发现AS并予以干预治疗对于改善T2DM患者预后显得尤为重要。早期AS在未造成动脉管腔狭窄之前,病变主要在内膜层,即在AS斑块出现之前,颈动脉内-中膜厚度(IMTc)即可表现异常,IMTc作为动态观察早期AS进展或消退的指标已得到普遍认可^[8-10]。在此背景下,本研究探讨了七味白术散合补阳还五汤对T2DM患者IMTc和IR的影响,为早期防治大血管病变提供新的试验依据。

1 资料和方法

1.1 一般资料

选入我院2020年9月~2022年9月收治的T2DM患者80例,根据治疗方法不同分为常规组和联合组,各40例。常规组中,男24例,女16例,年龄37~73岁,平均年龄(54.64±9.93)岁;BMI值19.23~27.91 kg/m²,平均(24.47±3.94)kg/m²;病程8个月~15年,平均(7.68±3.55)年。联合组中,男22例,女18例,年龄34~76岁,平均年龄(54.81±10.25)岁;BMI值19.17~27.86 kg/m²,平均(24.39±3.77)kg/m²;病程1~13年,平均(7.59±3.46)年。两组一般资料无差异($P>0.05$)。

纳入标准:(1)根据临床症状及体征、血糖水平检测等确诊为T2DM;(2)颈部血管彩超提示IMTc增厚(>0.9 mm);(3)入组前未接受任何抗DM治疗,或停药至少2w;(4)无其他严重心、脑血管疾病;(5)知情同意。

排除标准:(1)T1DM,继发性DM,妊娠期DM及其他特殊型DM;(2)有DM急性并发症(如酮症酸中毒、高血糖高渗性综合征等),或近3个月内发生过严重的心脑血管、肝、肾疾病;(3)合并急性慢性其他内分泌疾病(如甲亢、皮质醇增多症等),或近期使用过肾上腺皮质激素、减肥降脂类药物;(4)有明显消化吸收障碍的慢性肠功能紊乱;(5)对研究药物过敏;(6)长期酗酒、药物依赖或有精神疾病。

1.2 治疗方法

常规组:采用常规基础治疗,即根据患者具体情况采用口服降糖药(二甲双胍)或胰岛素皮下注射治疗控制血糖水平,同时要求患者严格控制饮食,适当运动,保持平和的心态和情绪稳定。

联合组:在常规组基础上加用七味白术散合补阳还五汤,方剂组成,(1)七味白术散:葛根15g,茯苓、炒白术、藿香叶各12g,人参、木香各6g,甘草3g;(2)补阳还五汤:黄芪(生)20g,当归尾10g,赤芍10g,地龙3g,川芎10g,红花10g,桃仁10g。将所有药材用水煎服,1剂/d,分早晚两次温服。

两组均以30d为1疗程,连续治疗3个疗程。

1.3 观察指标

1.3.1 实验室检查 分别于治疗前后采集患者空腹外周静脉血,利用全自动生化分析仪检测空腹血糖(FBG)、糖化血红蛋白(HbA1c)等血糖指标以及总胆固醇(TC)、甘油三酯(TG)、低密度脂蛋白胆固醇(LDL-C)和高密度脂蛋白胆固醇(HDL-C)等血脂指标;同时采用放射免疫法检测空腹胰岛素(FINS)水平,并应用稳态模型法(HOMA)评估IR指数(HOMA-IR)和胰岛β细胞功能指数(HOMA-β),计算公式分别为:HOMA-IR=FPG×FINS/22.5, HOMA-β=20×FINS/(FPG-3.5)。

1.3.2 IMTc测定 患者取仰卧位,肩部垫高头后仰,充分暴露颈部;应用彩色多普勒超声仪,探头(频率5.0~10.0)沿胸锁乳突肌外缘扫查,取动脉管壁最厚、距此近心1cm及远心1cm³处,测量颈动脉管腔-内膜界面之前缘到中层-外膜界面之前缘的距离,其平均值即为IMTc值。

1.3.3 统计不良反应情况 恶心呕吐,腹痛,腹泻,消化不良,头晕,头痛

1.4 疗效判定

(1)显效:多食易饿、倦怠乏力等临床体征完全消失,血糖指标恢复正常;(2)有效:临床症状改善,血糖指标明显下降但达正常范围;(3)无效:临床症状、各项指标检测等无明显变化,甚至加重。以(显效+好转)计算治疗总有效率。

1.5 统计学处理

采用SPSS 21.0统计软件,检验标准 $\alpha=0.05$;计量资料表示为"平均数±标准差",两组间比较采用t检验;计数资料表示为例数(百分比),组间比较采用 χ^2 检验。

2 结果

2.1 两组血糖、血脂指标比较

与治疗前相比,治疗后两组FPG、HbA1c、TC、TG、LDL-C和HDL-C均改善($P<0.05$),而联合组改善幅度明显大于常规组($P<0.05$),见表1。

2.2 两组胰岛功能指标比较

治疗前,两组HOMA-IR和HOMA-β无明显差异($P>0.05$);治疗后,联合组HOMA-IR明显低于常规组、HOMA-β显著高于常规组($P<0.05$),见表2。

2.3 两组IMTc值比较

治疗后,联合组IMTc值显著低于常规组($P<0.05$),见表3。

2.4 两组临床疗效比较

联合组治疗总有效率92.50%,显著高于常规组的72.50%($P<0.05$),见表4。

2.5 不良反应情况

联合组不良反应发生率明显低于常规组($P<0.05$),见表5。

3 讨论

T2DM是一组临床综合征,引起以血糖升高为基础的代谢紊乱,常伴有代谢障碍,可致各种组织长期损害、功能异常和衰竭^[11-13],同时长期药物治疗、急性慢性并发症等原因使得患者容易出现各种不良情绪,危害患者的身心健康,降低生活质量。近年来,受到人们生活习惯、饮食结构、人口老龄化等诸多因素的影响,T2DM的发病率逐年升高,已成为仅次于心血管疾病和肿

表 1 治疗前后血糖及血脂指标比较($\bar{x} \pm s$)

Table 1 Comparison of blood glucose and lipid indicators before and after treatment ($\bar{x} \pm s$)

Index	Time	Conventional group (n=40)	Combination group (n=40)	t	P
FBG(mmol/L)	Before treatment	9.86± 1.51	9.91± 1.44	0.151	>0.05
	After treatment	7.22± 1.29 ^a	6.10± 1.21 ^a	5.793	<0.05
HbA1c(%)	Before treatment	8.61± 1.13	8.58± 1.17	0.117	>0.05
	After treatment	7.33± 0.85	6.58± 0.76	4.160	<0.05
TC(mmol/L)	Before treatment	7.15± 1.90	7.18± 1.84	0.072	>0.05
	After treatment	6.40± 1.15 ^a	5.10± 1.11 ^a	5.144	<0.05
TG(mmol/L)	Before treatment	2.52± 0.49	2.55± 0.53	0.263	>0.05
	After treatment	2.11± 0.42 ^a	1.66± 0.37 ^a	5.085	<0.05
LDL-C(mmol/L)	Before treatment	4.02± 1.18	4.00± 1.16	0.076	>0.05
	After treatment	3.63± 0.92	2.91± 0.64 ^a	4.063	<0.05
HDL-C(mmol/L)	Before treatment	0.93± 0.30	0.91± 0.35	0.274	>0.05
	After treatment	1.04± 0.46	1.35± 0.44 ^a	3.080	<0.05

Note: Compared with before treatment in this group, ^a P<0.05.

表 2 胰岛功能指标比较($\bar{x} \pm s$)

Table 2 Comparison of pancreatic islet function indicators ($\bar{x} \pm s$)

Groups	HOMA-IR		HOMA-β	
	Before treatment	After treatment	Before treatment	After treatment
Conventional group(n=40)	3.99± 1.02	3.23± 1.05 ^a	17.31± 3.74	19.09± 5.27
Combination group(n=40)	4.02± 1.10	2.44± 0.67 ^a	17.24± 3.65	23.86± 7.96 ^a
t	0.126	4.011	0.085	3.160
P	>0.05	<0.05	>0.05	<0.05

Note: Compared with before treatment in this group, ^a P<0.05.

表 3 治疗前后 IMTc 值变化比较($\bar{x} \pm s$, mm)

Table 3 Comparison of changes in IMTc values before and after treatment ($\bar{x} \pm s$, mm)

Groups	Before treatment	After treatment	t value	P value
Conventional group(n=40)	1.22± 0.46	1.16± 0.27	0.711	>0.05
Combination group(n=40)	1.25± 0.52	0.91± 0.23	3.782	<0.05
t	0.273	4.458		
P	>0.05	>0.05		

表 4 临床疗效比较[n(%)]

Table 4 Comparison of clinical efficacy [n (%)]

Groups	Markedly effective	Effective	Ineffective	Total effective rate(%)
Conventional group(n=40)	13(32.50)	16(40.00)	11(27.50)	72.50
Combination group(n=40)	23(57.50)	15(37.50)	2(5.00)	95.00
t				7.440
P				<0.05

瘤的第 3 大非传染性疾病^[14]。虽然 T2DM 的发病机制尚未完全阐明，但胰岛 β 细胞功能衰退和 IR 是其发病的基础环节却是

肯定的^[15,16]，二者是 T2DM 病情恶化的驱动力，导致血糖水平居高不下，而持续的高血糖状态又会加重 IR，形成恶性循环。研

表 5 不良反应情况比较[n(%)]
Table 5 Comparison of adverse reactions [n (%)]

Groups	Nausea/vomiting	Abdominal pain/diarrhea	Dyspepsia	Dizziness/headache	Total
Conventional group(n=40)	2(5.00)	2(5.00)	1(2.50)	1(2.50)	6(15.00)
Combination group(n=40)	1(2.50)	0(0.00)	0(0.00)	0(0.00)	1(2.50)
t					3.914
P					<0.05

究证实^[17],有效控制血糖是改善胰岛功能、缓解 IR 的关键。目前,现代医学对于 T2DM 的治疗以健康宣教、饮食及运动管理、口服降糖药、抗凝、抗氧化等对症治疗为主^[18],虽具有一定的疗效,但药物副作用、耐药等情况使治疗效果受到影响。中医药作为我国的国粹,在治疗 DM 中具有一定见解。

T2DM 属中医“消渴病”范畴,发病与脾虚热盛,津液停留,脾失运化有关,治疗应以化湿健脾、活血通络、治糖与治络并重为主要原则^[19,20]。七味白术散出自《小儿药证直诀》^[21],方中人参甘温益气,健脾养胃,为君药;白术苦温,健脾燥湿,加强益气助运之力,为臣药;茯苓甘淡,健脾渗湿,葛根升阳生津,藿香化湿止呕,木香调理中焦气机,诸药合用共同为佐,奏健脾祛湿理气之功;炙甘草甘温,益气和缓,调和诸药,为使药。全方共奏健脾益气、和胃生津之功效。补阳还五汤是益气活血法的代表方^[22],本方重用生黄芪,补益元气,意在气旺则血行,瘀去络通,为君药;当归尾活血通络而不伤血,为臣药;赤芍、川芎、桃仁、红花协同当归尾以活血祛瘀,地龙通经活络,亦为佐药。诸药合用,使气旺血行以治本,祛瘀通络以治标,标本兼顾;且补气而不壅滞,活血又不伤正,发挥补气、活血、通络之功效。

本研究将七味白术散合补阳还五汤用于 T2DM 的临床治疗,结果显示:两组治疗后各血糖(FPG 和 HbA1c)、血脂(TC、TG、LDL-C 和 HDL-C)指标较治疗前均有不同程度的改善,而联合组改善幅度明显大于常规组($P<0.05$)。同时,联合组治疗总有效率较常规组高(92.50% vs. 72.50%, $P<0.05$),不良反应发生率较常规组低(2.50% vs. 15.00%, $P<0.05$)。提示,七味白术散合补阳还五汤可有效改善 T2DM 的糖脂代谢,提高临床疗效,且不良反应少,与张洁^[23]的研究结果一致。此外,相较于治疗前,两组治疗后 HOMA-IR 明显下降、HOMA- β 显著升高($P<0.05$),而联合组下降/升高幅度更大,与常规组差异显著($P<0.05$)。究其原因:七味白术散能行能守,升降和调,脾脏运化顺畅,气血津液运行,从而促进新陈代谢及生理性胰岛素分泌恢复,进而改善 IR,有效降糖;而补阳还五汤活血通络,加速脂质代谢,同时还能抗凝、抑制血小板聚集,改善血液流变学。两方合用可协同发挥降糖、降脂、改善胰岛功能等多种作用。

T2DM 最严重的并发症为大血管病变,其病理基础为 AS^[24,25]。因此,早期发现 AS、了解 AS 程度对 T2DM 非常重要。选择性经皮冠脉造影(coronary angiography, CAG)是诊断冠脉 AS 的“金标准”^[26],而研究表明 AS 早期由于血管重构的原因使冠状动脉尚未狭窄,即 CAG 正常,但超声检查已存在广泛的 AS 病变^[27,28]。AS 最早期的病理改变是内膜增厚,但超声下因内膜菲薄不易辨认,因此需加上中膜层的测量来观察其变化。近年来,IMTc 作为一项良好的反应全身 AS 程度的指标得到广泛认

可,而且其检测具有方便、无创、可定量、重复性好等优势^[29]。结合本研究结果:治疗前,两组 IMTc 值无明显差异($P>0.05$),而治疗后,联合组 IMTc 值显著低于常规组($P<0.05$)。提示七味白术散合补阳还五汤通过活血化瘀、促进新城代谢、降低 IR 等功效减少 IMTc 值,改善 AS,预防并发症的发生。

综上所述,七味白术散合补阳还五汤可有效提升 T2DM 的治疗效果,改善糖脂代谢及 β 细胞功能,减少 IR 及 IMTc 值,且不良反应少。但本研究仍存在一定的不足,如样本量较小、观察时间较短等。因此,确切结论还需进一步研究证实。

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