经节以刺激支配心脏的交感神经纤维末梢芽生(sympathetic nerve sprouting),可引起心室颤动和猝死;星状神经节自发放电增加可直接导致陈旧性心肌梗死犬发生室性期前收缩和室性心动过速;电刺激陈旧性心肌梗死犬的星状神经节可诱发室性期前收缩、室性心动过速和心室颤动[10~12]。本研究表明,Glu 可增大 SH-SY5Y 细胞的 I_h 电流,提示 Glu 可能诱发交感神经元的传出冲动,从而增加心律失常的风险。有些人食用含味精(主要成分为谷氨酸单钠)量高的食物会发生中国餐馆综合征,个别人甚至会发生心律失常[13]。如果再考虑到前述的病理性组织局部"谷氨酸泄漏",由 Glu 引起的交感神经不正常兴奋和(或)心肌电生理不稳定可能在某些心脏病(特别是心肌梗死)患者中容易发生。因此,依据本研究和以往研究的结果,减少味精摄入或抑制 Glu-iGluRs 信号通路可能对 Glu 引发的 I_h 通道开放概率增高以及由此引起的交感神经兴奋起到一定的抑制作用,从而减少心肌梗死或其他心脏病患者心律失常的风险。

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2 型糖尿病合并下肢动脉闭塞症患者手术前后血糖控制情况的研究

许建萍 肖新华

摘 要 目的 观察一组糖尿病下肢动脉闭塞症患者手术前后的血糖控制情况。**方法** 选取 2002~2012 年在北京协和医院血管外科行手术治疗的糖尿病下肢动脉闭塞症患者,并以同期门诊就诊的 2 型糖尿病且不合并下肢动脉闭塞的患者为对照组,监测血压、血糖和血脂。观察两组患者的空腹、3 餐后 2h 及平均血糖差异,并比较有动脉闭塞症的患者手术前后血糖变化情况。同时比较基线时两组的血压和血脂。组间比较采用 t 检验和方差分析。**结果** 共纳入有下肢动脉闭塞症的 2 型糖尿病患者

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作者单位:100730 中国医学科学院/北京协和医学院北京协和医院内分泌科、国家卫生和计划生育委员会(原卫生部)内分泌重点实验室
通讯作者:肖新华,电子信箱:xiaoxinhua@medmail.com.cn

60 例,对照组 65 例。两组患者年龄比较,差异无统计学意义(65.8 ± 8.9 岁 vs 63.0 ± 10.0 岁),合并下肢动脉闭塞的患者病程较长(12.2 ± 7.1 vs 7.7 ± 5.9 年),下肢动脉闭塞组与对照组术前血糖相比两组空腹血糖(8.3 ± 2.7 vs 7.7 ± 2.3mmo/L)、早、午餐后(10.7 ± 2.9 vs 9.0 ± 2.4mmol/L、10.6 ± 3.1 vs 8.9 ± 4.1mmol/L)和平均血糖闭塞组(9.7 ± 2.1 vs 7.6 ± 3.6mmol/L)显著高于对照组,晚餐后血糖(8.9 ± 2.3 vs 9.9 ± 3.2mmol/L)差异无统计学意义。下肢动脉闭塞组手术前后所用胰岛素剂量不变的情况下,空腹血糖(7.7 ± 2.1 vs 6.8 ± 2.8mmol/L)、早餐后血糖(10.5 ± 2.5 vs 8.5 ± 3.4mmol/L)、午餐后血糖(10.5 ± 3.1 vs 8.7 ± 3.8mmol/L)和平均血糖(9.6 ± 1.8 vs 8.2 ± 2.9mmol/L)有明显下降,晚餐后血糖(9.8 ± 3.1 vs 9.0 ± 4.0mmol/L)差异无统计学意义。**结论**　2 型糖尿病合并下肢动脉闭塞症的患者与对照组相比,糖尿病的病程相对较长,血糖控制较差。在治疗不变的情况下,行手术治疗下肢动脉闭塞症可使血糖控制情况明显改善。当糖尿病患者血糖控制不良时,应寻找病因,及时处理合并症,可使血糖控制得更加理想。

关键词　2 型糖尿病　外周动脉疾病　手术　血糖

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Investigation on Glycemin Control in Type 2 Diabetes Patients with Lower Extremity Arterial Occlusive Disease

Xu Jianping, Xiao Xinhua. Department of Endocrinology, Peking Union Medical College Hospital, Peking Union Medical College, Chinese Academy of Medical Sciences, Beijing 100730, China

Abstract　**Objective**　To investigate the status of glycemic control in a group of type 2 diabetes mellitus patients combined with peripheral arterial disease before and after operation. **Methods**　Patients with lower extremity arterial occlusive disease who were in charge in vascular surgery of Peking Union Medical College Hospital from 2002 to 2012 were involved. Type2 DM out patient without lower extremity arterial occlusive disease were involved as control. We measured blood pressure, blood glucose and blood lipid. Fasting, 2hPG and average plasma glucose of two groups patients were Compared, at the same time we observed the difference of plasma glucose before and after operation. The Student's *t* test and ANOVA analysis were used to compare the difference of before and after operation and between groups. **Results**　Total of sixty DM patients with lower extremity arterial occlusive disease were involved, and sixty five patients were involved in control group. There was no difference in age between two groups(65.8 ± 8.9 vs 63.0 ± 10.0years). The DM patients with lower extremity arterial occlusive disease had longer duration of DM(12.2 ± 7.1 vs 7.7 ± 5.9years). PAD group had higher fasting plasma glucose(8.3 ± 2.7 vs 7.7 ± 2.3mmol/L), post breakfast and lunch plasma glucose (10.7 ± 2.9 vs 9.0 ± 2.4mmol/L, 10.6 ± 3.1 vs 8.9 ± 4.1mmol/L) than control group. There was no significant difference in post dinner plasma glucose of two groups. Patients with PAD obtained a good plasma glucose after they made an operation but insulin volumn had no change, which was as fasting plasma glucose(7.7 ± 2.1 vs 6.8 ± 2.8mmol/L), breakfast (10.5 ± 2.5 vs 8.5 ± 3.4mmol/L), lunch(10.5 ± 3.1 vs 8.7 ± 3.8mmol/L) and average plasma glucose(9.6 ± 1.8 vs 8.2 ± 2.9mmol/L). Post dinner plasma glucose had no difference in two groups. **Conclusion**　Type 2 DM patients combined with lower extremity arterial occlusive disease had a longer duration of diabetes and higher plasma glucose. At the same, therapy and operation can improve blood glucose control. If a DM patient has a poor plasma glucose, we should find its reason, and deal with complication, then plasma glucose can be controlled better.

Key words　Type 2 diabetes mellitus; Peripheral arterial disease; Operation; Plasma glucose

2 型糖尿病的发生率在全球呈现明显上升趋势。我国 2007 ~ 2008 年的流行病学调查显示,20 岁以上的人群糖尿病发生率为 9.7%,成人糖尿病患者总数达 9240 万[1]。糖尿病大血管病变是严重危害患者生命的慢性并发症之一。我国 50 岁以上糖尿病患者的下肢动脉病变的患病率高达 19.47% ~ 23.80%。下肢动脉硬化性闭塞症是动脉粥样硬化累及下肢动脉导致动脉狭窄或闭塞而引起肢体缺血症状的慢性疾病,是全身动脉硬化性疾病在下肢的表现。有症状的下肢动脉硬化性闭塞症发生率达 0.6% ~ 9.2%[2]。吸烟、糖尿病、血脂异常、高血压、高龄是下肢动脉疾病的危险因素,吸烟和糖尿病对下肢动脉疾病的影响最明显[3]。

本研究旨在了解合并下肢动脉闭塞症的 2 型糖尿病患者的血糖控制情况,并观察手术治疗前后患者血糖水平的变化。

对象与方法

1. 研究对象:选取 2002 ~ 2012 年在北京协和医院血管外科住院行手术治疗的合并下肢动脉闭塞症的 2 型糖尿病患者 60 例,并以同期内分泌科门诊就诊的 2 型糖尿病且无下肢动脉闭塞的患者 65 例为对照组,排除有下肢麻木、发凉、疼痛、间歇性跛行及感觉异常的患者。糖尿病的诊断标准采用 1999 年 WHO 糖尿病的诊断标准。下肢动脉闭塞症的确诊均为术前 CTA 造影检查的基础上经手术证实。

2. 研究方法:所有患者均测身高、体重、血压、总胆固醇

(TC)、甘油三酯(TG)、高密度脂蛋白(HDL)、低密度脂蛋白(LDL)、糖化血红蛋白(HbA1c)、空腹(FBG)、早、午、晚餐后 2h 血糖(2hPG)、观察两组患者的空腹、3 餐后及平均血糖差异,同时比较有动脉闭塞症的患者手术前后胰岛素用量及血糖控制情况。根据患者的病变情况分别采取 DEEP 球囊扩张术、动脉插管溶栓、支架置入术等手术方式。

3. 统计学方法:统计分析应用 SPSS 19.0 软件。计数资料组间比较用 χ^2 检验,计量资料用均数 ± 标准差($\bar{x} \pm s$)表示,组间比较用 t 检验。以 $P<0.05$ 为差异有统计学意义。

结 果

1. 基本情况:下肢动脉闭塞症患者的临床资料见表 1。

表 1 合并下肢动脉闭塞症的 2 型糖尿病患者与对照组临床资料的比较

指标	动脉闭塞组	对照组
n(男性/女性)	60(38/22)	65(40/25)
年龄(岁)	65.8 ± 8.9	63 ± 10
病程(年)	12.2 ± 7.1	7.7 ± 5.9**
BMI(kg/m^2)	24.4 ± 2.1	23.7 ± 1.7
收缩压(mmHg)	138.8 ± 22.3	127.5 ± 15.8*
舒张压(mmHg)	73.8 ± 10.3	76.7 ± 8.7
空腹血糖(mmol/L)	8.3 ± 2.7	7.7 ± 2.3*
HbA1c(%)	8.2 ± 1.5	6.7 ± 0.8*
TC(mmol/L)	4.56 ± 1.22	4.56 ± 0.99
TG(mmol/L)	1.59 ± 1.06	1.38 ± 0.70*
HDL(mmol/L)	1.0 ± 0.22	1.47 ± 1.43
LDL(mmol/L)	2.91 ± 0.93	2.82 ± 0.86

与动脉闭塞组比较,* $P<0.05$,** $P<0.001$;1mmHg = 0.133kPa;BMI. 体重指数;HbA1c. 糖化血红蛋白;TC. 总胆固醇;TG. 甘油三酯;HDL. 高密度胆固醇;LDL. 低密度胆固醇

两组患者年龄、性别、体重指数和舒张压比较差异无统计学意义,但患有下肢动脉闭塞症的患者病程显著长于对照组($P<0.01$),并且平均收缩压显著高于对照组($P<0.05$)。空腹血糖及糖化血红蛋白动脉闭塞组显著高于对照组($P<0.05$)。血脂方面,总胆固醇以及高密度和低密度胆固醇两组控制的情况相当,但是甘油三酯在闭塞症显著高于对照组($P<0.05$)。

2. 血糖水平的比较:(1)术前血糖与对照组相比:下肢动脉闭塞症组术前各点血糖水平与对照组相比,结果见表 2。结果表明患有下肢动脉闭塞症组空腹血糖、早、午餐后 2h 血糖及平均血糖均显著高于对照组。晚餐后血糖两组差异无统计学意义。(2)术前术后血糖的比较:合并下肢动脉闭塞症的 2 型糖尿病患者在手术前后每日应用的胰岛素量相同,均为 42 ± 20U/d。下肢动脉闭塞症组患者手术前后血糖水平的变化见表 3。术后的空腹血糖水平较术前平均下降约 1mmol/L,差异有统计学意义。早餐后、午餐后 2h 及平均血糖水平较术前下降,差异有统计学意义。晚餐后 2h 血糖术前术后差异无统计学意义。

表 2 术前血糖水平的比较(mmol/L)

血糖	动脉闭塞组	对照组
FPG	8.3 ± 2.7	7.7 ± 2.3
早餐后 2h PG	10.7 ± 2.9	9.0 ± 2.4
午餐后 2h PG	10.6 ± 3.1	8.9 ± 4.1
晚餐后 2h PG	8.9 ± 2.3	9.9 ± 3.2
平均血糖	9.7 ± 2.1	7.6 ± 3.6*

与动脉闭塞组比较,* $P<0.05$;FPG. 空腹血糖;2h PG. 餐后 2h 血糖

表 3 手术前后血糖水平的比较(mmol/L)

血糖	术前	术后
FPG	7.7 ± 2.1	6.8 ± 2.8*
早餐后 2h PG	10.5 ± 2.5	8.5 ± 3.4*
午餐后 2h PG	10.5 ± 3.1	8.7 ± 3.8*
晚餐后 2h PG	9.8 ± 3.1	9.0 ± 4.0
平均血糖	9.6 ± 1.8	8.2 ± 2.9**

与术前比较,* $P<0.05$,** $P<0.01$

讨 论

下肢动脉病变是外周动脉疾病(peripheral arterial disease,PAD)的一个组成成分,严重者表现为下肢动脉的狭窄或闭塞。有明确的证据证实,下肢动脉疾病患者心血管事件的风险增加,如心肌梗死和缺血性脑卒中[3]。糖尿病患者更易累及股深动脉及胫前动脉等中小动脉。糖尿病患者的下肢动脉病变较非糖尿病者进展快并且后果更加严重[4]。2 型糖尿病是外周动脉疾病的独立危险因素。研究表明,糖尿病的病程、年龄、高血压、高血脂、吸烟均是下肢动脉病变的危险因素[5]。增加锻炼及戒烟可改善 2 型糖尿病患者下肢动脉病变的预后[6,7]。本研究重点观察合并下肢动脉闭塞症的 2 型糖尿病患者的血糖控制情况,结果发现与没有下肢动脉闭塞的糖尿病患者相比前者的空腹血糖水平、早午餐后 2h 血糖及平均血糖水平均显著高于后者。两组的空腹血糖相差约 0.5mmol/L,平均血糖相差约 2mmol/L。这表明血糖控制不佳在下肢动脉闭塞症的发生中起到重要的作用。大量的研究显示外周动脉疾病与高水平的糖化

血红蛋白有相关性[8]。两项针对高血压人群的研究显示空腹血糖水平高和有糖尿病与踝肱指数(ABI)下降有关[9,10]。多项心血管病危险因素的大型研究显示 ABI 水平与血糖水平显著相关[11~13]。但是,也有两项研究认为 2 型糖尿病患者的下肢动脉病变与血糖水平不相关[14,15]。VADT 研究也显示强化降糖治疗未能降低大血管并发症的风险[16]。但本研究通过对比两组合并及不合并下肢动脉闭塞的 2 型糖尿病患者的血糖水平得出的结论是有相关性的。因此,良好地控制血糖是预防 2 型糖尿病患者发生下肢动脉闭塞症的重要措施。

本研究进一步分析了手术治疗下肢动脉闭塞症对糖尿病患者血糖水平的影响。结果发现,在胰岛素治疗剂量不变的情况下,单纯通过手术解除下肢动脉闭塞就可获得空腹、餐后 2h 及平均血糖的显著下降。这表明不仅高血糖可促进下肢动脉闭塞症的发生、发展,反之,下肢动脉发生闭塞后可导致血糖更加难以控制。据文献报道,胰岛素抵抗可以通过糖毒性、脂毒性和炎性作用损伤血管内皮造成周围动脉病变[17]。某些药物如 RAS 抑制剂可通过改善肌肉血流灌注,改善糖耐量,增加胰岛素敏感度,推测肌肉血供差增加胰岛素抵抗造成血糖难以控制[18]。行手术治疗以后,血流动力学恢复正常,减轻了血管的阻力,增加了骨骼肌的血供,增加了胰岛素的敏感度,使得血糖更加容易控制,显示出积极治疗血管并发症对良好控制血糖的重要意义。同时,已有研究表明,糖化血红蛋白的水平高低与下肢动脉疾病的进展呈明确相关,因此严格控制血糖对防止下肢动脉病变的恶化有着重要的意义[19]。

本研究中两组患者在病程方面差异有统计学意义,有动脉闭塞组的患者较非动脉闭塞组的患者病程更长,可见随着病程的逐渐延长罹患下肢动脉闭塞症的风险是增加的。血脂方面两组患者胆固醇控制的情况相当,可能与他汀类药物的广泛应用有关。血压方面也有差异,有动脉闭塞组的患者较非动脉闭塞组的患者收缩压显著增高,而舒张压则差异无统计学意义。分析可能由于有下肢动脉的闭塞造成血液循环阻力增大,合并动脉粥样硬化后动脉壁的弹性下降有关。

由于 PAD 与足部溃疡及心血管病变密切相关,临床医师应高度关注本病并给予积极治疗[20]。美国心脏病协会指南指出合并 PAD 的患者应积极处理动脉硬化的危险因素以减少发生心血管事件的概率[21]。2 型糖尿病合并下肢动脉闭塞症的患者与对照组相比,糖尿病的病程更长,血糖控制较差。在胰岛素剂量不变的情况下,行手术治疗下肢动脉闭塞症可使血糖控制情况明显改善。当糖尿病患者血糖控制不良时,应寻找病因,及时处理合并症,可使血糖控制得更加理想。

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(下转第 36 页)

讨。本研究样本量偏小,今后需要增加样本数,开展进一步研究。对房颤患者今后进行 PS 基因多态性研究,可能对房颤合并血栓栓塞提供新的治疗方向。

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