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类风湿关节炎患者血糖、血脂水平与骨密度的关系

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[摘要] 目的: 探究类风湿关节炎(rheumatoid arthritis, RA)患者血糖、血脂水平与骨密度的关系。方法: 选择2017年12月至2020年12月合肥市滨湖医院收治的RA患者60例作为RA组, 并选择同期健康体检患者60例作为对照组, 比较两组患者L1~L4以及两侧股骨颈的骨密度(bone mineral density, BMD)及血糖[空腹血糖(fasting blood-glucose, FBG)、糖化血红蛋白(hemoglobin A1c, HbA1c)]、血脂[三酰甘油(triglyceride, TG)、总胆固醇(total cholesterol, TC)、低密度脂蛋白胆固醇(low density lipoprotein cholesterol, LDL-C)、高密度脂蛋白胆固醇(high density lipoprotein cholesterol, HDL-C)]水平。根据BMD将RA组患者分成骨量正常组($n=27$)、骨量减少组($n=21$)、骨质疏松(OP)组($n=12$), 比较3组患者的血糖、血脂水平, 并探究BMD水平与血糖、血脂水平的关系。结果: RA组的FBG、HbA1c、TC、TG、LDL-C水平均高于对照组, 差异有统计学意义($P<0.05$); HDL-C水平低于对照组, 差异有统计学意义($P<0.05$); RA组的L1~L4及股骨颈BMD低于对照组, 差异有统计学意义($P<0.05$); RA组的OP发生率为21.67%, 高于对照组的8.33%; RA组中不同骨代谢水平的FBG、HbA1c、TC、TG、LDL-C、HDL-C水平比较, 组间差异有统计学意义($P<0.05$); OP组的FBG、HbA1c、TC、TG、LDL-C均高于骨量正常组及骨量减少组, 差异有统计学意义($P<0.05$), HDL-C水平均低于骨量正常组及骨量减少组, 差异有统计学意义($P<0.05$); L1~L4及股骨颈的BMD与FBG、HbA1c、TC、TG、LDL-C均呈负相关($P<0.05$), L1~L4及股骨颈的BMD与HDL-C水平呈正相关($P<0.05$)。结论: RA患者的血脂、血糖水平较健康人紊乱, BMD水平低于健康人, OP发生率较健康人高, OP发生与血糖、血脂代谢的紊乱相关, 因此预防RA发生血糖、血脂代谢紊乱对减少OP发生有重要意义。

[关键词] 类风湿关节炎; 脂代谢; 糖代谢; 骨密度; 骨质疏松

Relationship between blood glucose, blood lipid levels and bone mineral density in patients with rheumatoid arthritis

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Abstract **Objective:** To explore the relationship between blood glucose, blood lipid levels and bone mineral density

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(BMD) in patients with rheumatoid arthritis (RA). **Methods:** Sixty RA patients admitted from December 2017 to December 2020 were enrolled as a RA group, while other 60 healthy controls during the same period were enrolled as a control group. BMD of L1–L4 lumbar vertebrae and bilateral femoral necks, levels of blood glucose [fasting blood glucose (FBG), hemoglobin A1c (HbA1c)] and blood lipid [triglyceride (TG), total cholesterol (TC), low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C)] were compared between the 2 groups. According to different BMD, patients in RA group were divided into normal bone mass group ($n=27$), osteopenia group ($n=21$) and osteoporosis (OP) group ($n=12$). The levels of blood glucose and blood lipid among the three groups were compared. The relationship between BMD levels and blood glucose, blood lipid levels in RA group was explored. **Results:** The levels of FBG, HbA1c, TC, TG and LDL-C in RA group were higher than those in control group ($P<0.05$), while HDL-C level was lower than that in control group ($P<0.05$). BMD of L1–L4 lumbar vertebrae and femoral neck in RA group was lower than that in control group ($P<0.05$), while incidence of OP was higher than that in control group (21.67% vs 8.33%) ($P<0.05$). The differences in levels of FBG, HbA1c, TC, TG, LDL-C and HDL-C were statistically significant among patients with different bone metabolism level in RA group ($P<0.05$). FBG, HbA1c, TC, TG and LDL-C in OP group were higher than those in normal bone mass group and osteopenia group ($P<0.05$), while HDL-C level was lower than that in normal bone mass group and osteopenia group ($P<0.05$). BMD of L1–L4 lumbar vertebrae and femoral neck was negatively correlated with HbA1c, TC, TG and LDL-C ($P<0.05$), while positively correlated with HDL-C ($P<0.05$). **Conclusion:** Compared with the healthy people, RA patients showed more disordered levels of blood lipid and blood glucose, with lower BMD level and higher incidence of OP. The occurrence of OP is related to the disorders of blood glucose and blood lipid metabolism. Therefore, preventing the occurrence of glucose-lipid metabolism disorders is of great significance for reducing the incidence of OP.

Keywords rheumatoid arthritis; lipid metabolism; glucose metabolism; bone mineral density; osteoporosis

类风湿关节炎(rheumatoid arthritis, RA)是常见自身免疫性疾病,能导致骨质破坏,呈进行性、对称性及侵蚀性,致残率较高,同时容易诱发心血管事件,其病死率较一般人群高1.5~1.6倍^[1]。骨质疏松(osteoporosis, OP)是其常见并发症,易导致骨折,影响患者生命安全,骨密度(bone mineral density, BMD)是诊断OP的金标准,能反映患者的骨丢失程度^[2]。RA患者发生OP的机制较为复杂,RA患者的炎症状态及病理活动会影响其糖脂代谢,而有研究表明糖脂代谢与骨代谢间存在一定关系,对骨量减少及OP的发生有一定影响^[3]。因此本文探究我院收治的60例RA患者的糖脂代谢水平与骨密度的关系,以期从控制血脂、血糖水平方面,为预防RA患者的OP发生提供一定参考。

1 对象与方法

1.1 对象

选择2017年12月至2020年12月合肥市滨湖医

院风湿免疫科收治的RA患者60例作为RA组,纳入标准:符合RA^[4]诊断标准。排除标准:1)伴有肝、肾功能障碍患者;2)伴有甲状腺或甲状旁腺疾病患者;3)伴有恶性肿瘤患者;4)长期卧床患者;5)长期服用钙剂等影响骨密度药物患者;6)伴有其他风湿性疾病患者;7)严重高血压及其他代谢性疾病患者。本研究经合肥市滨湖医院医学伦理委员会(批号:20170135)同意。

1.2 RA组用药情况

患者均口服两种免疫抑制剂,并联合小剂量激素或非甾类抗炎药,同时配合合理饮食,减少高脂肪、高胆固醇食物的摄入,注意控糖,患者均治疗3个月。

1.3 方法

1)BMD检查:采用双能X线骨密度仪(Hologic QDR-4500A骨密度仪,美国HOLOGICX公司)测量受试者L1~L4以及两侧股骨颈的BMD。OP诊断标准^[5]:基于BMD结果,以T值[(测定值-骨峰值)/

正常成人骨密度标准差]评分判断, T值 ≤ -2.5 标准差(SD)即为OP, -1.0 SD \leq T值 ≤ -2.5 SD为骨量减少, ≥ -1.0 SD为骨量正常, 根据该标准将RA组患者分成骨量正常27例, 骨量减少21例, OP组12例。2)血脂水平检测: 受试者入院后, 清晨采集其空腹静脉血3 mL, 离心分离上层血清, 采用日立7180全自动生化检测仪测定血清中的三酰甘油(triglyceride, TG)、总胆固醇(total cholesterol, TC)、低密度脂蛋白胆固醇(low density lipoprotein cholesterol, LDL-C)、高密度脂蛋白胆固醇(high density lipoprotein cholesterol, HDL-C)。3)血糖水平检测: 受试者入院后, 清晨采集其空腹静脉血3 mL, 离心分离上层血清, 采取亲和层析微柱法检测糖化血红蛋白(hemoglobin A1c, HbA1c), 采取德国罗氏血糖仪测定空腹血糖(fasting blood glucose, FBG)。

1.4 统计学处理

采用SPSS 20.0统计学软件进行数据分析, 计量资料以均数 \pm 标准差($\bar{x}\pm s$)表示, 组间比较采用 t 检验; 计数资料以例(%)表示, 采用 χ^2 检验; RA组BMD水平与血糖、血脂水平的相关

性采用Pearson分析, 以 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 两组患者一般资料比较

两组患者的一般资料比较, 差异均无统计学意义($P>0.05$, 表1)。

2.2 RA组和对照组的血糖、血脂水平比较

RA组的FBG、HbA1c、TC、TG、LDL-C水平平均高于对照组, 差异有统计学意义($P<0.05$); HDL-C水平低于对照组, 差异有统计学意义($P<0.05$, 表2)。

2.3 RA组和对照组的BMD比较

RA组的L1~L4及股骨颈BMD低于对照组, 差异有统计学意义($P<0.05$, 表3)。

2.4 RA组和对照组的OP发生情况比较

RA组的OP发生率为21.67%, 高于对照组的8.33%, 差异有统计学意义($P<0.05$, 表4)。

表1 两组患者一般资料比较($n=60$)

Table 1 Comparison of general data between the 2 groups ($n=60$)

组别	男/女/例	年龄/岁	收缩压/mmHg	舒张压/mmHg
RA组	15/45	53.47 \pm 7.06	131.42 \pm 26.21	78.13 \pm 18.44
对照组	18/42	53.29 \pm 7.18	130.18 \pm 25.56	77.58 \pm 17.19
t	0.376	0.138	0.262	0.169
P	0.540	0.890	0.794	0.866

1 mmHg=0.133 kPa.

表2 RA组和对照组的血糖、血脂水平比较($n=60$)

Table 2 Comparison of blood glucose and blood lipid levels between RA group and control group ($n=60$)

组别	FBG/(mmol·L ⁻¹)	HbA1c/%	TC/(mmol·L ⁻¹)	TG/(mmol·L ⁻¹)	LDL-C/(mmol·L ⁻¹)	HDL-C/(mmol·L ⁻¹)
RA组	5.68 \pm 1.67	8.29 \pm 2.16	5.57 \pm 1.49	1.74 \pm 0.51	2.65 \pm 0.54	1.41 \pm 0.39
对照组	4.84 \pm 1.43	5.67 \pm 1.58	4.28 \pm 1.25	1.31 \pm 0.39	2.39 \pm 0.42	1.62 \pm 0.45
t	2.959	7.583	5.138	5.188	2.944	2.732
P	0.004	<0.001	<0.001	<0.001	0.004	0.007

表3 RA组和对照组的BMD比较($n=60$)Table 3 Comparison of BMD between RA group and control group ($n=60$)

组别	L1~L4/(g·cm ⁻²)	股骨颈/(g·cm ⁻²)
RA组	0.71 ± 0.18	0.64 ± 0.17
对照组	0.96 ± 0.25	0.85 ± 0.21
<i>t</i>	6.286	6.021
<i>P</i>	<0.001	<0.001

2.5 RA组中不同骨代谢水平的血糖、血脂比较

RA组中不同骨代谢水平的FBG、HbA1c、

TC、TG、LDL-C、HDL-C水平比较, 组间差异有统计学意义($P<0.05$); OP组的FBG、HbA1c、TC、TG、LDL-C均高于骨量正常组及骨量减少组, 差异有统计学意义($P<0.05$), HDL-C水平均低于骨量正常组及骨量减少组, 差异有统计学意义($P<0.05$, 表5)。

2.6 BMD值与血糖、血脂水平的相关性

L1~L4及股骨颈的BMD与FBG、HbA1c、TC、TG、LDL-C均呈负相关($P<0.05$), L1~L4及股骨颈的BMD与HDL-C水平呈正相关($P<0.05$, 表6)。

表4 RA组和对照组的OP发生情况比较($n=60$)Table 4 Comparison of OP occurrence between RA group and control group ($n=60$)

组别	骨量正常	骨量减少	骨质疏松	总发生率/%
RA组	25	22	13	21.67
对照组	43	12	5	8.33
χ^2				4.183
<i>P</i>				0.041

表5 RA组中不同骨代谢水平血糖、血脂比较

Table 5 Comparison of blood glucose and blood lipids in patients with different bone metabolism levels in RA group

组别	<i>n</i>	FBG/(mmol·L ⁻¹)	HbA1c/%	TC/(mmol·L ⁻¹)	TG/(mmol·L ⁻¹)	LDL-C/(mmol·L ⁻¹)	HDL-C/(mmol·L ⁻¹)
骨量正常组	27	4.58 ± 1.41	5.46 ± 1.53	4.24 ± 0.91	1.25 ± 0.37	2.34 ± 0.61	1.51 ± 0.42
骨量减少组	21	6.24 ± 1.67 [#]	9.35 ± 2.59 [#]	5.78 ± 1.45 [#]	1.67 ± 0.46 [#]	2.65 ± 0.54 [#]	1.40 ± 0.35 [#]
OP组	12	7.69 ± 2.28 ^{*#}	11.57 ± 3.25 ^{*#}	7.23 ± 1.64 ^{*#}	2.31 ± 0.68 ^{*#}	3.17 ± 0.42 ^{*#}	1.14 ± 0.27 ^{*#}
<i>F</i>		15.076	33.452	24.325	20.924	9.415	4.136
<i>P</i>		<0.001	<0.001	<0.001	<0.001	<0.001	0.021

与骨量正常组比较, [#] $P<0.05$; 与骨量减少组比较, ^{*} $P<0.05$ 。

Compared with the normal bone mass group, [#] $P<0.05$; Compared with the osteopenia group, ^{*} $P<0.05$.

表6 BMD值与血糖、血脂水平的相关性

Table 6 Correlation between BMD and blood glucose, blood lipid levels

相关因素	L1~L4的BMD		股骨颈的BMD	
	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>
FBG	-0.427	<0.001	-0.523	<0.001
HbA1c	-0.519	<0.001	-0.611	<0.001
TC	-0.743	<0.001	-0.703	<0.001
TG	-0.611	<0.001	-0.612	<0.001
LDL-C	-0.574	<0.001	-0.636	<0.001
HDL-C	0.681	<0.001	0.707	<0.001

3 讨论

RA是一种进行性的自身免疫疾病,对人体关节损害较大,部分患者出现关节畸形,并发不同的关节外系统疾病,严重影响患者的生存质量^[6]。RA患者常伴有骨量减少,甚至发生OP,OP是全身性代谢疾病,表现为骨量减少,骨组织结构紊乱,骨脆性增加,易发生骨折,一旦发生骨折,将给患者及其家庭带来沉重负担^[7-8]。而OP的发生机制较为复杂,目前有研究^[9]表明RA患者机体的炎症因子水平升高,作用于外周组织如血管内皮、脂肪等,引起机体的血糖、血脂代谢紊乱,而血糖、血脂代谢与骨代谢的关系正是目前的研究热点。BMD是诊断OP的金标准,研究^[10]表明随RA病程延长、疾病活动,患者的BMD值下降,OP患病率增加。在本研究中,RA组的L1~L4及股骨颈BMD低于对照组,同时RA组的OP发生率为20.00%,高于对照组的6.67%,说明RA组的BMD水平低于健康人,OP发生率较健康人高。RA患者炎症因子水平升高,骨吸收增强,抑制骨破坏的保护因素明显减少,导致RA患者较高的OP发生率^[11]。

血糖代谢不仅为机体提供能量,也参与机体的多种生理过程。糖代谢障碍阻碍RA患者体内骨基质的生长,导致骨量减低^[12-13]。在本研究中,RA组的FBG、HbA1c水平均高于对照组,说明RA患者的血糖水平高于健康人。同时OP组的FBG水平高于骨量正常组及骨量减少组,L1~L4及股骨颈的BMD与FBG、HbA1c均呈负相关,说明RA患者的OP发生与糖代谢的紊乱相关。RA患者存在炎症反应和免疫系统异常,最终会导致物质代谢紊乱^[14]。RA患者血糖升高,可引起渗透性利尿,导致钙、磷排泄增加,刺激甲状旁腺激素分泌,骨钙动员,溶骨作用加强,骨质脱钙,导致BMD下降,进而导致OP的发生^[15]。同时大量的高血糖致糖基化终末产物在骨胶原蛋白上堆积,改变了成骨细胞的功能及其分化和增殖^[16];且高血糖会影响骨血管分布,使得毛细血管的通透性增强,影响骨形成及吸收过程。胰岛素因糖代谢紊乱而与RA患者OP的发生相关,临床上需进行针对性治疗,对于RA患者在生活提示其注重饮食摄入,注意控糖,对于血糖较高者,采用合理药物进行治疗,从而有效避免OP的发生。

目前已发现成骨细胞和脂肪细胞具有共同的前体细胞,因而有学者^[17-18]认为BMD与脂代谢存在一定关系,RA患者通常伴随着脂代谢紊乱。本研究中,RA组TC、TG、LDL-C水平均高于对照

组,HDL-C水平低于对照组说明RA患者的血脂水平高于健康人。同时OP组的TC、TG均高于骨量正常组及骨量减少组;L1~L4及股骨颈的BMD与FBG、HbA1c、TC、TG、LDL-C均呈负相关,L1~L4及股骨颈的BMD与HDL-C水平呈正相关,说明RA组中OP的发生与血脂水平紊乱相关。脂代谢会造成骨组织的病理变化,体外实验^[19]证明:胆固醇代谢对于成骨细胞的分化起重要作用,其代谢紊乱会影响成骨细胞的功能,导致骨矿物质含量下降。还有研究^[20]表示:血脂代谢能通过多种途径影响骨代谢,通过影响体内脂溶性维生素D和K的运转而促进成骨细胞增殖;同时能导致动脉粥样硬化、骨量丢失;且高血脂会导致骨髓微循环障碍,骨代谢能力下降,从而发生OP。

综上,RA患者中BMD低于健康人,OP发生率较健康人高,且血脂、血糖水平紊乱,而患者的OP发生与血糖、血脂代谢的紊乱相关,因此了解RA患者血糖及血脂代谢异常情况,有利于正确选择药物,对预防OP发生有重要意义。

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