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糖尿病视网膜病变患者血清炎症因子、脂肪因子及氧化应激指标的变化

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[摘要] **目的:**探讨糖尿病视网膜病变患者血清炎症因子、脂肪因子及氧化应激指标的水平变化。**方法:**选取我院收治的2型糖尿病患者130例,分为糖尿病无视网膜病变组(NDR)41例、非增殖期视网膜病变组(NPDR)44例和增殖期视网膜病变组(PDR)45例,另选取同期于我院体检的健康志愿者40名作为对照组(NC),检测各组的血清IL-6、TNF- α 、hs-CRP、瘦素、脂联素、MDA和SOD水平。**结果:**各组IL-6、TNF- α 、hs-CRP水平比较差异有统计学意义($P < 0.05$);PDR组均显著高于NC组、NDR组、NPDR组,NPDR组均显著高于NC组、NDR组,NDR组均显著高于NC组,差异均有统计学意义($P < 0.05$)。各组瘦素、脂联素水平比较,差异有统计学意义($P < 0.05$),PDR组瘦素高于NC组、NDR组、NPDR组,脂联素低于NC组、NDR组、NPDR组,NPDR组瘦素高于NC组、NDR组,脂联素低于NC组、NDR组,NDR组瘦素高于,脂联素低于NC组,差异均有统计学意义($P < 0.05$)。各组MDA、SOD水平比较差异有统计学意义($P < 0.05$),PDR组MDA高于NC组、NDR组、NPDR组,SOD低于NC组、NDR组、NPDR组,NPDR组MDA高于NC组、NDR组,SOD低于NC组、NDR组,NDR组MDA高于NC组,SOD低于NC组,差异均有统计学意义($P < 0.05$)。**结论:**糖尿病视网膜病变与炎症因子、脂肪因子及氧化应激指标具有密切关联。

[关键词] 糖尿病视网膜病变;炎症因子;脂肪因子;氧化应激

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Changes of serum inflammatory factors, adipokines and oxidative stress in patients with diabetic retinopathy

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View from specialist: It is creative, and of certain scientific and educational value.

[ABSTRACT] **Objective:** To investigate the changes of serum inflammatory factors, adipokines and oxidative stress in patients with diabetic retinopathy. **Methods:** A total of 130 patients with type 2 diabetes mellitus admitted to our hospital were selected and divided into 41 cases with diabetic retinopathy (NDR), 44 cases with nonproliferative retinopathy (NPDR) and 45 cases with proliferative retinopathy group (PDR). Besides, 40 healthy volunteers in our hospital were selected as control group

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(NC). The serum levels of IL-6, TNF- α , hs-CRP, leptin, adiponectin, MDA and SOD were detected. **Results:** There were significant differences in the levels of IL-6, TNF- α and hs-CRP in groups ($P < 0.05$). The levels of IL-6, TNF- α and hs-CRP in PDR group were (18.19 ± 3.84) pg/mL, (197.48 ± 13.78) ng/L and (8.13 ± 0.74) mg/L, respectively, which were significantly higher than those in NC group, NDR group and NPDR group. The levels of IL-6, TNF- α and hs-CRP in NPDR group were (14.07 ± 3.62) pg/mL, (115.29 ± 20.08) ng/L and (5.62 ± 0.83) mg/L, respectively, which were significantly higher than those in NC and NDR groups. As for these levels in NDR group, they were (12.67 ± 3.93) pg/mL, (89.49 ± 10.49) ng/L and (3.91 ± 0.49) mg/L, respectively, which were significantly higher than those in NC group. The difference was statistically significant ($P < 0.05$). There were significant differences among groups of leptin and adiponectin ($P < 0.05$). The leptin level in PDR group was (23.19 ± 6.48) μ g/mL, which was significantly higher than that in NC group, NDR group and NPDR group. However, adiponectin was (3.70 ± 1.02) g/mL, which was lower than those in other three groups. The level of leptin in NPDR group was higher than those in NC group and NDR group while adiponectin was lower than the two groups. Leptin level in NDR group was significantly higher than that in NC group while adiponectin was lower than that in NC group. The differences were statistically significant ($P < 0.05$). Moreover, the levels of MDA and SOD in each group were significantly different ($P < 0.05$). MDA in PDR group was (17.77 ± 4.33) nmol / mL, which was higher than NC group, NDR group and NPDR group, but SOD was (62.35 ± 11.43) U/mL, lower than those in these three groups. MDA in NPDR group was higher than NC group and NDR group but SOD was lower than NC group and NDR group. MDA level in NDR group was higher than that in NC group while SOD in NDR group was lower than that in NC group ($P < 0.05$). **Conclusions:** Diabetic retinopathy is closely related to inflammatory factors, adipokines and oxidative stress.

[KEY WORDS] Diabetic retinopathy; Inflammatory factor; Fat factor; Oxidative stress

2型糖尿病是临床上常见的代谢性疾病,患者以慢性高血糖为主要表现^[1]。在长期高血糖的影响下,患者常常发生微血管并发症,其中以视网膜病变最为常见,随着病程的进展,发病率也不断升高,病程10年以上者的发病率高达69%~90%^[2]。糖尿病视网膜病变已成为糖尿病患者失明最主要的原因^[3],然而多数患者确诊时已出现严重视力下降^[4]。因此,本研究着重分析糖尿病视网膜病变患者血清炎症因子、脂肪因子及氧化应激指标的变化,旨在通过血清学检测为糖尿病视网膜病变提供一种新的诊疗手段。

1 资料与方法

1.1 一般资料

选取2015年1月~2016年6月我院收治的2型糖尿病患者130例,均符合世界卫生组织(WHO)于1999年制订的糖尿病诊断标准,并排除伴有糖尿病急性并发症、心脑血管并发症、肝肾功能障碍、青光眼、脉络膜脱离等眼部疾病、恶性肿瘤及近期服用糖皮质激素、免疫抑制剂类药物及无噻唑烷二酮类药物者。根据糖尿病视网膜病变的国际临床分级标准^[5]将130例患者分为糖尿病无视网膜病变组(NDR)、非增殖期视网膜病变组(NPDR)和增殖期视网膜病变组(PDR)。NDR组41例,其中男性21例,女性20例;年龄最小者43岁,最大者75岁;糖尿病病程年限为6~12年;NPDR组44例,其中男性23例,女性21例;年龄最小者40岁,最大者73岁;糖尿病病程年限为6~11年;PDR组45例,其

中男性22例,女性23例;年龄最小者45岁,最大者72岁;糖尿病病程年限为7~13年。另选取同期于我院体检的健康志愿者40名作为对照组(NC),其中男性21例,女性19例;年龄最小者40岁,最大者73岁;排除伴有心、肝、肾等脏器系统及眼部疾病者。各组性别、年龄、体质指数等基础资料均无统计学差异($P > 0.05$),具有均衡可比性。

1.2 方法

采集各组对象禁食12小时后的空腹肘静脉血3 mL,应用ELISA法检测血清白介素-6(IL-6)、肿瘤坏死因子- α (TNF- α)、超敏C反应蛋白(hs-CRP)的含量,试剂盒购自深圳晶美生物工程有限公司;应用ELISA法检测血清瘦素(Leptin,LP)、脂联素(Adiponectin,ADPN)水平,试剂盒购自美国R&D公司;应用硫代巴比妥酸法检测丙二醛(MDA),应用黄嘌呤氧化酶法检测超氧化物歧化酶(SOD),试剂盒购自南京建成生物工程公司。

1.3 统计学处理

所有检测数据均应用SPSS19.0软件进行统计学处理,计量资料以 $(\bar{x} \pm s)$ 表示并进行单因素方差分析, $P < 0.05$ 为差异具有统计学意义。

2 结果

2.1 各组炎症因子比较

各组IL-6、TNF- α 、hs-CRP水平比较差异有统计学意义($P < 0.05$),PDR组均显著高于NC组、NDR组、NPDR组,NPDR组均显著高于NC组、NDR组,NDR组均显著高于NC组,差异均有统计学意义($P < 0.05$)。见表1。

表 1 各组炎症因子比较($\bar{x} \pm s$)

组别	n	IL-6 (pg/mL)	TNF- α (ng/L)	hs-CRP (mg/L)
NDR 组	41	12.67 \pm 3.93 ^a	89.49 \pm 10.49 a	3.91 \pm 0.49 ^a
NPDR 组	44	14.07 \pm 3.62 ^{a,b}	115.29 \pm 20.08 ^{a,b}	5.62 \pm 0.83 ^{a,b}
PDR 组	45	18.19 \pm 3.84 ^{a,b,c}	197.48 \pm 13.78 ^{a,b,c}	8.13 \pm 0.74 ^{a,b,c}
NC 组	40	11.05 \pm 2.75	35.31 \pm 7.52	2.09 \pm 0.38

注:与 NC 组比较,^a $P < 0.05$;与 NDR 组比较,^b $P < 0.05$;与 NPDR 组比较,^c $P < 0.05$ 。

2.2 各组瘦素、脂联素比较

各组瘦素、脂联素水平比较差异有统计学意义($P < 0.05$),PDR 组高于 NC 组、NDR 组、NPDR 组,脂联素低于 NC 组、NDR 组、NPDR 组,NPDR 组瘦素高于 NC 组、NDR 组,脂联素低于 NC 组、NDR 组,NDR 组瘦素高于 NC 组,脂联素低于 NC 组,差异均有统计学意义($P < 0.05$)。见表 2。

表 2 各组瘦素、脂联素比较($\bar{x} \pm s$)

组别	n	LP	ADPN
		(μ g/mL)	(μ g/mL)
NDR 组	41	13.29 \pm 4.01 ^a	5.71 \pm 1.50 ^a
NPDR 组	44	17.68 \pm 5.79 ^{a,b}	4.32 \pm 1.21 ^{a,b}
PDR 组	45	23.19 \pm 6.48 ^{a,b,c}	3.70 \pm 1.02 ^{a,b,c}
NC 组	40	9.48 \pm 3.47	6.51 \pm 1.90

注:与 NC 组比较,^a $P < 0.05$;与 NDR 组比较,^b $P < 0.05$;与 NPDR 组比较,^c $P < 0.05$ 。

2.3 各组氧化应激指标比较

各组 MDA、SOD 水平比较差异有统计学意义($P < 0.05$),PDR 组 MDA 高于 NC 组、NDR 组、NPDR 组,SOD 低于 NC 组、NDR 组、NPDR 组,NPDR 组 MDA 高于 NC 组、NDR 组,SOD 低于 NC 组、NDR 组,NDR 组 MDA 高于 NC 组,SOD 低于 NC 组,差异均有统计学意义($P < 0.05$)。见表 3。

表 3 各组氧化应激指标比较($\bar{x} \pm s$)

组别	n	MDA	SOD
		(nmol/mL)	(U/mL)
NDR 组	41	11.47 \pm 3.18 ^a	87.61 \pm 14.28 ^a
NPDR 组	44	14.95 \pm 3.60 ^{a,b}	74.27 \pm 12.95 ^{a,b}
PDR 组	45	17.77 \pm 4.33 ^{a,b,c}	62.35 \pm 11.43 ^{a,b,c}
NC 组	40	9.22 \pm 2.34	98.31 \pm 11.16

注:与 NC 组比较,^a $P < 0.05$;与 NDR 组比较,^b $P < 0.05$;与 NPDR 组比较,^c $P < 0.05$ 。

3 讨论

近年来,随着生活方式、饮食结构等的转变,2 型糖尿病在人群中流行甚广,由于其病程漫长、迁延难愈,患者极易并发糖尿病视网膜病变^[6]。散在微血管瘤伴小点片状出血是糖尿病视网膜病变的早期表现,随着病情进展,逐渐出现视网膜新生血管,视

网膜受玻璃体增殖膜的牵拉作用趋于剥离脱出,严重影响患者视力^[7-9]。2 型糖尿病进展为糖尿病视网膜病变的比例超过 60%^[10],但多数患者未能及时就诊,确诊时已出现严重视力损害。血清学检查操作简便易普及,分析糖尿病视网膜病变患者血清炎症因子、脂肪因子及氧化应激指标的变化对糖尿病视网膜病变的血清学筛查具有重要参考价值。

IL-6、TNF- α 、hs-CRP 是机体重要的炎症因子,其中 IL-6 是炎症级联反应过程中的核心因子^[11],高浓度 IL-6 可通过损害胰岛 β 细胞功能降低胰岛素的分泌,使机体处于胰岛素抵抗状态^[12];TNF- α 是 IL-6 的触发因子,可诱导产生 IL-6^[13],本身亦具有影响胰岛素信号链的作用^[14];hs-CRP 是典型的急性时相反应蛋白,受 IL-6 刺激作用明显,也可影响胰岛素信号链,造成胰岛素抵抗^[12]。本研究结果显示,各组 IL-6、TNF- α 、hs-CRP 水平比较差异有统计学意义($P < 0.05$),PDR 组均显著高于 NC 组、NDR 组、NPDR 组,NPDR 组均显著高于 NC 组、NDR 组,NDR 组均显著高于 NC 组,差异均有统计学意义($P < 0.05$)。说明糖尿病患者 IL-6、TNF- α 、hs-CRP 水平异常升高,且随着糖尿病视网膜病变损害加重,其水平也随之升高,进一步提示了以上炎症因子对糖尿病视网膜病变的促进作用^[14]。脂肪组织既可存储脂肪,又有分泌作用,是胰岛素作用的重要靶器官之一^[15]。脂肪组织分泌的脂肪因子参与糖类、脂类代谢,是胰岛素敏感性、炎症、免疫等过程的重要调节因子^[16]。瘦素作为肥胖基因在脂肪细胞的表达产物不仅参与代谢、能量消耗等过程,还可促进新生血管的生成^[7]。本研究结果显示,各组瘦素水平比较差异有统计学意义($P < 0.05$),PDR 组瘦素高于 NC 组、NDR 组、NPDR 组,NPDR 组瘦素高于 NC 组、NDR 组,NDR 组瘦素高于 NC 组,差异均有统计学意义($P < 0.05$)。提示瘦素对糖尿病视网膜病变新生血管具有重要促进作用,其浓度可用于判断视网膜病变的严重程度^[17]。脂联素是一种特异性血浆蛋白,由脂肪组织分泌,参与糖类代谢,具有降血糖作用^[18]。本研究结果显示,各组瘦素脂联素水平比较差异有统计学意义($P < 0.05$),PDR 组脂联素低于 NC 组、NDR 组、NPDR 组,NPDR 组脂联素低于 NC 组、NDR 组,NDR 组脂联素低于 NC 组,差异均有统计学意义($P < 0.05$)。提示脂联素水平降低有利于糖尿病视网膜病变的进展,

推测其是糖尿病视网膜病变的保护因子^[19]。

大量研究证实,氧化应激损伤是糖尿病视网膜病变的重要病理环节,高血糖下氧化应激作用增强,氧自由基含量增多,过氧化作用生成MDA,SOD等抗氧化酶不断消耗,最终引起视网膜组织损伤^[20-23]。本研究结果显示,各组MDA,SOD水平比较差异有统计学意义($P < 0.05$),PDR组MDA高于NC组、NDR组、NPDR组,SOD低于NC组、NDR组、NPDR组,NPDR组MDA高于,SOD低于NC组、NDR组,NDR组MDA高于,SOD低于NC组,差异均有统计学意义($P < 0.05$),说明随着糖尿病视网膜病变的进展,氧化应激作用逐渐增强,与上述内容一致。

综上所述,糖尿病视网膜病变与炎症因子、脂肪因子及氧化应激指标具有密切关联,通过上述指标的血清学检测可为有效诊治糖尿病视网膜病变提供科学依据。

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