· 论著 ·

原发性干燥综合征患者睡眠障碍的相关影响因素

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[摘 要] **目的**:探讨原发性干燥综合征(primary Sjögren's syndrome,pSS)患者中睡眠障碍的发生率及其相关的影响因素。**方法**:选取就诊于北京大学人民医院符合纳入及排除标准的 186 例 pSS 患者作为研究对象进行回顾性研究,采用匹兹堡睡眠质量量表(the Pittsburgh sleep quality index, PSQI)、抑郁症筛查量表(patient health questionnaire-9, PHQ-9)、广泛性焦虑量表(generalized anxiety disorder-7,GAD-7)进行调查,收集一般资料及临床数据,以欧洲抗风湿病联盟干燥综合征疾病活动度评分(the European League Against Rheumatism Sjögren's syndrome disease activity index,ESSDAI)评估疾病活动度。以 pSS 患者的 PSQI 分值 >7 分为界,分为 152 例睡眠障碍组和 34 例睡眠正常组。采用 Mann-Whitney U 秩和检验、卡方检验、t 检验,Spearman 相关分析以及 Logistic 回归进行统计学处理。**结果**:pSS 患者中睡眠障碍的发生率为 81.7%(152/186),其中 52.7%(98/186)的 pSS 患者存在中重度睡眠障碍。睡眠障碍组 pSS 患者的 PSQI 平均得分为(12.29 ± 3.30)分,睡眠正常组 PSQI 平均得分为(5.50 ± 1.20)分。睡眠障碍组患者的 PSQI 评分、PHQ-9 评分及 GAD-7 评分均明显高于睡眠正常组患者,并且差异均具有统计学意义,P 值分别为 0.000、0.035、0.031。睡眠障碍组的 PSQI 量表评分在睡眠质量、入睡时间、睡眠时间、睡眠效率、睡眠障碍、催眠药物使用及日间功能障碍等七个方面均明显高于睡眠正常组,并且两组间的差异均具有统计学意义(P <0.05)。疾病病程、焦虑程度、抑郁评分与 PSQI 评分呈正相关(r 值分别为 0.151、0.240、0.421,P <0.05),而补体 C3、C4 与 PSQI 评分呈负相关(r 值分别为 −0.021、−0.235,P <0.05)。二元 Logistic 回归分析显示病程、PHQ-9 评分为 pSS 患者睡眠障碍的预测指标,其中病程 OR = 2.809, 95% CI: 1.21 ~ 6.52;PHQ-9 评分,OR = 1.422, 95% CI: 1.04 ~ 1.94(P <0.05)。**结论**:pSS 患者睡眠障碍的发生率较高,且与疾病病程、抑郁、焦虑情绪等因素密切相关。

[关键词] 原发性干燥综合征;睡眠障碍;焦虑;抑郁;危险因素
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Investigation of sleep disturbance and related factors in patients with primary Sjögren's syndrome

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ABSTRACT **Objective**: To investigate the prevalence of sleep disorders and the relevant determinants in a cohort of primary Sjögren's syndrome (pSS) patients. **Methods**: One hundred and eighty-six pSS patients were included in the study, who were admitted to Peking University People's Hospital and met the criteria of inclusion and exclusion. Sleep quality was assessed using the Pittsburgh sleep quality index (PSQI). Depression, anxiety were evaluated by patient health questionnaire (PHQ)-9, generalized anxiety disorder(GAD)-7, respectively. The demographic and clinical data were also recorded. Disease activity and damage were evaluated with the European League Against Rheumatism Sjögren's syndrome disease activity index (ESSDAI). According to the PSQI score >7, the pSS patients were divided into 152 cases of sleep disorder group and 34 cases of normal sleep group. Mann-Whitney U test, Chi-square test or Fisher's exact test, independent samples t test, Spearman correlation analysis and Logistic regression were used for statistical analysis. **Results**: The prevalence of sleep disturbance (PSQI >7) was 81.7% (152 / 186) in the pSS patients, and 52.7% (98/186) had moderate or severe sleep disorders (PSQI ≥ 11). The mean PSQI score of sleep disordered group was (12.29 ± 3.30), while the normal sleep group PSQI score was (5.50 ± 1.20). The PSQI score, PHQ-9 score and GAD-7 score in the sleep-disordered group were significantly higher than those in the normal sleep group (P = 0.000, 0.035, 0.031). The PSQI score in the sleep disordered group were significantly higher than those in the normal sleep group in

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seven aspects: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disorders, hypnotic drug use and daytime dysfunction. All of them had statistical significance. According to the results of Spearman correlation analysis, PSQI had significantly positive correlation with course of disease, anxiety, depression score ($r = 0.151$, 0.240, 0.421, $P < 0.05$), but negatively correlated with C3, C4 ($r = -0.021$, -0.235, $P < 0.05$). Logistic analysis identified the course of disease ($OR = 2.809$, 95% CI: 1.21 – 6.52) and PHQ-9 score ($OR = 1.422$, 95% CI: 1.04 – 1.94) as predictors of sleep disorders. **Conclusion**: The incidence of sleep disorder in the pSS patients was higher, which was closely related to the course of disease, anxiety, depression and other factors. It is critical to assess and manage comprehensively the disease.

KEY WORDS Sjögren's syndrome; Sleep disorders; Anxiety; Depression; Risk factors

原发性干燥综合征(primary Sjögren's syndrome, pSS)是一种以淋巴细胞浸润和泪腺、唾液腺等外分泌腺受累为特征的慢性自身免疫性疾病[1],其主要表现为口干、眼干。据国外文献报道,约20% ~40%的患者存在广泛的腺体外受累,可累及多个脏器,如引起肺间质病变、肾小管功能受损、血液系统受累、周围神经病等[2-4]。近年来,pSS 患者中越来越常见的疲劳、焦虑、抑郁、睡眠困难等问题逐渐引起临床医师们的关注[5-7],其中睡眠障碍问题尤为突出。据国外文献报道,75% 的 pSS 患者存在中到重度睡眠障碍[8],且已对患者的日常生活造成影响。pSS 在我国患病率为 0.29% ~0.77%,高于国外文献报道的患病率[9-10],我国 pSS 患者人数庞大,而国内尚未检索到对于该方面完整的研究。本研究旨在采用回顾性研究分析我国 pSS 患者的睡眠障碍的发生率及相关影响因素,包括一般资料、血清学、疾病活动度、焦虑及抑郁心理状况等多个方面,进一步更为全面地认识 pSS,特别是患者的睡眠情况,以期指导临床治疗,必要时可予相应的睡眠指导和治疗早期干预,提高患者整体生活质量。

1 资料与方法

1.1 研究对象

对 2018 年 2 月至 2019 年 6 月在北京大学人民医院风湿免疫科门诊就诊及住院的 pSS 患者进行回顾性研究,所有纳入患者均符合 2002 年美国-欧洲联盟指定的干燥综合国际分类标准(American-European Consensus Group, AECG)或 2012 年美国风湿病学会(American College of Rheumatology, ACR)发表的干燥综合征分类标准(ACR 标准)。排除标准:①有精神神经类疾病史,影响睡眠;②有药物滥用史、吸毒史;③病情严重不能独立完成问卷者;④有阻塞性睡眠呼吸暂停低通气综合征病史;⑤有鼻窦炎、鼻中隔偏曲等影响睡眠的疾病史;⑥近期有外伤、手术史等。

1.2 研究方法

由专科医生评估 pSS 的病情活动度,在医生指导下患者自行完成睡眠质量、抑郁情况、焦虑程度等调查量表,专人负责发放问卷与问卷回收。

一般资料:包括性别、年龄、身高、职业、病程,计算体重指数(body mass index, BMI)。病情评估:包括血常规、红细胞沉降率(erythrocyte sedimentation rate, ESR)、C-反应蛋白(C-reactive protein, CRP)、补体、免疫球蛋白、抗核抗体(anti-nuclear antibody, ANA)、类风湿因子(rheumatoid factor, RF)、抗 SSA 抗体(anti-SS-A antibody)、抗 SSB 抗体(anti-SS-B antibody)、抗 α-胞衬蛋白(anti-α-fordrin antibody)、γ 球蛋白、尿视黄醇结合蛋白(retinol binding protein, RBP)、尿 β2-微球蛋白(β2-microglobulin, β2-MG)、尿 N-乙酰 β-D 氨基葡萄糖苷酶(N-acetyl β-D glucosidase, NAG), pSS 疾病活动度采用欧洲抗风湿病联盟(European League Against Rheumatism, EULAR)发表的 EULAR-SS 疾病活动度评分(the EULAR SS disease activity index, ESSDAI)评估。

睡眠质量及其他相关量表:①匹兹堡睡眠质量量表(Pittsburgh sleep quality index, PSQI):评估患者近 1 个月的睡眠质量,共包括 19 个条目,具体分为睡眠质量、入睡时间、睡眠时间、睡眠效率、睡眠障碍、催眠药物使用及日间功能障碍 7 个部分,各部分累计得分为 PSQI 总分。参照国内睡眠质量研究常模及结缔组织病睡眠障碍的相关研究[11],总分 >7 分评定为有睡眠障碍,11 ~15 分为中度睡眠障碍,16 ~21 分为重度睡眠障碍。②抑郁症筛查量表(patient health questionnaire-9, PHQ-9):由 9 个条目构成,用于评估患者近 2 周内抑郁情况,每个条目均赋值 0 ~3 分,各条目得分累计为 PHQ-9 总分,其中 0 ~4 分:无抑郁;5 ~9 分:有抑郁症状;10 ~14 分:明显抑郁症状;15 ~27 分:重度抑郁。总分越高,表明抑郁程度越重。③广泛性焦虑量表(generalized anxiety disorde-7, GAD-7):由 7 个条目构成,用于评估研究对象近 2 周内焦虑情况。每个条目均赋值

0 ~ 3 分,各条目得分累计为 GAD-7 总分,其中 0 ~ 4 分:无焦虑;5 ~ 9 分:轻度焦虑;10 ~ 14 分:中度焦虑;15 ~ 27 分:重度焦虑。总分越高,表明焦虑程度越重。

1.3　统计学分析

采用 SPSS 22.0 软件包进行统计分析。正态性检验采用 Shapiro-Wilk 检验,符合正态分布的计量资料以 $\bar{x} \pm s$ 表示,组间比较采用独立样本 t 检验;不符合正态分布的计量资料以[$M(P_{25}, P_{75})$]表示,组间比较采用 Mann-Whitney U 轶和检验;计数资料以百分比表示,组间比较采用卡方检验或者 Fisher 确切概率法进行分析;变量之间的相关性分析采用 Spearman 相关分析,采用二元 Logistic 分析探究睡眠质量预测因素的影响,以 $P < 0.05$ 作为变量间差异具有统计学意义。

2　结果

2.1　一般资料

共发放问卷 230 份,回收 204 份问卷,剔除无效问卷,有效问卷共 186 份。共入选 pSS 患者 186 例,其中女性 180 例,男性 6 例。以 pSS 患者的 PSQI 分值 >7 分为界,将入选 pSS 患者分为睡眠障碍组(152 例)和睡眠正常组(34 例),女性在各组中所占比例分别为 96.1%(146 例)、100%(34 例),见表 1;血红蛋白(hemoglobin,HGB)、免疫球蛋白 IgA、补体 C3 在 pSS 患者睡眠障碍组和睡眠正常组相比,组间差异无统计学意义($P > 0.05$)。睡眠障碍组的 CRP、抗 α-胞衬蛋白、RF、IgA、RBP、β2-MG 均高于睡眠正常组,HGB、IgG、γ 球蛋白、NAG 均低于睡眠正常组,且 CRP 在两组间的差异具有统计学意义($P < 0.05$),见表 2。

表 1　pSS 患者睡眠障碍组和睡眠正常组基本资料比较

Table 1　Comparison of general data between the two groups of pSS patients

Items	Sleep-disordered group	Normal sleep group	P value
Total cases, n	152	34	
Female/%	96.1	100	0.538
Age/years, M (P_{25}, P_{75})	59.5 (54.25,65)	64.0 (54.5,67)	0.456
Disease duration/ years, M (P_{25}, P_{75})	7.5 (3,7.5)	3 (3,7.5)	0.024*
BMI/(kg/m^2), M (P_{25}, P_{75})	21.8 (20.1,23)	23.4 (22,25.3)	0.061

BMI, body mass index; * $P < 0.05$ has statistical significance.

表 2　pSS 患者睡眠障碍组和睡眠正常组临床资料比较

Table 2　Comparison of laboratory features between the two groups of pSS patients

Items	Sleep-disordered group	Normal sleep group	P value
WBC/($\times 10^9$/L), M (P_{25}, P_{75})	5.0 (4.6,5.4)	4.9 (4.5,5.4)	0.351
HGB/(g/L), $\bar{x} \pm s$	127 ± 19.9	130 ± 11.8	0.366
PLT/($\times 10^{12}$/L), M (P_{25}, P_{75})	194 (180,208)	196 (168,227)	0.846
ESR/(mm/h), M (P_{25}, P_{75})	21.2 (17.0,25.4)	21.7 (12.5,30.8)	0.727
CRP/(mg/L), M (P_{25}, P_{75})	5.0 (0.9,9.0)	1.6 (0.3,3.5)	0.016*
α-fodrin/(RU/mL), M (P_{25}, P_{75})	18.1 (13.3,23.1)	15.7 (5.9,25.5)	0.082
RF /(IU/mL), M (P_{25}, P_{75})	171 (13.8,329)	101 (19.0,184)	0.144
IgA/(g/L), $\bar{x} \pm s$	3.8 ± 4.1	2.9 ± 1.7	0.213
IgG/(g/L), M (P_{25}, P_{75})	14.6 (13.1,16.1)	16.6 (14.1,19.2)	0.211
IgM/(g/L), M (P_{25}, P_{75})	1.3 (1.1,1.5)	1.2 (0.9,1.6)	0.714
C3/(g/L), $\bar{x} \pm s$	0.9 ± 0.2	0.9 ± 0.1	0.925
C4/(g/L), $\bar{x} \pm s$	0.2 ± 0.1	0.3 ± 0.3	0.171
γ globulin/%, M (P_{25}, P_{75})	20.6 (19.1,22.1)	21.7 (19.1,24.3)	0.103
RBP/(mg/L), $\bar{x} \pm s$	1.12 ± 3.1	0.3 ± 0.1	0.085
β2-MG/(μg/L), M (P_{25}, P_{75})	695 (63.0,1327)	262 (87.8,437)	0.781
NAG(U/L), M (P_{25}, P_{75})	10.2 (8.7,11.7)	14.8 (9.0,20.5)	0.989

WBC, white blood cell; HGB, hemoglobin; PLT, platelet; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; α-fodrin; anti-α-fordrin antibody; RF, rheumatoid factors; IgA, immunoglobulin A; IgG, immunoglobulin G; IgM, immunoglobulin M; C3, complement 3; C4, complement 4; β2-MG, β2-microglobulin; RBP, urinary retinol binding protein; NAG, urine N-acetyl β-D glucosidase; * $P < 0.05$ has statistical significance.

2.2 PSQI、PHQ-9、GAD-7 评分比较

PSQI 评分 >7 分者,即有睡眠障碍的 pSS 患者共有 152 例,在本研究中 pSS 患者睡眠障碍的发生率为 81.7%,其中存在中重度睡眠障碍患者,PSQI 评分≥11 分,共 98 例,即 52.7%。pSS 患者睡眠障碍组在主观睡眠质量、入睡时间、睡眠时间、睡眠效率、睡眠障碍、催眠药物使用及日间功能障碍 7 个方面的评分,均明显高于睡眠正常组,且组间差异均具有统计学意义(P <0.05),见表 3。此外,睡眠障碍组在 PHQ-9、GAD-7 二者的总分均明显高于 pSS 患者睡眠正常组,且差异具有统计学意义(P <0.05),见表 4。

表 3 pSS 患者睡眠障碍组和睡眠正常组 PSQI 评分比较

Table 3 The PSQI score of pSS patients of sleep-disordered group and normal sleep group

Items	Sleep-disordered group	Normal sleep group	P value
Total cases, n	152	34	
Subjective sleep quality, M (P_{25}, P_{75})	1 (1,2)	1 (0,1)	<0.001*
Sleep latency, M (P_{25}, P_{75})	2 (2,3)	1 (1,1)	<0.001*
Sleep duration, M (P_{25}, P_{75})	1.5 (1,2)	1 (0,1)	0.004*
Sleep efficiency, M (P_{25}, P_{75})	3 (2,3)	1 (0,1)	<0.001*
Sleep disturbance, M (P_{25}, P_{75})	1 (1,1)	1 (1,1)	0.027*
Hypnotic drug use, M (P_{25}, P_{75})	1 (1,2)	1 (0,1)	<0.001*
Daytime dysfunction, M (P_{25}, P_{75})	2 (2,3)	1 (1,2)	0.001*
PSQI global, $\bar{x} \pm s$	12.29 ± 3.30	5.50 ± 1.20	<0.001*

PSQI, Pittsburgh sleep quality Index; * P <0.05 has statistical significance.

表 4 pSS 患者睡眠障碍组和睡眠正常组 PHQ-9、GAD-7 评分比较

Table 4 The PHQ-9 score and GAD-7 score of pSS patients of two groups

Items	Sleep-disordered group	Normal sleep group	P value
Total cases, n	152	34	
PHQ-9, M (P_{25}, P_{75})	6 (4,8)	4 (2,5)	0.035*
GAD-7, M (P_{25}, P_{75})	3.5 (2,6)	2 (1,4)	0.031*

PHQ-9, patient health questionnaire-9; GAD-7, generalized anxiety disorde-7; * P <0.05 has statistical significance.

2.3 睡眠障碍的相关因素分析

对 pSS 患者进行相关性分析,结果显示,病程、焦虑情绪、抑郁倾向评分与 PSQI 评分呈正相关(病程 r =0.151, P =0.042;GAD-7 评分 r =0.240, P =0.001;PHQ-9 评分 r =0.421, P <0.001),而补体 C3、C4 与 PSQI 评分呈负相关(补体 C3: r = −0.021, P =0.006;补体 C4: r = −0.235, P =0.002)。

2.4 pSS 患者睡眠障碍影响因素的二元 Logistic 回归分析

选取 PSQI 总分单因素分析中差异有统计学意义的指标以及已有前期文献报道的有意义的指标,包括病程、PHQ-9、GAD-7、BMI、WBC、C3、C4 等因素为自变量,以 PSQI 总分为因变量,建立模型进行二元 Logistic 回归分析,结果显示病程、PHQ-9 评分为该模型中影响患者睡眠障碍贡献最大的变量;病程,OR =2.809, 95% CI: 1.21 ~ 6.52) (P <0.05);PHQ-9 评分, OR =1.422, 95% CI: 1.04 ~ 1.94) (P <0.05),而焦虑及实验室相关指标与睡眠障碍无明显相关。

3 讨论

目前睡眠障碍的机制不甚明确,但结缔组织病患者的睡眠障碍发病率越来越突出,国外文献曾报道类风湿关节炎(rheumatoid arthritis, RA)和系统性红斑狼疮可增加罹患睡眠障碍的风险[12-14],且曾有文献报道,与 RA 患者相比,pSS 患者睡眠障碍患病率显著较高[8,15-16]。而关于 pSS 睡眠障碍的发病率问题,国外的研究发现,Tishler 等[8]报道在一项以色列的有 65 例 pSS 患者的研究中有 75% pSS 患者有中至重度睡眠障碍;Gudbjornsson 等[15]阐述了 40 例瑞典 pSS 患者的研究中有 72% 的人主诉的睡眠时间较少;另外,一项 29 例意大利 pSS 患者的研究中,有高达 82.8% 的人有睡眠障碍,且 PSQI 平均得分(8.62 ± 4.58)分[7,15]。pSS 患者存在较为严重的

睡眠障碍,甚至已影响到患者的日常生活,这已经成为不可否认的事实,我国患病人数众多,但尚未检索到对于我国 pSS 患者的睡眠情况较为完整的研究。本研究纳入了较多的患者,在总结归纳了 186 例 pSS 患者的研究中,睡眠障碍的发生率为 81.7%[(PSQI 平均(12.29±3.30)分],这一数据与国外文献相符,同时,PSQI 平均得分高于国外,52.7% 的 pSS 患者存在中、重度睡眠障碍。本研究证实了我国 pSS 患者亦存在较为严重的睡眠障碍,该问题需引起我们的重视和关注。

导致睡眠障碍发生的因素是多方面的,在一般人群中,体质量增加、抑郁、疼痛、免疫功能受损等因素均可增加发生睡眠障碍的风险[17]。在 pSS 患者中抑郁情绪、疲劳、焦虑、嗜睡等均明显高于对照组,白天过度嗜睡尤为明显[15,18-19],这与本研究中患者的焦虑、抑郁状态与 PSQI 总分成正相关结论一致。在一篇关于风湿性疾病睡眠障碍的综述中指出,pSS 患者与健康对照组和 RA 患者相比,pSS 患者白天嗜睡明显增多,约为 RA 组 5 倍,约为对照组的 3 倍,并且更容易疲劳和午睡[18];与骨关节炎患者对照组相比,通过 Epworth 嗜睡量表测量的女性 pSS 患者白天明显过度嗜睡[20]。更有国外文献分析指出,pSS 患者的睡眠障碍患病率增加,主要表现在白天嗜睡、主观睡眠障碍、夜间觉醒和睡眠持续时间短等方面[21]。曾有研究表明,口干症状对睡眠有着明显的干扰作用,口干是睡眠质量的独立危险因素,并且有研究尝试提出了采取对口干的干预,缓解口干症状以改善睡眠质量的措施[22]。也有研究认为,夜间觉醒可能与觉醒饮水以缓解口干症状有关[20]。有研究显示干眼症患者睡眠欠佳,睡眠质量与干眼的程度有关[23]。疼痛,尤其是夜间疼痛,在 pSS 睡眠障碍患者中较为常见,研究提示疼痛程度增加时睡眠质量明显下降,因此,我们可以通过缓解疼痛的方法,改善患者睡眠质量[16]。此外,夜尿、睡眠期间腿动或肢体运动与睡眠障碍有关,其中睡眠周期性肢体运动可能会导致白天嗜睡[15,20]。

国外一项以使用睡眠多导图监测的研究中提示,pSS 睡眠障碍患者的呼吸暂停-低通气指数可达到健康对照组的两倍,并且睡眠呼吸暂停综合征的患病率显著更高(64% *vs.* 28%),并且建议 pSS 睡眠障碍患者需完善睡眠多导图评估睡眠客观指标,包括监测睡眠期腿动、夜间唤醒事件、呼吸暂停-低通气指数等,如患者出现严重阻塞性睡眠呼吸暂停综合征,建议接受持续气道正压通气(continuous positive airway pressure, CPAP)治疗以改善睡眠质量[18,21],而且有研究提示 pSS 患者发生睡眠呼吸暂停与 EULAR-SS 患者报告指数(EULAR Sjögren's syndrome patient reported index, ESSPRI)评分相关,尤其是口干、疼痛[24],其机制可能与 pSS 患者唾液和上气道衬里表面张力增加有关[25]。也有研究提示未观察到睡眠障碍与 ESSDAI 之间的独立关联[26],这与本研究结论一致,ESSDAI 不是发生睡眠障碍的独立危险因素。因评估患者疾病活动度量表不一致,目前考虑睡眠障碍与疾病活动度关系暂不明确。

国外已有研究表明,睡眠剥夺组与睡眠正常组相比,患者血清 CRP 浓度明显升高[27]。Emami Zeydi 等[28]在血液透析患者中进行了一项睡眠质量与 CRP 水平相关性的研究,结果显示患者睡眠质量下降与血清 CRP 水平明显相关($P<0.05$)。Ho 等[29]的研究中证明了在血清 CRP<3 mg/L 分组中,即血清 CRP 水平较低组中,患者的失眠情况与较高 CRP 水平明显相关。Irwin 等[30]在 2016 年对全世界范围内已出版的全部英文文献做了全面的系统回顾和荟萃分析,基于全世界人群的样本,近 34 000 参与者,综合所有现有的睡眠障碍的评估方法,明确证实了睡眠障碍与较高血清 CRP 水平显著相关,且差异具有统计学意义,并提出了 CRP 升高可能是由于更持久或更严重的睡眠障碍的结果。这与本研究中血清 CRP 水平在两组间差异具有统计学意义的结果一致。而对于因患者睡眠障碍导致血清 CRP 升高,抑或是血清 CRP 升高提示机体慢性炎症活动而进一步加重睡眠障碍的机制,目前不甚明确,仍需进一步探究。

睡眠障碍很可能与 pSS 或者自身免疫病患者的慢性免疫性炎症相关,而与此同时,长期睡眠障碍也可能会反过来影响机体的免疫和炎症反应,增加患自身免疫性疾病的风险[19,31]。Irwin 等[32]的研究显示,睡眠剥夺可引起患者体内白细胞介素-2(interleukin-2, IL-2)减少及 IL-6、肿瘤坏死因子(tumor necrosis factor, TNF)等细胞因子增多,在实验性睡眠剥夺的健康人中,Treg 的抑制活性减少,这提供了睡眠障碍与自身免疫疾病之间联系的证据[33]。目前,已有研究证实 pSS 等自身免疫病患者中,TNF-α 和干扰素-α 等促炎因子与疲劳有关[34]。后续我们会进一步探究 pSS 睡眠障碍的患者血清中细胞因子及 T 细胞的变化,监测患者睡眠障碍程度与促炎因子或免疫调节细胞水平是否具有明确相关性,进而探究是否可通过调节细胞因子等方式改善患者睡眠质量。

pSS 患者中睡眠障碍的发生率如此之高,需引起临床医师的关注和重视。临床医师需在诊治 pSS 疾病本身的同时,关注患者睡眠情况及抑郁、焦虑等相关影响因素,整体评估和管理病情,以期早期干预,积极干预,并通过改善口干、疼痛、抑郁、焦虑等相关因素来改善患者睡眠质量,进一步提高患者整体生活质量,改善预后。

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