

重症患者谵妄管理专家共识

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【提要】 谵妄是ICU中常见的一种急性临床综合征,可导致患者病死率增加,机械通气时间和住院时间延长,引起长期的认知功能障碍,增加医疗费用,严重影响患者的预后。为规范重症患者的谵妄管理,由中国冷静治疗研究组根据国内外最新文献资料和多年来的应用推广经验,组织相关重症医学专家在充分讨论和沟通基础上制定了“重症患者谵妄管理专家共识”。旨在改进重症患者的谵妄管理,优化镇痛镇静治疗,改善患者的预后。

【关键词】 谵妄; 重症

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Experts consensus on the management of delirium in critically ill patients

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【 Summary 】 To establish the experts consensus on the management of delirium in critically ill patients. A special committee was set up by 15 experts from the Chinese Critical Hypothermia-Sedation Therapy Study Group. Each statement was assessed based on the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) principle. Then the Delphi method was adopted by 36 experts to reassess all the statements. (1) Delirium is not only a mental change, but also a clinical syndrome with multiple pathophysiological changes. (2) Delirium is a form of disturbance of consciousness and a manifestation of abnormal brain function. (3) Pain is a common cause of delirium in critically ill patients. Analgesia can reduce the occurrence and development of delirium. (4) Anxiety or depression are important factors for delirium in critically ill patients. (5) The correlation between sedative and analgesic drugs and delirium is uncertain. (6) Pay attention to the relationship between delirium and withdrawal reactions. (7) Pay attention to the relationship between delirium and drug dependence / withdrawal reactions. (8) Sleep disruption can induce delirium. (9) We should be vigilant against potential risk factors for persistent or recurrent delirium. (10) Critically illness related delirium can affect the diagnosis and treatment of primary diseases, and can also be alleviated with the improvement of primary diseases. (11) Acute change of consciousness and attention deficit are necessary for delirium diagnosis. (12) The combined assessment of confusion assessment method for the intensive care unit and intensive care delirium screening checklist can improve the sensitivity of delirium, especially subclinical delirium. (13) Early identification and intervention of subclinical delirium can reduce its risk of clinical delirium. (14) Daily assessment is helpful for early detection of delirium. (15) Hypoactive delirium and mixed delirium are common and should be emphasized. (16) Delirium may be accompanied by changes in electroencephalogram. Bedside electroencephalogram monitoring should be used in the ICU if conditions warrant. (17) Pay attention to differential diagnosis of delirium and dementia / depression. (18) Pay attention to the role of rapid delirium screening method in delirium management. (19) Assessment of the severity of delirium is an essential part of the diagnosis of delirium. (20) The key to the management of delirium is etiological treatment. (21) Improving environmental factors and making patient comfort can help reduce delirium. (22) Early exercise can reduce the incidence of delirium and shorten the duration of delirium. (23) Communication with patients should be emphasized and strengthened. Family members participation can help reduce the incidence of delirium and promote the recovery of delirium. (24) Pay attention to the role of sleep management in the prevention and treatment of delirium. (25) Dexmedetomidine can shorten the duration of hyperactive delirium or prevent delirium. (26) When using antipsychotics to treat delirium, we should be alert to its effect on the heart rhythm. (27) Delirium management should pay attention to brain functional exercise. (28) Compared with

non-critically illness related delirium, the relief of critically illness related delirium will not accomplished at one stroke. (29) Multiple management strategies such as ABCDEF, eCASH and ESCAPE are helpful to prevent and treat delirium and improve the prognosis of critically ill patients. (30) Shortening the duration of delirium can reduce the occurrence of long-term cognitive impairment. (31) Multidisciplinary cooperation and continuous quality improvement can improve delirium management. Consensus can promote delirium management in critically ill patients, optimize analgesia and sedation therapy, and even affect prognosis.

【Key words】 Delirium; Critical care

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谵妄是ICU中常见的一种急性临床综合征,可导致患者病死率增加,机械通气时间和住院时间延长,引起长期的认知功能障碍,增加医疗费用,严重影响患者的预后。随着对其认识的不断深入,早发现、早诊断、早治疗可有效缩短谵妄持续时间,减少谵妄的不良影响。虽然近几年临床医护人员对谵妄的重视程度不断增加,但在实践过程中仍暴露出许多认识上的偏差和防治的疏漏。因此,中国冷静治疗研究组根据国内外最新文献资料和多年来的应用推广经验,组织相关重症医学专家在充分讨论和沟通基础上制定了本共识。

共识形成

2016年12月成立了来自全国各地的15名重症医学专家组成的重症谵妄管理共识小组,并召开工作会议,讨论相关问题。经专家讨论认为,重症谵妄管理作为提高医疗质量、保障医疗安全的重要组成部分,目前有必要并有条件形成共识,以促进谵妄的规范诊疗和学术推广。根据既往工作经验、会议讨论和沟通结果,专家们确定了重症谵妄管理共识应包括4方面内容,即谵妄概述、谵妄的原因和相关危险因素、谵妄的诊断、谵妄的防治。由10名重症医学专家组成工作组,完成相关文献的查找、阅读、专家意见的收集和共识条目初稿的书写。经过3次讨论,形成31条基本条目。

通过电子问卷的形式将共识基本条目发给36名专家。根据共识条目的理论依据、科学性、创新性、可行性及专家权重进行综合评分,同时对临床相关结果类条目,参考推荐意见分级的评估、制定及评价(grading of recommendations assessment, development and evaluation, GRADE)系统评价方法,评估过程基本符合GRADE系统推荐原则。最终综合评分以0~9计分,确定各条目的推荐强度。其中,0~3分为不推荐,4~6分为弱推荐,7~9分为推荐。然后通过改良的德尔菲法,组织8名专家,结合最新的临床医学证据和重症医学发展前沿,分别对共识条目的相关专题进行审阅。并于2018年6月24日召开会议集中讨论。根据会议所有专家达成一致的条目及其内容描述要求,在综合评分的基础上,形成最终推荐意见。之后,共识条目撰写小组根据会议意见,再次查阅及增补最新文献,于2018年8月初形成最终稿。

谵妄概论

谵妄是多种原因引起的一过性意识混乱状态,主要特

征为意识障碍和认知功能改变。虽然谵妄的表现以精神症状为主,但其产生和发展是全身疾病与脑功能共同作用的结果。

1. 谵妄不仅是精神改变,还是一种多伴有病理生理改变过程的临床综合征[推荐强度:(7.63±0.94)分]

谵妄的临床表现多种多样,均可归于精神改变范畴。人们往往仅关注于具体的症状,而忽略了谵妄内在的病理生理机制。谵妄发生的机制有许多学说,如乙酰胆碱合成受损、胆碱能突触的损伤、多巴胺水平升高、血浆氨基酸(色氨酸、酪氨酸)浓度的改变^[1-3]等。此外,脓毒症等引起的系统炎症反应还可通过内皮细胞活化、脑血流受损、血脑屏障破坏等神经毒性反应促进谵妄的发生^[4-5]。一项对90例颅内出血患者进行谵妄预测的研究发现:右侧大脑半球皮层下白质或海马旁回出血,谵妄发生率明显升高,提示特定位置的脑损伤与谵妄密切相关^[6]。由此可见,谵妄未来的管理不应仅满足于控制精神症状,而应像其他疾病一样,从病理生理机制出发,寻找根本上的解决方法。

2. 谵妄是意识障碍的一种亚型,是脑功能异常的表现[推荐强度:(7.59±0.88)分]

人的意识活动由意识水平和意识内容两部分组成,二者之一出现异常均属于意识障碍。谵妄患者意识水平高低不等,意识内容杂乱无章,因此谵妄是意识障碍的具体表现形式之一,能反映脑功能的异常。有研究认为,暴露于应激源后,脑功能的崩溃及大脑连通性和可塑性的损害最终导致了谵妄的发生^[7]。而谵妄持续时间的延长亦与影响脑功能的组织学改变,如脑容量下降、脑白质破坏等密切相关^[8-9]。因此,加强谵妄管理,缩短谵妄持续时间,是保护脑功能的重要手段。

谵妄的原因与相关危险因素

临床中促发或影响谵妄的因素多种多样,对谵妄的影响程度也各不相同(表1)。一类是易患因素,与患者基础状况直接相关,由患者的既往健康背景所决定,如老年痴呆、高龄、酗酒、高血压等。这些因素是患者固有的,有些无法干预,有些即使能干预,也无法在短期内彻底解除其影响。另一类是躯体、心理的急性疾病损伤及治疗干预措施造成的脑功能异常,如严重感染、创伤、休克、呼吸衰竭、体外循环(CBP)等,对这类情况,原发病的治疗对于谵妄至关重要。第三类是促发因素,在患者原发病的基础上,并存促发

表 1 谵妄的病因和影响因素

分类	因素
易患因素	高龄
	酗酒
疾病因素	高血压
	老年痴呆
	严重感染
	创伤
	休克
	呼吸衰竭
	代谢性酸中毒
	体外循环
促发因素	疼痛
	焦虑
	抑郁
	药物
	制动

谵妄的因素,如疼痛、焦虑、抑郁、药物等。在ICU中若未重视这些因素的干预,谵妄的发生率会大大提高。

3. 疼痛是重症患者发生谵妄的常见原因,抑制疼痛可延缓谵妄的发生发展[推荐强度:(7.56±1.01)分]

大部分患者在ICU期间会经历中至重度的疼痛,疼痛作为能产生不良应激的躯体刺激因素,是引起重症患者谵妄的重要原因^[10]。有研究发现,手术后静息疼痛与术后谵妄的发生密切相关,且疼痛程度越严重,相对危险度越高^[11]。一项关于疼痛、镇痛与谵妄发生间关系的研究,纳入了541例髋关节手术患者,发现疼痛处理不当的患者发生谵妄的危险度约是疼痛控制良好者的9倍^[12]。重症患者由于机械通气、麻醉苏醒延迟等原因,常无法主动表达,导致患者的疼痛常被忽略,反复的疼痛刺激以及长时间置身于陌生嘈杂环境的影响,易诱发和加重谵妄的临床症状,甚至对临床预后产生不良影响。缓解患者疼痛是降低谵妄发生率行之有效的方法之一。

4. 焦虑或抑郁是重症患者发生谵妄的重要因素[推荐强度:(7.19±1.18)分]

谵妄的发生是患者的易感性(易患因素)、疾病本身和应激事件(促发因素)综合作用的结果。在ICU,患者要面对死亡的恐惧、潜在的永久功能丧失、无亲属的陪伴、睡眠的剥夺、灯光噪音的干扰等,均会成为心理及精神创伤的应激因素,产生或加重焦虑或抑郁。二者相互作用,导致记忆力下降及睡眠障碍,影响大脑皮质功能,进而导致谵妄的发生。而焦虑或抑郁本身又可加强疼痛感觉,增加谵妄的发生率^[13]。因此焦虑或抑郁是引发院内谵妄的重要原因,应引起足够重视。

5. 镇痛镇静药物与谵妄发生的相关性不确定[推荐强度:(6.66±1.64)分]

镇痛镇静药物能有效缓解疼痛、焦虑等症状,预防谵妄的发生。但亦有研究显示,使用镇痛镇静药物可使ICU谵妄发生的风险明显增加。目前对镇痛镇静药物诱发谵妄的

机制尚不清楚,而众多研究提示,不合理的应用镇痛镇静药物可能与谵妄更加相关。在成人ICU患者中,阿片类药物的使用与谵妄之间的关系临床证据相互矛盾,而与增加药物剂量及药物蓄积有关^[14]。苯二氮草类(咪达唑仑或劳拉西泮)药物似乎是可引起ICU谵妄的危险因素,但其原因亦是药物应用/使用方法不当所致,且与药物剂量相关^[15-16]。而丙泊酚影响谵妄的发生机制目前尚未完全阐明,且目前鲜有报道ICU中使用丙泊酚镇静对谵妄发生率的影响。

6. 应重视谵妄与撤药反应的关系[推荐强度:(7.75±0.88)分]

撤药反应是指使用某种药物后,机体对药物产生了适应性,一旦停药或减量过快使机体调节功能失调,而导致的功能紊乱,病情或症状反跳、回升,疾病加重等现象。ICU中常用的阿片类药物及镇静催眠药均可引起撤药反应,与镇痛镇静治疗时间、药物总剂量密切相关。撤药反应可表现为躁动、定向力障碍、幻觉等,常被认为是谵妄中的一种亚类。但其相对其他类型的谵妄,又有相对明确的病因,即镇痛镇静药物撤药速度过快所致。治疗上恢复使用该药物即可使症状消失。因此重视重症患者谵妄与撤药反应的关系,关注镇痛镇静药物的选择、用法、用量及镇静深度。从低剂量开始,滴定至有效镇静目标为止,定期回顾用药剂量,逐渐减量、停药,或采用不同镇静药物的序贯疗法^[17],才能从根本上避免撤药引起的谵妄。

7. 应重视谵妄与依赖/戒断反应的关系[推荐强度:(7.47±0.92)分]

依赖反应是一组认知、行为和生理症状群,包括躯体依赖和心理依赖。躯体依赖是由于反复使用成瘾物质所造成的一种病理性适应状态。心理依赖是指长期应用成瘾物质者会产生一种愉快满足的或欣快的感觉,驱使其为寻求这种感觉而反复使用,表现所谓的渴求状态。戒断反应是在依赖的基础上产生的,是酒精、烟草、毒品等成瘾后突然停止或减少使用成瘾物质所出现的特殊症状群,引起精神症状、躯体症状、或社会功能受损。ICU患者可能因酒精戒断而使去甲肾上腺素释放增多,导致脑内神经递质失衡而诱发谵妄。最新的研究显示,创伤患者出现酒精戒断后发展为谵妄的几率为11%,且这部分人群的病死率明显升高^[18]。而既往吸烟的患者,由于烟草戒断,其在ICU发生躁动、意外拔管的几率明显高于非吸烟者^[19]。急性脑损伤患者,烟草戒断可能是谵妄的潜在致病原因之一^[20]。对酒精和海洛因依赖的髋关节置换患者,术后谵妄发生率明显升高^[21]。此外,长期应用阿片类镇痛药物也可产生类似依赖反应,因此,重视重症患者谵妄与依赖/戒断反应的关系,选择合适的镇痛镇静药物。当超过预定剂量时,可选用其他药物,以延迟耐药和依赖性的发生,并采取合理的有计划的撤药方法。

8. 睡眠剥夺可诱发谵妄[推荐强度:(8.06±0.62)分]

ICU的患者很容易出现睡眠剥夺。虽然患者有足够的睡眠时间,但是睡眠时间常被碎片化,且睡眠结构异于正

常,主要为 N_1 期、 N_2 期增多,而 N_3 期及快速眼动期减少。睡眠剥夺作为强烈的应激,可促使谵妄的发生,是谵妄的危险因素之一^[22],且睡眠剥夺与谵妄的危险因素具有很大程度上的重叠^[23]。此外睡眠剥夺、睡眠-清醒周期紊乱还可导致褪黑素昼夜分泌紊乱。有研究证实,褪黑素分泌紊乱与ICU谵妄有明显的相关性^[24]。睡眠剥夺还可造成认知功能损害,抑郁或焦虑的精神状态,进而引起谵妄。因此采取改善睡眠质量的非药物措施,包括控制灯光、噪音;提倡护士避免睡眠时间进行常规护理活动,操作动作轻柔等减少对患者睡眠周期的刺激;使用眼罩和耳塞等改善睡眠环境,也可有效预防谵妄的发生^[25-27]。

9. 对持续存在或反复发作的谵妄,需警惕尚未发现的潜在危险因素[推荐强度:(7.63±1.16)分]

谵妄是脑功能异常的表现。在重症患者中,脑功能异常既可能是已有疾病(无论其是否已控制)的后果,也可能是尚未发现的潜在疾病及易患因素的临床表现,因此对持续存在或反复发作的谵妄,除已知重症疾病外,还应注意其他病症的筛查。Siew等^[28]发现,急性肾损伤2期患者发生谵妄的相对危险度为1.55,而3期患者相对危险度则升至2.56,提示急性肾损伤是谵妄的潜在危险因素。此外,谵妄持续时间越久,认知功能损伤越重,有时需排除潜在的中枢神经系统病变的存在,因为部分持续谵妄的存在,可能是大脑本身储备能力减少的表现,如发病前即有认知功能障碍的患者(如痴呆)^[29],会加重谵妄病情,延长谵妄持续时间。因此,所有类型的谵妄,均需鉴别危险因素和病理生理状态,尤其对反复发作或持续存在的谵妄更加重要。

10. 重症相关的谵妄可影响原发病的诊治,也可随原发病的好转而缓解[推荐强度:(7.62±1.10)分]

相较于镇痛镇静药物撤药反应或成瘾物质戒断引起的谵妄,ICU中更常见的是重症相关的谵妄(图1)。其原发病位点不一定在大脑,而是由于重症疾病内在的病理生理机制影响脑功能,临床表现为谵妄症状。可以讲谵妄是此类重症疾病脑功能异常的体现。如脓毒症,可通过破坏血脑屏障、细胞因子激活、神经递质失衡等机制,引起脓毒症相关性谵妄,其发生率可高达50%^[30]。谵妄的存在会恶化病情,使原发病的治疗更加复杂和棘手,延长患者住院时间及住ICU时间,增加镇静药物使用时间及医疗费用,升高短期与长期认知功能障碍的发生率^[31],甚至能影响ICU的病死

率^[32]。如果将谵妄的管理视为重症疾病整体治疗策略的一部分,尽快干预、解决原发病,可将谵妄的危害降至最低。如对脓毒症相关性谵妄,其治疗的核心始终是脓毒症本身的管理^[33]。随着脓毒症的控制,谵妄也可表现为逐渐减轻,直至彻底缓解。

谵妄的诊断

谵妄的临床表现错综复杂、多种多样。既有普遍规律,又掺杂着各种不典型症状。早期、准确的诊断对后续的干预治疗、疗效随访、预后判断均具有重要的意义。目前临床常用的谵妄诊断工具均存在各自的优势和弊端,而日益增长的诊治需求已不满足于简单的诊断“是”或“否”,而希望能划分出不同的严重程度,甚至在临床诊断前,更早地预测筛查出谵妄人群,达到治未病的目的。

11. 急性意识改变和注意力受损是诊断谵妄的必要条件[推荐强度:(7.84±0.99)分]

注意力是指人的心理活动指向和集中于某种事物的能力。注意力受损表现为患者对各种刺激的警觉性及指向性下降,不能集中注意力,同时注意力保持、分配和转移也有障碍。谵妄时意识的改变则表现为意识水平和/或意识内容出现波动。谵妄的诊断有各种诊断标准,目前公认的精神疾病诊断与统计手册第5版(DSM-5)、中国精神障碍分类与诊断标准第3版(CCMD-3)、国际疾病分类第10版(ICD-10)、意识模糊评估法(CAM)、ICU患者意识模糊评估法(CAM-ICU)、重症监护谵妄筛查量表(ICDSC)诊断标准中^[34],均必须存在意识障碍和注意力受损,因此急性意识改变和注意力受损是诊断谵妄的必要条件。

12. CAM-ICU和ICDSC联合评估有利于提高谵妄,尤其是亚临床谵妄诊断的敏感性[推荐强度:(7.53±1.48)分]

CAM-ICU和ICDSC两种评估方法的制定,开辟了ICU谵妄评估的新纪元,两者在评估谵妄患者的效用上具有高度的一致性^[35],因此被推荐为ICU谵妄评估的常用工具。CAM-ICU评估条目少,简便易行,因此在临床上应用广泛,但其只能做出阳性和阴性的定性诊断。而ICDSC包含了定向力、幻觉、不恰当的言语和情绪、睡眠-觉醒周期等多种因素的评估,因此对谵妄筛查的阳性率更高^[36-37],且可以对谵妄程度进行划分,区分临床谵妄和亚临床谵妄,丰富了评估内容。两者结合,才能最大程度地兼顾效率和效果。一项对ICU患者采用ICDSC进行谵妄评估的研究显示,亚临床谵妄与临床谵妄的住院时间接近,住ICU时间和住院时间均高于无谵妄患者。因此应提高对亚临床谵妄的重视及早期筛查干预,以减少对预后的影响。

13. 早期识别和干预亚临床谵妄,可降低其进展为临床谵妄的风险[推荐强度:(7.59±1.41)分]

亚临床谵妄是介于正常意识与谵妄之间的过渡状态。虽然依照诊断标准,其尚不能划入临床谵妄的范畴,但其已表现出谵妄的某些征象,应引起足够重视。Al-Qadheeb

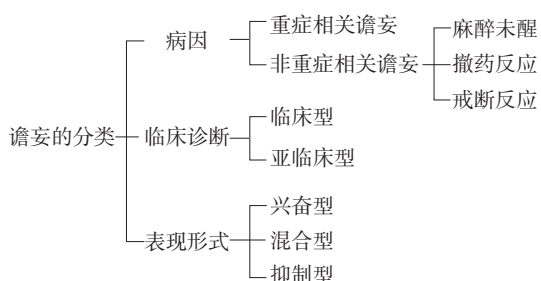


图1 谵妄的分类

等^[38]研究了低剂量氟哌啶醇与安慰剂相比,是否可降低亚临床谵妄进展为临床谵妄的风险。虽然最终结果提示,两组临床谵妄的发生率差异无统计学意义,但氟哌啶醇组的 Ricker 镇静-躁动评分(SAS)更低,提示氟哌啶醇组应用镇静药物更少,而镇静药物的大量使用是谵妄发生的重要危险因素,因此对亚临床谵妄的干预价值尚不可完全否定。谵妄能通过预防措施改善临床结局,从这个角度看,早期识别和干预亚临床谵妄,避免其进展为临床谵妄,应成为重要的治疗要求^[39]。

14. 每日评估有助于早期发现谵妄[推荐强度:(7.63±1.04)分]

谵妄与患者的预后密切相关,且谵妄持续时间与老年患者的一年病死率直接相关^[40]。因此早期筛查,并尽可能缩短谵妄持续时间,是改善预后的关键。2013 年美国成人疼痛、躁动、谵妄管理指南(PAD 指南)提出,对成年重症患者应使用有效可靠的评估工具常规对其进行谵妄监测^[41]。已有研究发现,每日评估可发现更多需要治疗的谵妄患者^[42],让医生准确治疗谵妄,减少谵妄带来的不良后果。

15. 抑制型谵妄和混合型谵妄并不少见,应给予重视[推荐强度:(7.91±0.78)分]

美国精神病协会制定的 DSM-5 将谵妄分为 3 个亚型,即兴奋型、抑制型和混合型。兴奋型谵妄以躁动、烦躁不安、试图拔除各种管路为特征;抑制型谵妄以感情淡漠、言语减少、嗜睡为特征;混合型则是患者具备两者的典型特征^[43]。有报道显示,重症谵妄患者中,兴奋型谵妄占 1.6%,抑制型占 43.5%,混合型则占 54.1%^[44]。而之后的研究发现,不同亚型的谵妄在重症患者中所占比例差别很大。尽管抑制型或混合型谵妄发生率较高,但兴奋型谵妄患者更易受到医护人员的关注,主要是因为兴奋型谵妄患者的症状,如焦虑、躁动等易引发医疗护理不良事件,甚至对患者自身或医护人员造成伤害。而抑制型谵妄患者少有兴奋表现,混合型谵妄呈间断发作,在临床也常被忽视。有研究表明,相较于其他两种类型,混合型谵妄持续时间最长^[45]。因此对常见且存在严重危害的抑制型和混合型谵妄,应给予重视。

16. 谵妄可伴有脑电的改变,有条件的 ICU 可使用床旁脑电监测[推荐强度:(6.88±1.43)分]

目前谵妄的发现及评估均无直接客观数据指导诊断和治疗,只能依赖 CAM-ICU 等评估量表。有研究发现,脑电的变化可反映疼痛程度、情绪状态、睡眠质量等谵妄影响因素,手术中脑电抑制是术后谵妄的独立危险因素。脑电的监测对精准镇痛、平复焦虑(他人无法察觉的内、外专注过高)、保证充足睡眠等方面可起到准确指导作用。同时对临床症状不典型、不易发觉的脑异常放电也可早期发现,有助于排除癫痫等脑部疾病引起的精神障碍,避免盲目治疗。目前有限的研究提示,大多数脓毒症患者存在脑电图异常,并与是否存在脓毒症相关性脑功能障碍及其严重程度有关^[46],此类患者脑电图可表现为背景异常、周期律改变、

癫痫样活动或癫痫持续状态^[47-48]。对临床症状不典型,不易发觉的脑功能异常可行持续脑电监测评估,从而提高谵妄的管理质量。

17. 重视谵妄与痴呆、抑郁症的鉴别[推荐强度:(7.16±1.17)分]

痴呆和抑郁症均是谵妄发生的高危因素,而其临床表现与谵妄的症状也有部分重合。由于其诊疗存在一定的差异,因此在临床中有必要对三者进行一定的甄别^[49-50]。首先,痴呆和抑郁症均呈慢性渐进性病程,而谵妄一般表现为急性脑功能损害,在患病时间上会有明显差异,因此病史的采集尤为重要。其次,痴呆患者多伴有智力进行性减退,且意识水平波动不明显。抑郁患者突出表现为情绪低落和快感缺乏,且有时会伴有妄想、自杀等行为,而谵妄患者意识内容多杂乱无章。再次,谵妄会出现睡眠周期紊乱,而抑郁仅会表现为入睡困难,不会出现昼夜颠倒。需要强调的是,谵妄可与痴呆、抑郁并存,因此区分三者有利于治疗有的放矢,促进可逆疾病(谵妄、部分抑郁症)尽快恢复。

18. 重视谵妄的快速筛查方案在谵妄管理中的作用[推荐强度:(7.84±0.92)分]

DSM-5 是目前诊断谵妄的金标准。近年来超过 10 种谵妄筛查方案出现,均是为了使临床医生提高对谵妄的警惕。筛查阳性有助于进一步明确谵妄的诊断与后续处理措施。目前谵妄的快速筛查方案包括:3 min 谵妄诊断量表(3D-CAM)^[51](3 min 内,包括 3 个定向力项目、4 个注意力项目、3 个症状项目、10 项可观察项目)和 4 项谵妄快速诊断(4AT)方案^[52][包括警觉性、认知(定向力及注意力)及精神状态的急性改变]。这两个方案与目前公认的标准相比,有很高的契合度,应用也更加广泛。快速筛查方案的应用可简化谵妄的标准诊断流程,有助于谵妄的早期发现与管理。

19. 谵妄严重程度的评估是诊断谵妄必不可少的组成部分[推荐强度:(7.31±1.51)分]

明确诊断谵妄的患者,其临床表现、危害程度等均存在很大差异,直接影响医护人员对其的重视程度和治疗的紧迫性,因此评估谵妄严重程度对指导后续治疗具有重要的指导意义。目前最常用的评估工具是谵妄分级量表-98 版(delirium rating scale-revised-98, DRS-R-98)^[53],许多研究均已证实其具有良好的可靠性^[54]。将 DRS-R-98 纳入谵妄评估流程,可使谵妄诊断更加具体化,治疗有的放矢。

谵妄的防治

谵妄对重症患者预后的影响深远,因此谵妄的预防和治疗成为了重症患者谵妄管理的核心。所有的镇痛镇静治疗策略均应围绕着控制应激反应、降低谵妄发生率、减少谵妄危害来制定。谵妄的防治是一个多项目、多目标、多手段组成的系统诊疗方案,既涵盖了 ICU 固有环境的改进,又包含了重症康复的理念,甚至突出强调了以往易被重症医生忽略的人文关怀和精神慰藉,是对重症治疗整体化的完美诠释。

释。近些年在谵妄防治方面的研究探索,为全面认知、早期干预谵妄指明了方向,展现出一片广阔的新天地。

20. 对因治疗是谵妄管理的关键[推荐强度:(7.78±1.16)分]

脓毒症、休克、呼吸衰竭等疾病造成的脑功能异常,是重症患者并发谵妄的主要原因。多种病理生理改变如炎症反应、脑灌注、神经变性,均是脑功能障碍的影响因素^[33,55],这些因素使得严重感染及低灌注的患者更易出现谵妄。研究表明,谵妄的发生与疾病的严重程度存在明显的相关性^[56],积极处理原发病在谵妄的管理过程中至关重要。疼痛、焦虑、不合理镇静均是促发谵妄的因素^[57],有效的镇痛及合理镇静对减少应激所致的生理和心理功能障碍可起到积极作用。而谵妄的对症治疗只是在对因治疗发挥作用过程中的有效辅助和补充。

21. 改善 ICU 环境因素、提高患者舒适度有助于减少谵妄的发生[推荐强度:(7.91±0.89)分]

ICU 患者面临诸多诱导谵妄发生的高危因素,包括因自身病情所决定的基线因素,以及医疗相关因素^[58]。基线因素与患者原发疾病相关,而医疗相关因素往往与治疗措施和 ICU 管理相关,是可以干预和控制的。通过灯光的昼夜调节、降低病房内噪音、维持舒适的温度等可减少患者的不适主诉^[45]。因此改善环境因素、提高患者舒适度有助于减少谵妄的发生。

22. 早期活动既可降低谵妄的发生率,又可缩短谵妄的持续时间[推荐强度:(8.09±0.73)分]

早期活动目前主要指患者患病后 2~5 d 内开始进行活动^[59]。运动可以促进肢体血液循环,改善脑部供血,预防大脑发生缺血性损害;还可以增加皮质内胆碱能纤维密度,增加体内抗炎物质的产生^[60]。有研究显示,早期活动可缩短谵妄持续时间^[61]。而早期活动的安全性和可行性在临床中也得到了很好地证实。在对 103 例机械通气时间>4 d 的 ICU 患者 1 449 次早期活动的调查研究显示,跌倒、营养管脱出、高血压[收缩压>200 mmHg(1 mmHg=0.133 kPa)]、低血压(收缩压<90 mmHg)等不良事件发生率为 0.96%,但未增加并发症的发生率和医疗费用^[62]。ICU 活动分级使患者的早期活动水平有了更为具体和明确的可衡量的指标。早期活动既可给予患者心理支持,也可增强躯体器官功能,减少并发症,已成为谵妄患者集束化管理策略中的一项重要举措。

23. 重视和强化与患者的沟通和交流,家庭成员的参与有助于减少患者谵妄的发生,促进谵妄的恢复[推荐强度:(7.83±1.01)分]

重症患者在治疗过程中遭受着因机械通气、有创监测、睡眠剥夺等引起的各种身体不适,加之对病情及陌生环境的恐惧、交流受限等因素均加重其心理负担,使患者极易罹患谵妄。而谵妄本身也易导致抑郁、焦虑等心理应激^[63]。因此,医护人员应尽早进行解释沟通,最大程度减少来自疾病本身及治疗引起的精神创伤和心理应激,从而预

防谵妄的发生。家庭成员提供类似的干预措施,也有潜在的疗效。有研究发现^[64],通过延长 ICU 探视时间,增加家属与患者接触机会,即对谵妄的管理有明显的促进作用。

24. 应强调睡眠管理在谵妄防治中的作用[推荐强度:(8.22±0.75)分]

在 ICU,由于各种声音、光线和监护治疗措施的干扰,以及疼痛、焦虑情绪的影响,患者常常无法保证正常的睡眠^[65-66]。有研究显示,ICU 患者的睡眠紊乱与谵妄的发生密切相关。一旦 ICU 医护人员发现患者存在睡眠障碍,总是习惯性给予镇静药物。然而,镇静药物经常不能改善睡眠,有时还会使睡眠质量进一步恶化。目前的研究已证实,无论是应用咪达唑仑还是丙泊酚,均会引起睡眠结构的改变,减少快眼睡眠和慢波睡眠时间^[67-69]。持续镇静治疗还会使睡眠-觉醒昼夜节律及褪黑素昼夜分泌节律消失^[70-71]。合理的睡眠管理推荐,通过声光的管控及放松疗法等非药物方式进行。Hu 等^[72]的研究发现,通过耳塞和眼罩,联合轻柔的音乐可以不同程度地改善睡眠(如睡眠深度、入睡难易程度、觉醒次数、觉醒后再次入睡等)。而有 Meta 分析^[73]也显示,通过耳塞改善睡眠能减少谵妄的发生。

25. 右美托咪啶可缩短谵妄持续时间,或可预防谵妄发生[推荐强度:(7.13±1.74)分]

右美托咪啶是一种高选择性 α_2 肾上腺素受体激动剂,其通过蓝斑内的受体,发挥镇静和抗焦虑作用,此外通过脊髓内 α_2 肾上腺素受体还可以发挥镇痛作用,还具有减轻应激反应的作用。相对于其他镇静药物,右美托咪啶在镇静的同时更易保持可唤醒力,极少诱发呼吸抑制,血流动力学影响小,且其快速消除的药代动力学特性,可减少药物蓄积。临床研究证实,右美托咪啶对应用机械通气的兴奋型谵妄患者,可明显缩短谵妄持续时间^[74]。对非心脏术后的老年患者,右美托咪啶对谵妄的发生还有一定的预防作用^[75]。但对心脏手术患者,与咪达唑仑+吗啡比,右美托咪啶虽然可以缩短住 ICU 时间,但对谵妄的发生率无影响^[76]。

26. 应用抗精神病药物治疗谵妄时,应警惕其对心律的影响[推荐强度:(7.34±0.97)分]

传统抗精神病药(主要是氟哌啶醇)和苯二氮草类药物均曾用于谵妄(特别是兴奋型谵妄)的治疗,但苯二氮草类药物的镇静作用及其对认知功能的影响,可能会恶化患者的清醒程度及行为障碍,因此除了镇静安眠药物和酒精戒断引起的谵妄,应避免单一使用苯二氮草类药物,而氟哌啶醇的锥体外系反应和抗胆碱作用也限制了其使用。近年来,有研究显示非典型抗精神病药,如奥氮平、喹硫平等,对谵妄有一定的疗效,但在应用时应权衡利弊,此类药物不但可导致过度镇静,还可引起尖端扭转型室性心动过速。因此,不建议对存在高风险尖端扭转型室性心动过速(QT 间期延长,或服用可导致 QT 间期延长药物的患者,或有心律失常病史)的患者使用非典型抗精神病药物^[77]。

27. 谵妄管理应关注脑功能锻炼[推荐强度:(7.13±1.19)分]

脑功能锻炼是指在限定的时间内通过重复特定的程序或活动来增强认知能力,其主要包括注意力训练、工作记忆、习惯纠正训练等^[78]。有研究显示,其对衰老或损伤后的神经功能重建均具有显著疗效^[79]。谵妄作为脑功能紊乱的一种表现形式,其发生不仅影响患者的近期预后,亦对患者远期预后造成严重影响,如影响患者的记忆功能、生活质量等。即使在谵妄缓解后,仍有许多患者会遗留认知功能障碍。有研究显示,相较于顶叶、前叶和皮层下,全脑综合征与谵妄的发生更加密切^[80]。侧面印证了全脑功能的异常与谵妄相辅相成。因此对谵妄患者的脑功能状态给予早期有效的管理,并进行脑功能锻炼尤为重要。

28. 与非重症相关谵妄比,重症相关谵妄的缓解不会一蹴而就[推荐强度:(7.06±1.11)分]

发生谵妄的危险因素众多,临床表现也多种多样,其纠正方法是个体化的、多维的。从疾病的治疗→生命体征的维持,从营造舒适环境→心理疏导等,涉及ICU治疗单元的方方面面。谵妄一旦发生,无论药物还是非药物的干预,只能缩短谵妄的持续时间,而意识的完全恢复需要各个环节配合协调,这需要一定的时间。对于镇静相关性谵妄,镇静药物停止使用后,随着药物代谢的过程,谵妄症状即可消失,对患者的预后不会造成严重的影响^[81]。而重症相关性谵妄的发生往往是多因素综合作用的结果^[82]。对这些因素的纠正需要一个过程,因此谵妄发生后,需要做到早期诊断与治疗,积极祛除病因。

29. ABCDEF、eCASH、ESCAPE 等综合管理策略有助于谵妄的防治,并改善重症患者的预后[推荐强度:(7.84±0.92)分]

重症疾病本身会导致机体内血流动力学及代谢紊乱,进而影响脑功能,诱发谵妄。而谵妄本身又会加重病情,不利于各项治疗的开展,延缓疾病的恢复。因此对重症相关谵妄,减少其发生和进展较降低已出现的谵妄带来的潜在损害风险更为重要。已有许多研究证实^[83-84]:采用一定的措施早期干预、预防谵妄可明显减少谵妄的发生。近几年来,以谵妄为核心的,包含早期活动的重症患者镇痛镇静集束化管理策略越来越受到重视,其中的代表是ABCDEF和eCASH策略。ABCDEF策略包括疼痛的评估、预防和管理;自主觉醒试验和自主呼吸试验;镇痛镇静的选择;谵妄的评估、预防和管理;早期活动及家庭关怀六方面。有研究证实,应用该策略可明显降低谵妄的发生率^[85],缩短谵妄持续时间^[86]。而与之类似的eCASH策略^[87],包含早期使用镇痛药物保持舒适、最小化镇静和最大化人文关怀,充分体现了集束化管理对谵妄预防的重要性。最近提出的ESCAPE策略^[88](图2),着重强调了早期活动、睡眠管理和精神状态评估(认知功能评估)在谵妄管理中的重要性,使谵妄患者的管理策略更加全面。

30. 缩短谵妄持续时间可减少远期认知功能障碍的发生[推荐强度:(7.50±0.98)分]

谵妄是一个可显著改变患者生活的事件,可能威胁到



图2 谵妄管理的ESCAPE集束化策略

患者的独立性和生活质量。谵妄的发生与炎症和凋亡相关,可能会引起脑萎缩。而脑萎缩和脑白质完整性的异常被认为与认知功能障碍密切相关。谵妄发作持续时间越长,认知功能障碍越明显^[89]。长时间的谵妄持续状态,是远期认知功能和执行能力下降的独立危险因素^[90]。由于谵妄对认知功能的不利影响,因此缩短谵妄时间对远期认知功能障碍具有重要意义。

31. 多专业合作、持续管理质量改进可提高谵妄管理水平[推荐强度:(7.58±1.24)分]

谵妄的管理涉及评估、监测、干预和预防等多方面内容。每一部分均需要有严格的质量控制体系以保证其实施到位,结果可靠。因此持续的管理质量改进是提高谵妄管理水平的重要保证。评估准确是谵妄诊断的前提,有研究发现^[91],护士主导的干预使谵妄评估的准确性由56%升至95%。而在治疗方面,临床药师参与的镇静、镇痛、谵妄管理策略明显缩短住ICU时间和住院时间^[92]。而麻醉医生的参与,术中注意监测麻醉深度和维持轻度镇静,对预防术后谵妄也有重要意义^[93]。由于谵妄的管理涉及神经、精神、麻醉、重症、药理等多系统、多专业理论,因此多学科合作展现出了越来越广阔的发展前景。

利益冲突 所有作者均声明不存在利益冲突

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