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Review Article

Stress, Trauma, Sepsis, Inflammation, Management in Asthma

Abstract

This review paper covered stress, management related to asthma, trauma, sepsis, inflammation along with anxiety, and depression that occurs both in women with asthma, traumatic children and adult patients. These areas, induce immune function changes, which can lead to both trauma and pro-inflammatory activation known as systemic inflammation response syndrome (SIRS). Related to sepsis. Stress management in trauma is based upon the notion that stress causes an immune imbalance in susceptible individuals. Various topics also covered were the neuroimmune system, oxidative stress, inflammation, innate immunity, the role of NF-kappa B related to inflammation, cytokines, procalcitonin related to sepsis.

adults in the US and caused by many factors. Genetic variation, innate immune genes, those involved in tissue remodeling and inflammatory mediators might contribute to its pathogenesis [3]. The relevant experimental data to verify the correctness of the theory is that severe asthma is characterized by major impairment of quality of life, poor symptom control and frequent exacerbations [4], Inflammatory, clinical and causative factors identify different phenotypes and endotypes of asthma. In the last few years, new treatment options have allowed for targeted treatments according to the different phenotypes of the disease. To accurately select a specific treatment for each asthmatic variant, the identification of appropriate biomarkers is required [4]. Eosinophilic asthma is a distinct phenotype characterized by thickening of the basement membrane and corticosteroid responsiveness. This review by Menzella reported the latest evidence on an anti-IL-5 monoclonal antibody, mepolizumab, a new and promising biological agent recently approved by the FDA specifically for the treatment of severe eosinophilic refractory asthma [4].

This recent review article discussed chronic rhinosinusitis, epidemiology, pathogenesis, innate adaptive immunology, nuclear factor-kappa B related to inflammation, sepsis, complement, reactive oxygen species, asthma, sinusitis, elderly pathogenesis, oxidative stress, depression, seasonal variation, and other topics related to trauma and stress [4].

A literature search was conducted from several articles, prospective studies, recent reviews and earlier reports [4]. A synergistic relationship develops between activation of the innate immune system and the loss of organ barrier functions. Asthma and sepsis, a common condition encountered in

Introduction

Stress

Stress due to psychological issues has long been recognized as a contributing factor to asthma symptom expression and disease progression. Neural mechanisms that underlie this relationship have addressed the pathophysiology and management of asthma. These authors compared asthmatic individuals with high and low levels of chronic life stress in their neural and peripheral physiological responses to the Trier Social Stress Test and a matched control task [1]. They also used fluoro-deoxyglucose positron emission tomography (FDG-PET) to measure neural activity during performance of the two tasks along with both circulating and airway-specific markers of asthma-related inflammation to assess the impact of acute stress in these two groups [1].

Psychological stress in women

The occurrence of depression with asthma is very common, especially in women, and can influence behavioral factors, such as treatment compliance, self-assessment, and management of environmental triggers that can collectively result in stress, poor asthma management and control [2].

Asthma management and prevention

Asthma is very heterogeneous; new theories and treatments are emerging. It is a growing epidemic among children and

hospital environments remains an important cause of death at intensive care units. . This earlier article reviewed current concepts of airway inflammation with a special emphasis on the epithelium, and airway remodeling.⁵ Future therapeutic strategies may involve these targets and a synergistic approach in preventing remodeling in selected asthmatic patients [5].

The management of pediatric asthma exacerbations is based on trials in children of all ages. Recent studies from 2009 raised the possibility that preschoolers (younger than 6 years) with viral-induced wheezing and children exposed to tobacco smoke might be at an increased risk of treatment failure [6].

With the increase in the global prevalence of obesity, there is a parallel rise in the proportion of obese patients admitted to the ICU's, referred for major surgery or requiring long-term non-invasive ventilation (NIV) at home for chronic respiratory failure. These authors addressed other aspects of care of obese patients, including antibiotic dosing and catheter-related infections [7]. Obstructive sleep apnea is associated with rhinitis and asthma and is highly prevalent in the general population worldwide, especially in its mild form [8]. Clinical manifestations correlate poorly with disease severity measured by the apnea-hypopnoea index (AHI), which complicates diagnosis. Full polysomnography might be more appropriate to assess suspected mild cases because limited ambulatory diagnostic systems are least accurate in mild disease. Treatment options in mild obstructive sleep apnea includes continuous positive airway pressure (CPAP) and oral appliance therapy, in addition to positional therapy and weight reduction.

Although a small number of asthmatics have severe disease, and it accounts for the majority of morbidity related to the illness. Severe asthma comprises a heterogeneous group of phenotypes. Targeted treatments for these phenotypes represent a major advancement in the management of severe asthma [9]. Omalizumab, improves asthma control in patients with a predominant allergic phenotype. Monoclonal antibodies targeted to interleukin 4 α and interleukin 5 have shown substantial benefit in patients with the eosinophilic asthma phenotype; so too have monoclonal antibodies targeted to interleukin 13 in patients with a type 2 allergic phenotype [9]. Bronchial thermoplasty, a new technique to decrease airway smooth muscle mass, improves symptoms and reduces exacerbations in patients with severe uncontrolled asthma and also in chronic airflow obstruction phenotype.

Eosinophilic airway inflammation is associated with increased corticosteroid responsiveness in asthma, but direct airway sampling methods are invasive or laborious. Minimally invasive markers for airway eosinophilia could present an alternative method, but estimates of their accuracy vary [10].

Korevaar conducted a systematic review and assessed the diagnostic accuracy of markers against a reference standard of induced sputum, bronchoalveolar lavage, or endobronchial biopsy in patients with asthma or suspected asthma. Reslizumab is a humanized anti-interleukin 5 monoclonal antibody that disrupts eosinophil maturation and promotes programmed cell death. Castro assessed the efficacy and

safety of reslizumab in patients with inadequately controlled, moderate-to-severe asthma [11]. Common adverse events on reslizumab were similar to placebo. The most common adverse events were worsening asthma symptoms 52% for placebo and 40% for reslizumab in one study [11].

Early life influences are crucial for the development of distinct childhood asthma phenotypes. Besides genetics, epigenetics and environmental factors have an effect on innate and adaptive immune regulatory networks. Crucial determining factors for complex immune regulation and barrier function include family history of atopy, respiratory infections, microbiome, and nutrition [12].

Neuroendocrine Immunology

Frieri reviewed concepts of neuroendocrine immunology, dysregulation, stress, and treatment of allergic and autoimmune diseases. Neuroendocrine hormones triggered during stress may lead to immune dysregulation resulting in atopic, autoimmune diseases or decreased host defense. The stress response and induction of a dysregulation of cytokine balance can trigger the hypothalamic-pituitary-adrenal axis and sympathetic nervous system that contains chiefly adrenergic fibers and tends to depress secretion, decrease the tone and contractility of smooth muscle, and increase heart rate [13].

These authors reviewed substance P at the neuro-immune crosstalk in the modulation of inflammation, asthma and antimicrobial host defense [14]. It modulates a variety of inflammatory processes, including asthma, trauma, systemic inflammatory response syndrome or sepsis [14].

Neuroendocrine hormones triggered during stress may lead to immune dysregulation or altered or amplified cytokine production, resulting in atopic, autoimmune diseases or decreased host defense [15]. The stress response and induction of a dysregulation of cytokine balance can trigger the hypothalamic-pituitary-adrenal axis and sympathetic nervous system [15]. The sympathetic nervous system is the part of the autonomic nervous system that contains chiefly adrenergic fibers and tends to depress secretion, decrease the tone and contractility of smooth muscle, and increase heart rate. The sympathetic nervous system and the parasympathetic nervous system constitute the autonomic nervous system. The multiple roles of Th2 cells in maintaining allergic inflammation and altering the balance between Th1 and Th2 responses are important mechanisms for allergic inflammation, and can also relate to stress [15]. Mast cells are important in allergic diseases and asthma, but they also have a role in trauma and neuroinflammation and contribute to end-organ damage after trauma related to complement activation [15].

Oxidative stress

Oxidative stress occurs in asthma as a result of inflammation but also from environmental exposure to air pollution which can occur in children [15]. The specific localization of antioxidants in the lung suggests the important role of oxidative stress, and therapeutic interventions that decrease exposure to the environment [16].

Pediatric stress

A recent paper by Ramirez reviewed evidence-based parent programs to support children hospitalized after a traumatic injury. Using qualitative methods in evaluation and intervention and completed a formative research study in 2012 to develop a new program of psychological first aid and held focus groups [17].

A recent pilot study by Biffl assessed the complexity of need and difficulty with obtaining services at the time of transition from inpatient to outpatient care for pediatric rehabilitation [18]. Current developments on the implementation of trauma informed care in a variety of service systems call for the surveillance of trauma, resiliency and health impact. This article by Oral reviewed childhood adversity and traumatic toxic stress and presented epidemiologic data on the prevalence of adverse childhood experiences and their physical and mental health impacts, and discussed intervention modalities for prevention [19].

Disasters have the potential to cause short- and long-term effects on the psychological functioning, emotional adjustment, health, and developmental trajectory of children [19]. Schonfeld provided practical suggestions on how to identify common adjustment difficulties in children in the aftermath of a disaster and to promote effective coping strategies as well as any associated bereavement and secondary stressors [20]. This information can serve as a guide to pediatricians as they offer anticipatory guidance to families or consultation to schools, child care centers for mental health.

Posttraumatic stress disorder

Arcaya examined associations between PTSD symptoms and self-reported post disaster asthma attacks [21]. A 1-point increase in the IES-R avoidance score, which corresponded to one standard deviation change in this sample, was associated with double the odds of reporting an asthma attack or episode since a hurricane.

Trauma

These authors addressed the hypothesis that intergenerational transmission may begin during intrauterine life via the effect of maternal childhood trauma exposure on placental-fetal stress physiology, specifically placental corticotropin-releasing hormone pCRH [22]. Maternal childhood trauma (CT+) was significantly associated with pCRH production.

Renal trauma

Blunt childhood renal trauma with pre-existing renal abnormalities was reviewed [23]. The injuries may appear to be disproportionate in relation to the severity of the trauma history, and recognition of both the underlying disease process as well as the manifestations of acute trauma is important [23].

A recent study compared the test characteristics of clinician suspicion with a derived clinical prediction rule to identify children at risk of intra-abdominal injuries [24]. The higher

specificity of clinician suspicion, however, did not translate into clinical practice, as clinicians frequently obtained abdominal CT scans in patients they considered very low risk. If validated, this prediction rule can assist in clinical decision-making around abdominal CT use in children with blunt torso trauma [24].

A toddler with a closed head injury six days prior to admission, recently diagnosed with post-concussive syndrome to the emergency department with complaint of uncontrollable shaking of the head and extremities. The authors presented this case, accompanied by a video of the patient, to help the emergency physician recognize this rare and often misdiagnosed syndrome [25]. A recent study developed by Connelly for simple clinical tool to predict the risk of developing VTE in pediatric trauma patients based on a model created using a large national database and was internally validated [26]. The clinical tool required external validation and provided an initial step toward the development of the specific VTE protocols for pediatric trauma patients.

Impact of trauma on neutrophil function

Hazeldine discussed the emerging role of the neutrophil, and the first line of defense against microbial challenge, in the initiation and propagation of the inflammatory response to trauma [27].

This means with trauma-induced changes in neutrophil biology are linked to the development of such post-traumatic complications as multiple organ failure and acute respiratory distress syndrome. This is an area of research within the field of trauma immunology that is gaining [27]. Considerable interest: the manipulation of neutrophil function as a means by which to potentially improve patient outcomes.

Polymorphonuclear phagocytes are the main effector-cells of the innate immune system that are involved in organ failure, controlled by cytokines,, complement and specific tissue signals [28].

Multiple organ failure

Tsukamoto described the pathophysiological approach for MOF after trauma studied so far and also introduced the prospects of this issue for the future [29].

Following major trauma, IL-6 release correlates with injury severity, complications, and mortality, Interleukin-10 (IL-10) can markedly inhibit lymphocyte and phagocytic functions, essential for an adequate immune response [29]. In this early study by Neidhardt, patients who died from injury or developed posttraumatic complications and had elevated IL-10 levels in comparison with injured patients with an uneventful posttraumatic course [30]. Trauma causes an enhanced release of IL-10 and increase IL-10 levels are significantly related to posttraumatic complications. A significant increase of both IL-6 and IL-10 concentrations was found with a significant correlation between the Injury Severity Score and the levels of both IL-6 and IL-10 at all sampling points [31]. Serum concentrations of IL-6 and IL-10 were significantly higher in patients not surviving 30 days.

IL-6, obesity and trauma

There is a relationship between obesity and trauma. Among children admitted after trauma, increased BMI percentile is associated with increased risk of death and potentially preventable complications. These findings suggest that obese children may require different management than nonobese counterparts to prevent complications [32].

Severe asthma is a complex heterogeneous disease associated with older age and obesity [32]. Peters considered the possibility that systemic inflammation, which arises in subgroups of obese and older patients, increases the severity of asthma [33].

Cellular stress is increased in adipose tissue of obese individuals. However, the relation between cellular stress and weight regain is unclear. Previously, Roumans observed increased adipose tissue cellular stress of participants regaining weight compared to participants maintaining weight loss [34]. These present findings indicate that the risk for weight regain is related to expression changes of distinct sets of stress-related genes during the first four weeks after returning to energy balance, and during dietary intervention. Further research is required to investigate the mechanistic significance of these findings and find targets for preventing weight regain.

Trauma is a leading cause of death in both military and civilian populations worldwide [34]. Pati provided a state of the science review regarding cellular therapies in trauma and critical care, and to provide a foundation from which the potential of this emerging field can be harnessed to mitigate outcomes in critically ill trauma patients [35]. A study by Tulloch was reported [36]. All adult patients who triggered a Code Sepsis in the emergency department (ED) were included. Hospital mortality and hospital loss of stay of sepsis are similar to those reported in other observational studies. This study confirmed a decline in the mortality of sepsis predicted by earlier longitudinal studies [36].

Arslan stated a large proportion of splenic injuries recover with conservative therapy and some of the advantages of conservative therapy includes short hospitalization time, less need for blood transfusion, and less morbidity and mortality [37].

Sepsis

SIRS with proven infection is referred to as sepsis, SIRS vital signs are common among medical pediatric patients presenting to an ED, and critical illness is rare [38]. The majority of patients with SIRS vital signs were discharged without IV therapy and without readmission. However, SIRS vital sign criteria did not identify the majority of patients with mortality or need for critical care.

Prediction models for neonatal health care-associated sepsis. Was studied [38]. The paper stated prediction models should be considered as guidance rather than an absolute indicator because they all have limited diagnostic accuracy [39].

Optimal amikacin dosing regimens for the empirical treatment of Gram-negative bacterial sepsis in pediatric patients with burn injuries was studied [40]. Amikacin pharmacokinetics are altered in patients with burn injuries, including a significant increase in clearance. In simulations, increased doses led to improved PD target attainment rates.

Children ages 2-17 years presenting to the PICU or ED with sepsis or for procedural sedation to the ED were enrolled by Mickiewicz [41]. Combining metabolomic and protein mediator profiling improved the model differentiating PICU sepsis from ED sepsis with accuracy of 0.87. Separation of PICU sepsis or ED sepsis from ED controls was even more accurate.

Procalcitonin

Septic children aged between 28 days and 14 years were divided into sepsis (SG; n = 46) and septic shock (SSG; n = 41) groups. CRP and procalcitonin (PCT) were measured at admission. At T₀, there was a higher frequency of SSG with PCT >10 compared to SG [SSG: 30 > SG: 14 (30.4%); P significantly higher for SSG patients with higher PCT than SG patients. . PCT was better than CRP for diagnosing sepsis and septic shock [41].

Zhou investigated the diagnostic value of the IL-8 in neonatal sepsis and an important cause of morbidity and mortality [42]. Eight studies in 548 neonates were evaluated. IL-8 had a moderate accuracy for the diagnosis of neonatal sepsis and IL-8 is a helpful biomarker for early diagnosis, but one should combine the results with clinical symptoms, laboratory and microbial results [42].

Sepsis is a major cause of morbidity and mortality. Without specific antisepsis therapies, management relies on infection control and organ support [43]. Reidel stated it is necessary to not only recognize the importance of critical clinical awareness and thorough physical patient examination, but to understand traditional microbiological methods to facilitate an early diagnosis and goal-directed therapy in patients suspected of sepsis [44].

These authors' recruited consecutively adult patients with SIRS admitted to an intensive care unit and divided them into sepsis and noninfectious SIRS based on clinical assessment with or without positive cultures [45]. Future studies should include clinical indices, for example, SOFA score, for prognostic evaluation of biomarkers [45].

In surgical intensive care unit (SICU) patients, it is difficult to distinguish bacterial sepsis from other causes of SIRS and biomarkers have proven useful to identify the presence of bacterial infection. In this paper, the combination of alpha 2 macroglobulin and procalcitonin discriminated bacterial sepsis from other SIRS among SICU patients with suspected sepsis [46].

Shiferaw showed that procalcitonin is a more accurate diagnostic parameter for sepsis and a better predictor of mortality [47]. Procalcitonin is a more reliable marker than other biomarkers including C-reactive protein, Interleukins and lactate levels.

The patient's immune surveillance could fail to eliminate the pathogen, allowing it to spread and there is a pro-inflammatory mediator release with, inappropriate activation [48]. Serum procalcitonin levels are elevated in patients with bacterial infections [49].

Conclusion

This review paper covered stress, management related to asthma, trauma, sepsis, inflammation, anxiety, and depression that occurs both in women with asthma, traumatic children and adult patients. These areas, induce immune function changes, leading to both trauma and pro-inflammatory activation known as SIRS. Related to sepsis. Stress management in trauma is based upon the notion that stress causes an immune imbalance in susceptible individuals. Various topics also covered were the neuroimmune system, oxidative stress, inflammation, innate immunity, the role of NF- κ B related to inflammation, cytokines, procalcitonin related to sepsis.

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