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EC GASTROENTEROLOGY AND DIGESTIVE SYSTEM

Review Article

Management of Systemic Inflammatory Response Syndrome (SIRS) and Sepsis in Children. A Systematic Literature Review

Yaser Reda Mandorah[1]*, May Mohammed Alkhezzi[2], Mazi Mohammed Alanazi[3], Maali Omar Alrashed[4], Noura Mohssen Alassaf[5], Mohammad Hassan Haroobi[6], Ayman Ali Albarrak[7], Abdullah Salah Alahmadi[8], Hasnaa Ahmad Alhussan[9] and Bader Abdulwahab Alamer[9]

[1]*King Abdulaziz University, Jeddah, Saudi Arabia*

[2]*Qassim University, Qassim, Saudi Arabia*

[3]*King Saud Medical City, Riyadh, Saudi Arabia*

[4]*King Saud Bin Abdulaziz University for Health Science, Riyadh, Saudi Arabia*

[5]*Qassim University, Qassim, Saudi Arabia*

[6]*Jazan University, Jazan, Saudi Arabia*

[7]*King Faisal University, Alahsa, Saudi Arabia*

[8]*Imam Mohammed Bin Saud Islamic University, Riyadh, Saudi Arabia*

[9]*King Saud bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia*

***Corresponding Author**: Yaser Reda Mandorah, King Abdulaziz University, Jeddah, Saudi Arabia.

Received: January 13, 2020; **Published:** January 22, 2020

Abstract

This review is aiming to discuss the management of systemic of inflammatory response syndrome (SIRS) and sepsis in children, the presented review was conducted between November 2018 to September 2019 by searching in Medline, Embase, Web of Science, Science Direct, BMJ journal and Google Scholar for, researches, review articles and reports, published over the past years. Were searched up to September 2019 for published and unpublished studies and without language restrictions, if several studies had similar findings, we randomly selected one or two to avoid repetitive results. On the basis of findings and results this review found the main goal of the management after the stabilizations of the patient hemodynamic; is to eliminate of the treat the triggering cause, then the use of pro-inflammatory and anti-inflammatory cytokine, interferon gamma-1b, and Insulin, are show evidences to be effective in the management of inflammatory response syndrome (SIRS) and sepsis in children.

Keywords: *Management; Systemic of Inflammatory Response Syndrome (SIRS); Sepsis; Children*

Abbreviations

SIRS: Systemic of Inflammatory Response Syndrome; TNF-CT: Tumor Necrosis Factor, IL-1: Interleukin-1.

Introduction

Sepsis is one of the most dangerous inflammatory body response to infection, it also been called as "blood poisoning", in which the infection can cause dysfuntion in the body organ activities [1].

Sepsis is a result of the body's response to an infection caused by an injury or disease rather than due to a specific bacteria or micro-organism responsible for the infection. Sepsis is the third leading cause of death in the United States [2]. However, sepsis can also occur in a hospital due to infections that arise after routine or elective surgery procedures. Despite advances in modern medicine, sepsis remains the leading cause of death due to infection throughout the world [2].

"Sepsis is the third leading cause of death in the United States" [2].

Through sophisticated feedback mechanisms the pro- and anti-slip cytokines are strictly controlled [3,4] primarily responsible for initiating an effective defense against external pathogens are pro-inductive cytokines. However, excessive production of these intermediaries can be harmful which leads to shock, multiple organ failure, and death [5,6]. On the other hand, inward anti-cytokines are crucial in regulating exacerbations and maintaining parallelism for the proper functioning of vital organs. An anti-extension response may lead to the level of but it may also suppress the immune function in the body [7-10].

Acknowledging that, in response to the internal toxins of bacteria, a single cell or macrophage releases a spectrum of intermediaries, including cytokines, and has stimulated great interest in the pro-blood response underlying the poisoning. Recently, in addition to this pro-inflammatory response, patients with sepsis also undergo an anti-inflammatory phase, and sometimes, a mixed response with both pro-inflammatory and anti-inflammatory components (mixed anti-response syndrome) [11]. As a result of the production of inflammatory cytokines, primary systemic hyperplasia occurs, especially tumor necrosis factor (TNF-CT) as well as interleukin-1 (IL-1), IL-6 and gamma interferon [12].

Acted synergistically with TNF-OT to trauma animal models However, treatment of patients with intoxication with antibodies against endotoxin or TNF IL-1 antagonist or platelet stimulating agent was not effective in Reducing mortality [13-19]. One possible explanation for these findings may be that highly inflammatory mediators are inducing a secondary anti-inflammatory response, which is characterized (among other results) by a decrease in the expression of the major complicated histocompatibility second major histocompatibility (< 30%) [20]. it's secondary phase, which can last for a many of days, is also associated with decreased monocytic antigen presenting function; reduced production of TNF-a, IL-1, and IL-6; energy; and alterations in lymphocyte activity. In patients with sepsis, the persistence of monocyte inactivation for more than 2 days' correlates with a mortality of 58% and for more than 5 days, with a mortality of 88% [22]. Once monocyte inactivation is established in patients with sepsis, agents designed to minimize hyper inflammation are not likely to be effective and may be harmful. However, we hypothesized that immunostimulation, through administration of an agent, such as interferon-gamma-lb, which has been shown to normalize monocyte function and phenotype in vitro, might be a useful therapeutic measure [21,22].

Recently, intensive insulin therapy has been shown to reduce serious mortality in patients with serious illnesses. insulin administered in doses to keep blood glucose less than 110 mg/dL prevented multi-organ failure and thus improved clinical outcomes and rehabilitation [23]. Insulin improves excess metabolism by influencing the production of pro-inflammatory cytokines and the expression of the hepatic transcription factor of the signal, and there is evidence for this [24].

Methods

The current review was conducted in November 2019 in accordance with the preferred reporting items for systematic reviews and meta-analyses (PRISMA) declaration standards for systematic reviews. We reviewed all the topics on management of systemic of inflammatory response syndrome (SIRS) and sepsis in children. Such as pro-inflammatory and anti-inflammatory cytokine, interferon gamma-1b, Insulin.

To find out what this goal is, Search Medline, Embase, Web of Science, Science Direct, and Google Scholar have searched for articles, articles, and reports published over the past 15 years.

This research was completed without language restrictions. Then we extracted data on study year, study design, and key outcome on diabetes. The selected studies were summarized and unreproducible studies were excluded. Selected data is shown in the table 1.

Author and year	Sample	Management	Key point	Level of evidence
P C Ng 2003 [25]	127 episodes of suspected clinical sepsis	Pro-inflammatory and anti -inflammatory cytokine	The results indicate that the counter-regulatory mechanism between the pro-inflammatory and anti-inflammatory cytokine pathways is probably operational in preterm infants of early gestation.	Level 2
Wolfgang J 1997 [26]	10 received interferon gamma-1b, 100 \ g=m\g per 0.5 Ml	Interferon gamma-1b	It also shows that interferon gamma-1b not only restored the levels of HLA-DR expression but also reestablished the ability of monocytes to secrete the cytokines interleukin-6 and tumor necrosis factor a.	Level 2
Marc G 2004 [27]	Thirteen thermally injured children received insulin	Insulin	Insulin attenuates the inflammatory response by decreasing the pro-inflammatory and increasing the anti-inflammatory cascade, thus restoring systemic homeostasis, which has been shown critical for organ function and survival in critically ill patients	Level 2

Table 1: *Results from Sequencing Studies.*

Studies has been rated as being high quality by an established evaluation process based on the Dyuna Med criteria and it's based on the level of evidence as following:

- **Level 1 (Likely Reliable) Evidence:** Representing research results addressing clinical outcomes and meeting an extensive set of quality criteria which minimize bias. example: Randomized controlled trial/meta-analysis.
- **Level 2 (Mid - Level) Evidence:** Representing results addressing clinical outcomes, and using some methods of scientific investigation but not meeting the quality criteria to achieve level 1 evidence labeling. Example: well-designed non-randomized clinical trials.
- **Level 3 (Lacking Direct) Evidence**: Representing reports that are not based on scientific analysis of clinical outcomes. Examples include case series, case reports, expert opinion and conclusions extrapolated indirectly from scientific studies.

Inclusion criteria

Inclusion criteria were systemic inflammatory response and sepsis: in children, management.

Exclusion criteria

Irrelevant articles [not related to the aim of this review and articles that did not meet the inclusion criteria in this review.

Data extraction and analysis

Information relating to each of the systematic review question elements was extracted from the studies and collated in qualitative tables. Direct analysis of the studies of management of systemic of inflammatory response syndrome(SIRS) and sepsis in children.

Results and Discussion

"Management is thus designed around a parallel search for the underlying etiology and its resolution along with time-sensitive interventions that may not be cause-specific, but get targeted towards preventing end-organ injury. The goal is to disrupt progression along the continuum of shock and multi-organ dysfunction syndrome" [28].

37 of 127 confirmed episodes of suspected clinical infection or necrotizing enterocolitis. Significant associations were observed between IL6 and TNFα or IL10 as well as IL10 and IFNγ in infected infants. Plasma concentrations of IL6, IL10 and TNFα, and IL10 / TNFα and IL6/IL10 ratios were significantly high in subgroup analysis in patients with intravascular thrombosis. IL10/TNFα rates decreased significantly 48 hours after the start, while the IL6/IL10 ratio only showed an insignificant declining trend. Furthermore, the IL6/IL10 ratio in the deceased infant was increased disproportionately in width and continued to increase despite treatment [25].

Decreasing levels of HLA-DR expression were restored on monocytes from interferon gamma-1b treatment. Of 10 patients, 8 responded to treatment within one day. On the first day of gamma-1b virus therapy, HLA-DR expression increased from mean (/m = + -/SEM) pretreatment levels of 27%/m = + -/6% to 62%/m = + -/8% (P <.01) It remained elevated during the 28-day period in 8 patients. Treatment was given to 2 patients the second time when the HLA-DR expression on monocytes was less than 30%. Recovery from mono-HLA-DR expression levels after gamma-interferon 1B administration was associated with restoration of monocytic function, which is reflected in a significant increase in interleukin-6 plasma (P <.05) and tumor necrosis factor a (P <.05)) levels in 9 patients [26].

Insulin administration decreased pro-inflammatory cytokines and proteins, while increasing constitutive-hepatic proteins (P<0.05). Burned children receiving insulin required significantly less albumin substitution to maintain normal levels compared with control (P<0.05). Insulin decreased free fatty acids and serum triglycerides when compared with controls (P<0.05). Serum IGF-I and IGFBP-3 significantly increased with insulin administration (P<0.05) [27].

The data showed the activation of anti-aging cymokines (IL2, IL6, IFNγ and TNFα) and anti-carcinogens (IL4, IL10) in response to sepsis and successful treatment in preterm and infant VLBW. The pro-enzyme and cytokine plate of enzymes was organized in response to the nature and severity of diseases, IL5, a cell essentially associated with hypersensitivity and hypersensitivity stress, remained largely unaffected. Reactions in the comparison between levels of uninfected infants on sepsis were particularly prominent in the activation of IL6 and IL10, which were 35-fold high and 22-fold respectively at 0 hours. Moreover, after treatment, cytokine levels decreased by 83% and 87% 48 hours. In addition, the interaction between pro- and anti-toxin cytokines in response to sepsis remains a controversial topic. Most of the current evidence and findings refer to the operation of the feedback mechanism or countermeasures mechanism. IL6 and TNFα are powerful pro-inside cytokines and are responsible for eliciting a strong reaction in the body, which may lead to severe hypotension if left unattended, dysfunction in multiple organs, and death [25].

There is increasing evidence of the important role of internal immune mediators, especially cytokines, in the inflammatory response against infection. 16, a complete inflammatory reaction of the body occurs when poisoning develops from a local infection and can be systematically detected on cytokines that are limited to areas of localized infection, where symptoms of septic shock cause [17]. The central mediator of pathophysiological changes associated with the early stages of sepsis is TNF-a [26].

Post-traumatic systemic inflammatory response leads to excessive metabolism and thus protein degradation and demolition. Accordingly, the structure and function of essential organs, such as muscles, skin, heart, immune system, and liver, are at risk, and contribute to failure and death of multiple organs. Catabolic, for example, by inhibiting the insulin-like growth hormone-like growth factor (I-IGF-I) - the insulin axis 12-14 after clinical failure of anti-inflammatory agents or antibodies against pro-inflammatory cytokines such as tumor necrosis (TNF), Interleukin-1 (IL-1β), or their receptors, have followed various methods to relieve excessive metabolism. Insulin in a dose that kept blood glucose levels less than 110 mg/dL, which resulted in a lower death rate and prevention of multiple organ failure in patients with serious diseases [10]. In an animal model, insulin had anti-inflammatory effects by decreasing pro-inflammatory signal transcription factors and pro-inflammatory cytokines, while increasing anti-inflammatory cytokines [11]. Insulin had anti-inflammatory effects by reducing pro-inflammatory signal transcription factors and pro-inflammatory cytokines in an animal model, while increasing anti-inflammatory cytokines [11]. Mediators or indirectly by modifying the glucose concentration. Numerous studies have suggested the extent of internal hyperparathyroidism and moderate metabolic hyperglycemia and that it increases shock aggravation [27].

Conclusion

This study demonstrated the management of inflammatory response syndrome (SIRS) and sepsis in children. Based on the findings and results, this review found pro-inflammatory, anti-inflammatory, cytokine, gamma-1b, children. And insulin, are used in the treatment of the systemic of inflammatory response syndrome (SIRS) and sepsis.

Conflict of Interest

The authors of this article hasn't receive and support for this work and it was completely self-funded.

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Volume 7 Issue 2 February 2020