MULTIPLE ORGAN DYSFUNCTION SYNDROME (MODS) IN THE MEDICAL ICU, CHALLENGES AND OPPORTUNITIES: INDIAN PERSPECTIVE

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INTRODUCTION

Multiple organ dysfunction syndrome (MODS) is characterized by organ injury and/or failure that is distant from the primary cause of illness or insult. It is an important cause of mortality in intensive care units (ICUs) globally (1,2). The recent years have witnessed changes in the epidemiology, outcome, and prognosis of MODS. In the published literature, the syndrome had been variously referred to as “multiple organ failure”, “multiple system organ failure”, and “multiple organ system failure”. The concept of MODS initially emerged in the context of sepsis and related syndrome. MODS develops due to uncontrolled infection, especially Gram-negative sepsis (3,4). Shock, infection and several other insults are postulated to set in motion an underlying cascade of reactions that would eventually lead to widespread endothelial damage, oedema resulting from increased vascular permeability, and impaired availability of oxygen (5).

DEFINITION

The term MODS was introduced in the 1991 ACCP-SCCM Consensus Conference (6) replacing the term "multiple organ failure" because MODS stresses the continuum of organ dysfunction rather than just its result. MODS was defined as “the presence of altered organ function in an acutely ill patient such that homeostasis cannot be maintained without intervention” (6).

Presently, MODS is defined as a clinical syndrome characterized by the development of progressive and potentially reversible physiologic dysfunction in 2 or more organs or organ systems that is induced by a variety of acute insults, including (but not limited to) sepsis. MODS has conventionally been defined in terms of involvement of six organ systems, namely, pulmonary, renal, hepatic, central neurologic, cardiovascular, and haematologic systems. As per the current understanding, MODS also includes derangements of the endocrine, metabolic, immunologic and gastrointestinal systems, which were not originally included in the description of the syndrome. Consensus definitions of “organ system involvement” regarding the above described six systems have been developed. However, consensus definitions to describe the involvement of the endocrine, metabolic, immunologic and gastrointestinal systems have not emerged and these have been variously defined.
KEY PATHOGENETIC MECHANISMS
The key concepts regarding the pathogenetic mechanisms underlying the evolution of MODS (3,4,7,8) include: Stage 1: Local response; Stage 2: Initial systemic response; Stage 3: Massive systemic inflammation; Stage 4: Excessive immunosuppression; and Stage 5: Immunologic dissonance. Various hypotheses such as oxygen delivery hypothesis, gut-origin hypothesis, two-hit hypothesis, mitochondrial dysfunction hypothesis have been postulated to explain the genesis of MODS. However, they have been disappointing when translated into clinical therapies for MODS (3,4,7,8).

AETIOLOGICAL CAUSES
Primary MODS occurs due to the direct result of a well-defined insult in which organ dysfunction occurs early and can be directly attributable to the insult itself. Secondary MODS develops as a consequence of a host response. MODS usually develops in patients with sepsis and related syndromes. Further, MODS due to other non-infectious causes, such as, severe trauma, burns, pancreatitis, and ischaemic reperfusion injury, among others is being recognized (3,4,7,8).

CLINICAL PRESENTATION
Clinical presentation of MODS is characterized by the underlying cause of MODS as well as the number and severity of organ system involvement. Fever, the cardinal manifestation of infection may not always be evident. When infection is the underlying cause, an obvious focus of infection is usually (but not always) discernible. Organ dysfunction in MODS usually becomes evident within 24 to 48 hours of the physiologic insult. The classic sequence of organ dysfunction begins with evidence of pulmonary dysfunction. This is followed by dysfunction of hepatic/gastrointestinal, renal and other systems usually in that order.

MANAGEMENT
Patients with MODs are very sick and often require admission into an ICU for diagnostic workup, invasive monitoring and institution of treatment. Laboratory evaluation including imaging should include assessment of involvement of relevant organs systems. In all patients
with MODS a diligent search must be undertaken to look for a focus of infection as focussed diagnostic testing can help in identifying the organism and its antibiotic susceptibility pattern and guide specific therapy.

*Organ system involvement*

Acute respiratory distress syndrome (ARDS) usually the first and earliest manifestation of MODS is defined in terms of the new Berlin Criteria (9). Hepatic involvement is characterized by initial elevation of transaminases, followed by hyperbilirubinaemia, and then synthetic dysfunction with increased international normalized ration (INR) that may progress eventually to severe hepatic failure (shock liver); or mild hyperbilirubinaemia, with or without cholestasis usually with preserved synthetic function. Acute kidney injury is defined in terms of the RIFLE classification (10,11). Cardiovascular abnormalities reflect the vascular features of systemic inflammatory and hypermetabolic state. Glasgow coma scale is used to assess neurological dysfunction. Common endocrine manifestations of MODS include derangements of the hypothalamic-pituitary axis and glucose and protein metabolism.

*Scoring systems*

Several scoring systems have been developed for clinical measurement and monitoring of MODS. These include *general physiological critical care scores* such Acute Physiological and Chronic Health Evaluation; (APACHE), Simplified Acquired Physiological Score (SAPS); Mortality Probability Model (MPM) or specific organ score to describe dysfunction/failure (e.g., *Marshall Multiple Organ Dysfunction Score*), Sepsis related Organ Failure Assessment (SOFA), Logistic Organ Dysfunction System (LODS), among others (4,12). The *specific organ dysfunction scores* classify organs as failed or dysfunctional using an ordinal scale (i.e., graded score). The aggregate score quantitates severity in any one organ and the overall severity of organ dysfunction. This aggregate score can then be interpreted as a likelihood of predicted mortality based upon the observed mortality in those study patients used to construct the original scoring system scoring system (4).

MODS as an outcome is considered to be a less-biased measurement of the original injury and subsequent care provided (3,4). These scoring systems broadly place the mortality between 60%
to 98% depending on age with dysfunction in three or more organs for at least a period of one week (4).

Treatment of MODS is complex and difficult. Sparse published evidence-based data on the efficacy of treatment strategies for MODS are available. Early goal-directed therapy, nutrition, and control of infection are considered to be the key determinants of outcome from MODS (1,13).

**MODS: CHALLENGES AND OPPORTUNITIES**

There is a need for generating reliable epidemiological data on the burden of MODS and various aetiological causes in the Indian setting. Further, the various scoring systems used in intensive care have been developed and validated in ICUs in the USA and Europe. Research into extrapolation and validation of these scoring systems in the Indian ICU setting also needs to be studied. While the understanding of the molecular mechanisms underlying the development of MODS is rapidly increasing, translation of this into drugs directed at these molecular targets that can significantly improve the outcome of patients with MODS are yet to emerge highlighting the knowledge gap between the bench and the bedside. Future research is required to answer these questions (13).
REFERENCES


