

The Curing Coma Campaign[®]: Concerns in the Indian Subcontinent

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ABSTRACT

Background: The Curing Coma Campaign (CCC) was launched by the Neurocritical Care Society (NCS) in 2019, with the purpose to bring together a diverse group of coma scientists, neurointensivists, and neurorehabilitationists.

Methods: The aim of this campaign is to move beyond the limitations imposed by current definitions of coma and identify mechanisms to improve prognostication, identify test therapies, and impact outcomes. At the moment, whole approach of the CCC appears ambitiously challenging.

Results: This could be true only for the Western world, such as the North America, Europe, and few developed countries. However, the whole concept of CCC may face potential challenges in the lower-middle income countries. India has several stumbling blocks that need to and can be addressed in the future, for a meaningful outcome, as envisaged in the CCC.

Conclusion: India has several potential challenges, which we aim to discuss in this article.

Keywords: Campaign, Coma, Curing, Neurocritical care.

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HIGHLIGHTS

Curing Coma Campaign aims for a better understanding of the entity called coma, in a global effort, and to bring the best of all health-related aspects of managing a comatose patient. India needs to address several issues for a meaningful outcomes envisaged in the CCC.

INTRODUCTION

The CCC was launched by the NCS in 2019 with a purpose to bring together diverse group of coma scientists, neurointensivists, neurorehabilitationists, and implementation experts into a Scientific Advisory Council (SAC) who met during the NCS Annual Meeting in Vancouver in October 2019.¹ The aim of this campaign is to move beyond the limitations imposed by current definitions of coma, such as sub-acute and chronic or disorder specific, and identify mechanisms to improve prognostication, identify test therapies, and impact outcomes.

The Council addressed the following three fundamental overarching pillars:

1. Endotyping: To develop a better understanding of the different types of comas
2. Biomarkers: To evaluate current tools and their shortcomings in understanding coma and its prognosis
3. Proof-of-concept clinical trials: To identify early interventional studies for evaluating new treatment protocols and inform clinical trial design

ENDOTYPING

We know different disease entities produce a similar clinical phenotype. This was considered a limitation in the current practice

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of coma assessment and treatment. Therefore, it was decided that endotyping would more accurately reflect the gap and challenges faced during coma management.

The Council opined that early recognition of different endotypes of coma may identify patients with recovery trajectories early in the intensive care unit (ICU), which may improve the accuracy of early neuro-prognostication.

The endotype-specific diagnosis and optimized endotype-specific treatment aim to improve the management of comatose patients.

Indian Viewpoint

In India, it's still a distant dream and various fronts need to be worked upon. The genome-wide association studies help identify genes associated with a particular disease. But despite a huge number of comatose patients available for study, our country lacks the facilities to carry out such testing except in good tertiary centers. These types of research require a large amount of funds as well as trained faculty. We need to have a centralized database of comatose patients, which allows us to study endotypes and associated phenotypes by phenowide association studies. This will help not only in the stratification of comatose patients but also in providing personalized care to individuals. In India, we essentially need a collaborative effort between researchers, clinicians, and funding agencies to achieve the desired results. The artificial intelligence (AI) has a major role to play by helping in dealing with "big data." It helps in analyzing information and accordingly stratifying the comatose patients to distinct endotypes, on basis of which we can prognosticate and even manage patients.

BIOMARKERS

The need to follow patients during the course of their disease is critically important. Currently used biomarkers for the assessment of consciousness include those assessing the brain at rest [brain magnetic resonance imaging (MRI)—fluid-attenuated inversion recovery (FLAIR), diffusion tensor imaging (DTI), computed tomography (CT), electroencephalography (EEG), positron emission tomography (PET), Xenon CT perfusion, magnetic resonance (MR) spectroscopy, brain microdialysis, S100 beta, neuron-specific enolase, glial fibrillary acid protein, and IgG electrophoresis], passive perturbation tasks [somatosensory evoked potentials (SSEP), brainstem auditory evoked potentials, motor evoked potentials, and transcranial magnetic stimulations], and active perturbation tasks (behavioral scores: FOUR score, Glasgow coma scale (GCS) and functional EEG or MRI).

Indian Viewpoint

The EEG is widely available in the country and can be applied at the bedside following a cardiac arrest. The EEG patterns that are consistently associated with a poor outcome are not clearly identified and have to be interpreted in conjunction with other markers. Telemonitoring may be an area where the early application of EEG analysis coupled with an expert advice contributes to better prognostication after a cardiac arrest. Somatosensory evoked potentials may be more reliable and consistent in predicting poor outcomes following a cardiac arrest. The concern regarding SSEP is its sensitivity (<50%); therefore, it has to be combined with other modalities. The emerging area of interest is in the field of biochemical biomarkers that have their origin from multiple sites of the neuroaxis. Neuron Specific Enolase and S-100B are biomarkers that are unaffected by sedation. The correct cut-off of these biomarkers to identify patients with a poor prognosis is yet to be identified. The availability of other biomarkers like Tau protein and

microRNAs in India is limited. An evaluation of the biomarkers in cerebrospinal fluid (CSF) and their temporal patterns following a cardiac arrest seem to be a feasible and potential area of work. At this time point, a combined approach using outcome scores, SSEP, and imaging appears to be the best option for assessing patients resuscitated from a cardiac arrest.^{2,3}

PROOF-OF-CONCEPT CLINICAL TRIALS

Several proof-of-concept trials have been conducted in the past using pharmacological and electrophysiological interventions. All these trials have been performed almost entirely in the subacute to the chronic stage of recovery. Irrespective of the etiology, CCC aims to advance the design and implementation of methodical proof-of-concept clinical trials in the ICU.

Indian Viewpoint

In addition to the various limitations of the available clinical trials on the management of this unique disorder, the conduction of trials in the Indian subcontinent has specific confounders in the form of variabilities in culture, psychosociology, religion, resource allocation, and many such issues. To address these loopholes in the management, the Indian Society of Critical Care Medicine (ISCCM) Coma Network Campaign convened a Coma Science Work Group to perform a gap analysis that would be more pertinent in the Indian subcontinent. To address the wide research gap, designing proof-of-concept trials that focus on identifying biomarkers and neurophysiological techniques will help to diagnose, prognose, treat, and cure coma in patients. The proof-of-trials should include both endotypes and phenotypes as a part of predictive enrichment strategies to maximize clinical trial success for specific populations. Biomarkers in clinical trials have great potential as an additional weapon in the existing armamentarium for the diagnosis and management of disorders of consciousness (DOC). Pragmatic clinical trials are the need of the hour because it promotes the later translation of trial findings into clinical practice. A multimodal approach will best track the outcomes of patients receiving treatments. To better evaluate the effects of treatment, the primary measure in these proof-of-clinical trials should include a standardized evaluation of behavioral assessment, preferably the Coma Recovery Scale, Revised, and patient-centered outcomes, such as quality of life measures. Neuroimaging and electrophysiological scans can then be used as secondary treatment assessments.

The epidemiological data of Indian patients with coma and DOC have not been investigated properly. According to an Indian preliminary survey developed through collaboration between Italian and Indian members of the World Federation of Neurorehabilitation (WFNR) from December 2017 to February 2018, the prevalence rates of traumatic and nontraumatic etiologies are equally distributed. The most commonly used clinical assessment scale in these patients is Glasgow Outcome Scale (GOS) followed by Coma Recovery Scale Revised (CRS-r), usage of which is reported very low.⁴

In India, care support for comatose patients is not on the priority list of healthcare system. Though various Coma Care Centers are available that take care of such patients, most of them are run by non-government organizations, which are few in number with limited resources. There are private hospitals which provide facility of creating home ICU to take care of comatose or unconscious patients where certain equipment are to be set up.

Parallel to the care of coma survivor patients, the controversial issue of euthanasia or mercy killing cannot be ignored. Active euthanasia is the administration of a lethal agent by another person to a patient for the purpose of relieving intolerable and incurable sufferings. In India, active euthanasia is an offense. However, a major development took place in 2011, when the Supreme Court of India set a tough guideline under which passive euthanasia can be legalized through a high-court monitored mechanism. The court further stated that parents, spouses, or close relatives of the patient can make such a plea to the high court.

In India, the concept of executing an advance directive (AD) is new and yet to be widely known. Advance directive is an instrument to enable an autonomous decision in the anticipation of the loss of capacity for making healthcare decisions directly at some point in the disease trajectory.⁵ Despite several ethical position statements and guidelines published since 2005, withholding or withdrawal of life support (WHLS or WDLS) and do not attempt resuscitation (DNAR) decisions are being practiced in very few centers.^{5,6}

Clinicians in Indian ICUs appear to be in favor of end-of-life-care (EOLC) practices when aggressive care is potentially inappropriate. Thus, clinicians face uncertainty while making EOLC decisions, perhaps due to sociocultural considerations (amplified by inappropriate and misleading use of the term “euthanasia” and “passive euthanasia”) but largely due to fear of legal implications of WHLS or WDLS.

The Indian Intensive Care Case Mix and Practice Patterns Study (INDICAPS) was a point prevalence study that included data of 4,038 adult patients from 120 Indian ICUs between 2010 and 2011.^{7,8} There were 546 deaths and 183 terminal discharges (TDs) including “left against medical advice (LAMA).” Of the 545 deaths, 35 patients (4.8%) had do-not resuscitate (DNR) orders, 45 (6.2%) had WHLS, and 13 (1.8%) had WDLS. INDICAPS-II was performed in 2018–2019 and included 4669 adult patients in 132 Indian ICUs. There were 737 deaths in ICU (15.8%) and 355 TDs (7.6%).⁴ Only 3.6%, 6.7%, and 1.4% of patients had DNR WHLS and WDLS, respectively.⁹

The ISCCM and the Indian Association of Palliative Care have produced a joint statement on EOLC.⁸ The All India Institute of Medical Sciences has introduced a palliative and EOLC pathway for their patients. The Indian Council of Medical Research has clarified the terminology around EOLC and also recognized DNR as a valid medical decision to be taken by the clinician when cardiopulmonary resuscitation is deemed inappropriate. Recent judgments by the Supreme Court recognize the legality of WHLS and WDLS as well as the living will but lay down a procedure that is too restrictive and virtually unimplementable.^{10,11} This has perhaps, unfortunately, led to the widespread practice of LAMA, which is seen to absolve the doctor and hospital of all responsibility for the consequences of WHLS and WDLS.

Long-term acute care (LTAC) is one of the first priorities for a patient with DOC, shifting them away from an acute care hospital to a facility focused on rehabilitation. Long-term acute care provides patients with DOC and the right environment to prevent secondary conditions like infections, muscle wasting, and ventilator dependence. However, there is a dearth of LTAC in India. Patients are dependent on acute care hospitals for ventilator weaning, and in the absence of specialized LTAC succumb to infection.

Pastoral care, a model of spiritual, emotional, and social care inclusive of nonreligious forms of support and religious support, is yet another important tool needed for recovery, which is absent and not provided for patients and their families with DOC.

The CCC was mooted with the idea of having a better understanding of the entity called a coma, in a global effort or collaboration, and to bring the best of all health-related aspects of managing a comatose patient. However, a country like India has several stumbling blocks that need to and can be addressed in the future, for a meaningful outcome, as envisaged in the CCC. The knowledge gap among the medical professionals and the paramedical encountering these patients, especially with causes like stroke or head injury, needs to be plugged in a scientific and rational manner. The logistics required in transporting such patients from home to hospital, such as ambulances with a stroke or trauma unit, dedicated lanes for ambulances, etc., need to be impressed by the government machinery. Further, public awareness regarding coma and its sequelae needs to be expanded.

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