Optimal micronutrient status for all

Determination of functional micronutrient status for precision medicine in critically ill patients

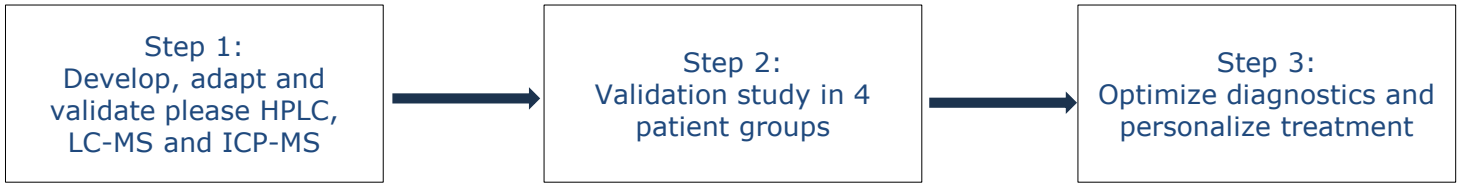
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Description of the initiative

Micronutrients (MN) are crucial for the recovery of critically ill patients, as they are essential for cellular metabolism, endocrine and immune functions, and reducing inflammation and oxidative stress. European guidelines strongly recommend compensating for MN deficiencies in critically ill patients, as these deficiencies are associated with worse outcomes. However, there is currently no accurate method to identify critically ill patients with significant MN deficiencies who may benefit from MN supplementation. In critically ill patients, inflammation and oxidative stress are typically severe and lead to organ damage, necessitating intense treatment. Inflammation also causes the redistribution of MN, temporarily shifting them out of the circulating compartment and decreasing plasma MN concentrations, while intracellular MN concentrations can be either decreased or normal. In practice, only plasma MN concentrations are available, but metabolic and biochemical reactions occur mostly within cells. Therefore, plasma concentrations are not informative of intracellular function in critically ill patients. Intracellular function could be better reflected by MN concentrations in body cells, such as erythrocytes and leukocytes, which are more accessible and less affected by inflammation. A recent study found that vitamin C concentrations in leukocytes of septic patients were similar to those in healthy volunteers, suggesting that high-dose vitamin C treatment may not be appropriate for these patients. More accurate MN measurements may help identify patients who are most likely to benefit from MN supplementation and estimate individual needs to enhance recovery.

Planned activities & deliverables

In this project, we aim to develop, adapt, and validate plasma HPLC, LC-MS, and ICP-MS assays for alternative sample matrices, such as erythrocytes and leukocytes. Vitamin B1/B6/B9/C/D/E, zinc, and selenium are selected from 23 MNs due to their potent anti-inflammatory and antioxidative roles in critically ill patients. Additionally, we will validate these new assays in a pilot study comparing MN concentrations in erythrocytes and leukocytes with plasma concentrations in four patient groups: 10 ICU patients (real or potential depletion), 10 patients undergoing major elective surgery (potential depletion), 10 patients on parenteral nutrition (medically fed), and 10 healthy adult volunteers (control group).



With this initiative we aim to improve recovery of critically ill patients and personalize micronutrient supplementation

Resources & enablers

A PhD-student will conduct the development and validation of the laboratory analyses of the MN in the new matrices and the pilot study. In addition, a laboratory technician (0.25 fte) is needed to assist with the development of these assays and the measurements of the samples of the pilot study. These personnel costs will be covered by the participating departments. The necessary equipment is available. However, substantial costs for processing of the samples and reagents for laboratory analyses will be made.
Costs consumable/reagents: processing samples: €10.000, laboratory analyses: €30.000

Results/outcomes & expected impact

Currently, plasma MN concentrations are the only method to diagnose MN deficiencies in association with history of losses in clinical practice. However, inflammation can alter plasma MN values, leading to misinterpretation and potentially harmful treatments. Administering MNs to patients without actual deficiencies is unlikely to yield benefit and may cause harm. MN concentrations in erythrocytes or leukocytes are less affected by inflammation, may more accurately reflect functional MN status in critically ill patients thereby facilitating personalized MN therapy. Supplementation based on these diagnostics could improve clinical outcome and can be applied to all patients with inflammation and to all countries with sufficient laboratory support.

V **Please tick to confirm the PEN letter of endorsement is attached. Incomplete submissions will not be considered.**