Antioxidant Treatment with Vitamin C in Cardiac Surgery Patients – A Pilot Study

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Description of the initiative

- **Background/context:** Vitamin C is an essential, water-soluble micronutrient, has many crucial functions in the human body, and is considered as the most important antioxidant, countering the influence of free radicals. Several studies demonstrated that vitamin C concentrations are lowered in severe illness and in patients recovering from surgery, in patients after cardiac surgery, and especially in patients developing multiorgan failure (MOF).
- **Rationale for the initiative:** The supplementation of antioxidants is suggested as a potent strategy to attenuate the oxidative stress during surgical procedures, thereby reducing the extent of postoperative systemic inflammatory response syndrome (SIRS) and the potential to develop MOF with tremendous significance for the patient´s postoperative outcome. Based on its redox-potential and powerful antioxidant capacity, vitamin C represents an inexpensive and safe antioxidant, with the potential to modify the inflammatory cascade and improve clinical outcome, which thus may be of special relevance for patients with significant inflammatory response and at risk to develop organ dysfunctions. As patients undergoing cardiac surgery commonly experience a SIRS, which ultimately often leads to organ dysfunctions, it remains speculative, if a high dose perioperative administration of vitamin C may reduce the development of SIRS and organ dysfunction after cardiac surgery.
- **Objectives and scope:** This pilot study aims to gather experience about the feasibility (including protocol adherence and violation), pharmacokinetics, efficacy, and efficiency of vitamin C administration in cardiac surgery patients.

Planned activities & deliverables

- **Outline the steps to be taken:** A multicenter, prospective, double blinded, randomized controlled clinical pilot trial will be conducted including n=30 high-risk adult cardiac surgery patients. Patients will be randomized (1:1 ratio) either to receive 6-hourly bolus of 50 mg/kg body weight vitamin C or placebo (before surgery, at the end of cardiopulmonary bypass, at ICU admission, and until 96 hours after surgery).
- **What are the concrete deliverables of the project?** This study aims to evaluate the feasibility of the trial protocol and the treatment efficacy (biological response measured by the oxidation-reduction-potential [ORP]). Further, we want to gather first evidence on the efficiency of vitamin C administration on blood vitamin C levels, oxidative stress, inflammation, and clinical outcome .
- **What achievements are possible in the next 12 and 24 months?** Start-up of the pilot trial, patient recruitment, data analysis, and publication of results will be performed over a period of 18 months, before transferring into a larger, international, multicenter confirmatory trial.

Resources & enablers

- **Describe personnel, financial needs:** Funding is required for overall project management (personnel) and materials (laboratory analysis).
- **Specify how the grant will be spent:** Funding will be spent for salary of the junior project manager and the biomarker analysis (ORP, vitamin C level) within the pilot study.
- **What factors will make it successful?** Measurement of safety, feasibility, compliance, contamination; measurement of biomarkers (ORP, vitamin C levels), evaluation of patient outcome; publication of results, establishment of a pilot phase with seamless adaptive design to confirmatory trial.

Results/outcomes & expected impact

- **How will the findings be implemented?** The findings will strengthen the evidence on perioperative high-dose vitamin C administration as a potent antioxidative strategy in cardiac surgery patients.
- **How will this project advance patient care/contribute to optimal nutritional care?** The patients may benefit from reduced extent of systemic inflammation, that may result in less organ dysfunctions, lower rates of complication, lower mortality/morbidity, better mid- to long-term outcome, and improved quality of life.
- **What makes the project innovative?** Neither perioperative high-dose vitamin C as an effective antioxidative strategy nor ORP as an appropriate biomarker to measure oxidative stress have been validated so far in this specific cohort of critically ill patients.
- **Will the project be likely to influence national nutrition policy?** Vitamin C currently represents the most promising candidate, which may reduce the inflammatory response and influence patients' outcomes. An effective antioxidant treatment strategy with perioperative high-dose vitamin C supplementation may reduce clinical complications after cardiac surgery leading to faster recovery periods and better outcomes. The results will be relevant for nutrition support practices worldwide and will provide evidence for international nutrition guidelines.
- **Is the project transferable to other settings/countries?** It is intended to transfer this pilot trial into an international multi-center confirmatory trial.