CRITICAL ROUNDS

MICRO LABS LIMITED

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Dear Doctor,

Greetings from Micro Labs limited. We are happy to bring "CRITICONNECT" containing latest information in the field of Critical care medicine.

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Best Regards,
Medical Team, Micro Labs Ltd

CRITICONNECT

Diuretics decrease fluid balance in patients on invasive mechanical ventilation: the randomized-controlled single blind, IRIHS study

Introduction:

Fluid overload has been associated with increased morbidity and mortality in critically ill patients. Positive fluid balance has been associated with worse outcome in critical care patients (sepsis, burns, major surgery, acute kidney failure and in critically ill children). Fluid balance is induced by systemic inflammatory response syndrome, volume expansion and cardiac and kidney failure and is present in the vast majority of patients. The efficacy and safety of systematic diuretics to decrease positive fluid balance has not been thoroughly investigated. Moreover, no guidelines are available regarding the timing and indication of diuretics from weaning of mechanical ventilation in ICUs.

Aim: To assess the efficacy and safety of a diuretic strategy to overcome positive fluid balance in patients on invasive mechanical ventilation.

Methods: Multicentre, single-blind, randomized-controlled study. Patients were randomized into a diuretic (furosemide) or a control group. Patients were eligible in case of fluid overload defined as in-ICU weight increase ≥3%, invasive mechanical ventilation ($FiO_2 \leq 60\%$ and $PEEP \leq 10$ cm H_2O on inclusion) and hemodynamic stabilization.

Primary outcome: Fluid balance, defined as weight variation from reference weight to successful extubation.

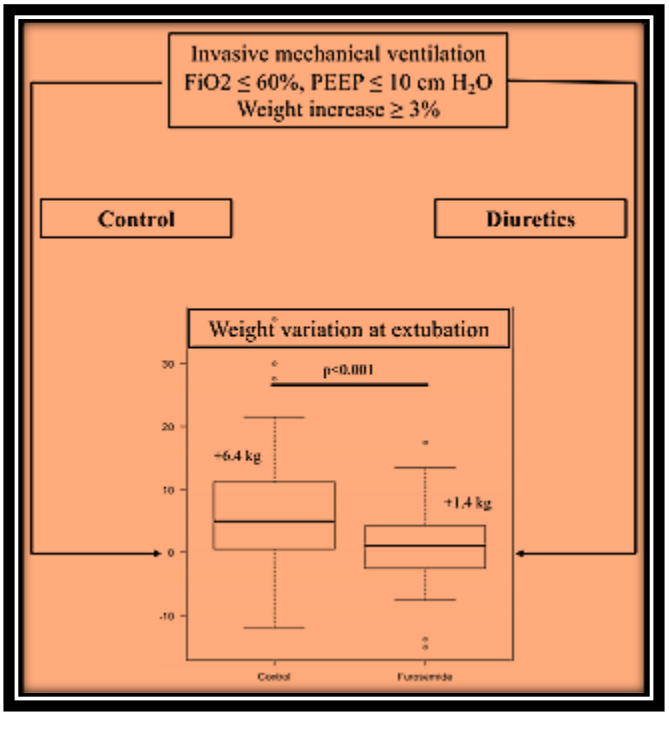
Secondary outcome: Safety of diuretic.

Results: Around 171 patients were randomized. After 5 exclusions, 166 patients were included in the analysis: 77 in the diuretic and 89 in the control group. Fluid balance was 1.4 [− 2.5 to 4.5] kg in the diuretic and 6.4 [0.5–11.2] kg in the control group ($p<0.001$).

Evolution of fluid balance between groups

	Control group $N=89$	Intervention group $N=77$	Mean difference 95% CI	p value
Primary analysis				
Multiple imputation ($N=166$)			−4.9 [−7.4;−2.5]	<0.001
Sensitivity analyzes				
Complete cases ($N=144$, 86.7%)	6.4 [5–11.2] kg	1.4 [1–4.5] kg	-5.1 CI_{95} [−7.4;−2.8]	<0.001
Worst case imputation ($N=166$)	4.5 [−1.5;10.5] kg	1.5 [−2;7.7] kg	−0.5 [−3.2;2.3]	0.7
Last observation carried forward ($N=166$)	7 [2;15.5] kg	1.5 [−2;7.7] kg	−8.4 [−16.6;−0.2]	0.047
Per protocol ($N=135$, 81.3%)	5 [0.5;11.3] kg	1 [−2.0;4.6] kg	−4.7 [−7.1;−2.3]	<0.001

Design and main result



Eleven (14%) patients died in the diuretic group and 16 (18%) patients in the control group (p=0.5). There was a worsening of Acute Kidney Injury in 67 (75.3%) patients of the control group versus 46 (59.7%) patients in the diuretic group (p=0.03). In the multiple imputation analysis, fuid balance was signifcantly decreased in the diuretic group

Conclusions: In this multicenter randomized-controlled study, diuretic therapy reduced fluid accumulation in patients receiving mechanical ventilation and was well tolerated with a favourable safety profile.

Source: Cinotti et al. Diuretics decrease fuid balance in patients on invasive mechanical ventilation: the randomized-controlled single blind, IRIHS study. Critical Care (2021); 25:98

Association of Intravenous Immunoglobulins Plus Methylprednisolone vs Immunoglobulins Alone With Course of Fever in Multisystem Inflammatory Syndrome in Children

Introduction:

Multisystem inflammatory syndrome in children (MIS-C) is the most severe paediatric disease associated with severe acute respiratory syndrome coronavirus 2 infection, is associated with a wide range of clinical features including persistent fever, digestive symptoms, rash, bilateral nonpurulent conjunctivitis, mucocutaneous inflammation signs, and frequent cardiovascular involvement. Many children with MIS-have received empirical treatment. Based on Kawasaki disease guidelines, with intravenous immunoglobulin (IVIG) alone or combined with corticosteroids. In some studies, children have required second-line treatment, such as tumor necrosis factor inhibitor or interleukin 1 inhibitor, which underscores the importance of defining optimal initial therapy

Objective: To compare intravenous immunoglobulins (IVIG) plus methylprednisolone vs IVIG Alone as initial therapy in MIS-C.

Methods: Retrospective cohort study drawn from a national surveillance system with propensity score–matched analysis. All cases with suspected MIS-C were reported to the French National Public Health Agency. Confirmed MIS-C cases fulfilling the world Health Organization definition were included. The study started on April 1, 2020, and follow-up ended on January 6, 2021.

Primary outcome: Persistence of fever 2 days after the introduction of initial therapy or recrudescence of fever within 7 days, which defined treatment failure

Secondary outcome: Second-line therapy, hemodynamic support, acute left ventricular dysfunction after first-line therapy, and length of stay in the paediatric intensive care unit. The primary analysis involved propensity score matching with a minimum caliper of 0.1.

Results: Among 181 children with suspected MIS-C. Five children did not receive either treatment. Overall, 3 of 34 children (9%) in the IVIG and methylprednisolone group and 37 of 72 (51%) in the IVIG alone group did not respond to treatment.

Primary and Secondary Analyses in the Propensity Score–Matched Cohorts

	After propensity score matching				
	No. (%)				
Outcomes	IVIG and methylprednisolone (n = 32)	IVIG alone (n = 64)	Absolute risk difference between groups (95% CI) [reference: IVIG alone]	Odds ratio (95% CI) [reference: IVIG alone]	*P* value
Primary outcome					
Treatment failure[a]	3 (9)	24 (38)	−0.28 (−0.48 to −0.08)	0.25 (0.09 to 0.70)	.008
Secondary outcomes					
Second-line treatment[b]	3 (9)	20 (31)	−0.22 (−0.40 to −0.04)	0.19 (0.06 to 0.61)	.004
Hemodynamic support[c,d]	2 (6)	15 (23)	−0.17 (−0.34 to −0.004)	0.21 (0.06 to 0.76)	.01
LVEF <55%[c]	2/12 (17)	14/40 (35)	−0.18 (−0.35 to −0.01)	0.20 (0.06 to 0.66)	.007
Duration of PICU stay, median (IQR), d	4 (2 to 5)	6 (4 to 8.5)	Reduction of days: −2.4 (−4.0 to −0.7)		.005

Treatment with IVIG and methylprednisolone vs IVIG alone was associated with lower risk of treatment failure (absolute risk difference, −0.28 [95%CI, −0.48 to −0.08]; odds ratio [OR], 0.25 [95%CI, 0.09 to 0.70]; *P* = .008). IVIG and methylprednisolone therapy vs IVIG alone was also significantly associated with lower risk of use of second-line therapy (absolute risk difference, −0.22 [95%CI, −0.40 to −0.04]; OR, 0.19 [95%CI, 0.06 to 0.61]; *P* = .004), hemodynamic support (absolute risk difference, −0.17 [95%CI, −0.34 to −0.004]; OR, 0.21 [95%CI, 0.06 to 0.76]), acute left ventricular dysfunction occurring after initial therapy (absolute risk difference, −0.18 [95%CI, −0.35 to −0.01]; OR, 0.20 [95%CI, 0.06 to 0.66]), and duration of stay in the paediatric intensive care unit (median, 4 vs 6 days; difference in days, −2.4 [95%CI, −4.0 to −0.7]).

Conclusions: Among children with MIS-C, treatment with IVIG and Methylprednisolone vs IVIG alone was associated with a more favourable fever course.

Source: Ouldali M et al. Association of Intravenous Immunoglobulins Plus Methylprednisolone vs Immunoglobulins Alone With Course of Fever in Multisystem Inflammatory Syndrome in Children. JAMA. 2021;325(9):855-864

Estimated Methicillin-Resistant Staphylococcus aureus Decolonization in Intensive Care Units Associated With Single Application Chlorhexidine Gluconate or Mupirocin

Intorduction:

Chlorhexidine gluconate (CHG) and mupirocin are widely used to decolonize patients with methicillin-resistant *Staphylococcus aureus* (MRSA) and reduce risks associated with infection in hospitalized populations. Quantifying the association of an application of CHG alone or in combination with mupirocin with risk of MRSA infection is important for studies evaluating alternative decolonization strategies or schedules and for identifying whether there is room for improved decolonizing agents.

Objective:

To estimate the proportion of patients with MRSA decolonized per application of CHG and mupirocin from existing population-level studies.

Methods:

Stochastic mathematical model of 18-bed intensive care unit (ICU) in an academic medical center operating over 1 year was used to estimate parameters for the proportion of simulated patients with MRSA decolonized per application of CHG and mupirocin. The model was conducted using approximate bayesian computation with data from an existing meta-analysis of studies conducted from February 2005 through January 2015. Data were analyzed from January 2018 through November 2019.

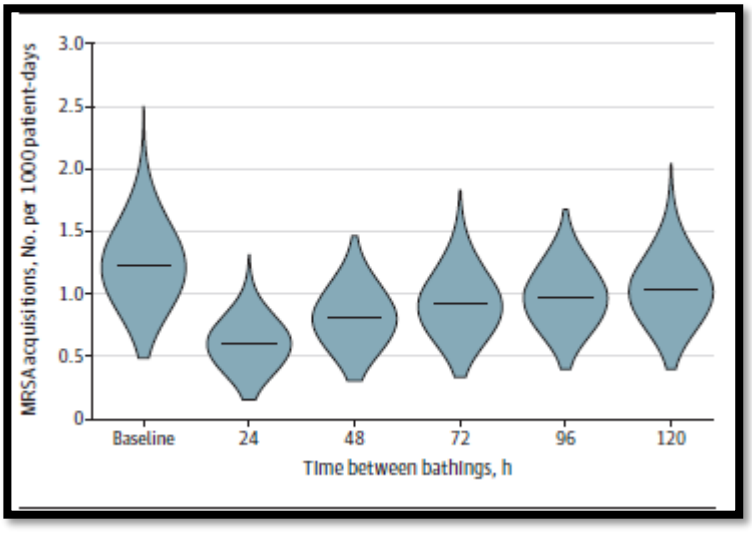
Outome: The proportion of patients with MRSA decolonized per application of CHG and mupirocin was estimated.

Results:

The estimated proportion of patients with MRSA decolonized per application of CHG was 0.15 (95%credible interval, 0.01-0.42), and the estimated proportion per application of mupirocin in conjunction with CHG was 0.15 (95%credible interval, 0.01-0.54). A lag in colonization detection was associated with decreases in the CHG estimate (0.11; 95%credible interval, 0.01-0.30) and mupirocin estimate (0.10; 95%credible interval, 0.00-0.34).

A 1%increase in the value of this parameter was associated with a 0.73% increase in the estimated combined outcomes associated with CHG and mupirocin (95%CI: 0.71, 0.75). Gaps longer than 24 hours in the administration of decolonizing agents were associated with a decrease of within-ICU MRSA transmission. Compared with a mean (SD) of 1.23 (0.27) acquisitions per 1000 patient-days in scenarios with no decolonizing bathing, a

Sensitivity of Decolonization Protocols to Changes in Timing



bathing protocol administering CHG and mupirocin every 120 hours was associated with a mean (SD) acquisition rate of 1.03 (0.24) acquisitions per 1000 patient days, a 16.3%decrease (95%CI, 14.7%- 18.0%; *P* > .001).

Conclusions:

These findings suggest that there may be room for significant improvement in anti-MRSA disinfectants, including the compounds themselves and their delivery mechanisms. Despite the decolonization estimates found in this study, these agents are associated with robust outcomes after delays in administration, which may help in alleviating concerns over patient comfort and toxic effects.

Eric t et al. Estimated Methicillin-Resistant Staphylococcus aureus Decolonization in Intensive Care Units Associated With Single Application Chlorhexidine Gluconate or Mupirocin. JAMA Network Open. 2021;4(3):e210652