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LETTER TO THE EDITOR

When fat-free parenteral nutrition is required: The strategy that becomes a double-edge sword

Cuando se requiere una nutrición parenteral libre de lípidos: la estrategia que se convierte en una espada de doble filo

Dear Editor:

Recently, several cases requiring the restriction or suppression of intravenous lipid emulsion (ILE) in parenteral nutrition (PN) have been presented in the ICU of our hospital.

Fat-restrictive strategies in PN should be applied in episodes of severe hypertriglyceridemia, commonly related to critical illness, or allergy to components of ILE. In this context, the solution applied to this clinical problem exposes the patient to a new potential risk of developing an essential fatty acid deficiency (EFAD), difficult to manage.

Linoleic acid (LA) (18:2ω-6) and α-linolenic acid (ALA) (18:3ω-3) are the essential fatty acids (EFAs) for humans and must be obtained from dietary intake.[1] EFAD can lead to various physiological consequences, such as the disturbances in biomembrane structures, cell signaling mechanisms, transduction/transcription procedures, susceptibility to oxidative stress, proinflammatory (n-6-derived eicosanoids), and anti-inflammatory (n-3-derived eicosanoids) processes.[1] Its clinical signs are diverse and mainly include skin and hair alterations, diminished immune system status, hematological alterations, and/or hepatic steatosis.[1]

EFAD is rarely described in the presence of a balanced diet because only 2–4% and 0.25% of total energy should come from LA and ALA, respectively.[1] However, this clinical entity was reported in 30%, 66%, 83%, and 100% of patients with fat-free PN after 1, 2, 3, and 4 weeks, respectively.[2] These data may be relevant, especially in those allergies directly related to soybean or indirectly (cross allergies), such as peanuts, when lipid administration is precluded in PN due to the lack of availability of soybean-free ILEs. A possible alternative could be the use of an ILE based solely on fish oil, as this emulsion has not shown any evidence of EFAD when used as the sole fat source in home PN.[3] However, it is not commercialized in Spain, so a request for its importation and for each case must be made to the Spanish Medicines Agency and wait for its approval.

Additional solutions are not good alternatives, either. Switching to enteral nutrition when possible is not feasible in cases of soybean or peanut allergy since all enteral diets marketed include soy lecithin. The topical administration of oils as a source of EFAs has no solid evidence in adult patients as it seems only to act at skin level.[4]

To provide an early diagnosis and as a monitoring tool of EFAD, we propose to rescue the almost forgotten triene/tetraene ratio (T:T-ratio) (eicosatrienoic acid/arachidonic acid), a biochemical marker of both.[5] Serum mead acid (20:3 n-9) to arachidonic acid (20:4 n-6) ratios greater than 0.2 suggest EFAD,[5] indicating increased metabolism of oleic acid to mead acid due to inadequate LA and ALA intake.

Biochemical evidence of EFAD with T:T-ratio usually can be detected two weeks before the clinical signs and symptoms appear.[5] However, EFAD in obese individuals develops over a longer term due to fat mobilization from adipose tissue.[1]

Given the complex management of EFAD and the current limited therapeutic arsenal available, we recommend closely monitoring this clinical entity in patients requiring lipid-restricted PN and establishing the T:T-ratio in hospital biochemical panels for early detection in high-risk situations.

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Comparisons are odious

Las comparaciones son odiosas

Dear Editor,

We would like to thank the authors of the article ''*Sepsis mortality prediction with Machine Learning Techniques*''[1] for their valuable contribution to mortality prediction in septic patients using machine learning, with the aim of shedding new light on the heterogeneity of sepsis.

The authors aimed to evaluate machine learning models based on a local database and a public database (MIMIC-III).[2] After their analysis, they found that lactate levels, urine output, and acid–base balance variables were the most relevant for predicting mortality.

The authors identified similar predictive variables across both databases, with strong results at the local level but mediocre outcomes when compared with the other dataset. They argue that this discrepancy is due to the differences in variables used in each model or the reduction in the number of variables, which is a mathematically sound explanation. However, we believe that a more in-depth analysis of the article's findings could provide greater insight, as medicine cannot always be fully explained through mathematical models.

1) COMPARED POPULATIONS: The data presented by the authors suggest that the two septic patient populations are markedly different. The local database shows an approximate mortality rate of 44%, while in MIMIC-III, the mortality rate is 16.25%. This difference in mortality likely reflects variations in patient populations, underlying pathologies, and healthcare systems. Therefore, we may be addressing different healthcare challenges under the same label. Mathematically, population heterogeneity affects the model's generalizability.
2) METRICS USED: The metric employed to evaluate the models is the area under the curve (AUC), which may be appropriate for measuring the event of interest in the local population, where the event rate is close to 50%. However, AUC becomes a ''less informative'' metric in MIMIC-III, where the event of interest is imbalanced.[3]
3) VARIABLE IMPORTANCE: Furthermore, the metrics used to quantify variable importance—namely, the ''*Mean Decrease Accuracy (MDA)/Gini (MDG)*'' complex—are a ''joint metric'' that provides a more robust view of variable importance, as each captures different aspects[4]: MDA measures how the variable affects the overall predictive accuracy, while MDG measures how it impacts the quality of splits in the model. A closer examination of the values reveals that, although the highlighted variables may be similar, the degree to which they improve prediction or reduce impurity differs quantitatively, implying a different classification capacities.

In summary, we would like to add to the discussion that not only the variables used explain the models' reduced accuracy but also the consideration of socio-health factors, event distributions, and the quantification of variable importance should be addressed.

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Conflicts of interest

The authors declare that none of them have any conflicts of interest.

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