LETTERS TO THE EDITOR

Lactic acidosis in patients treated with metformin is not always drug related

La acidosis láctica en pacientes en tratamiento con metformina no siempre se asocia al fármaco

To the editor:

We have read with interest the work recently published by Quesada Redondo et al.[1] This is a very interesting study considering how infrequent metformin associated lactic acidosis (MALA) is. However, we would like to make some comments on some aspects that can be debated.

The objective of the study was the detection of analytical parameters associated with mortality in patients with type 2 diabetes mellitus on chronic treatment with metformin who consult the emergency department due to an acute condition with lactic acidosis. The study included 16 patients, all grouped under the diagnosis of MALA, which is defined by three criteria[2]: 1) low pH value, 2) elevated serum lactate concentration and 3) detectable concentrations of metformin. As reported by the authors, there are numerous studies that show a relationship between metformin serum values and MALA severity, with a correlation between this concentration, pH and serum lactate levels[3]. In the work published by Quesada Redondo et al. there was a total of 3 deaths (19%); all had severe sepsis, associated with severe acidosis and extremely high concentrations of procalcitonin and lactate, which are considered as factors of poor prognosis in the septic patient[4]. However, serum metformin concentrations in the subgroup of deceased patients were much lower than in those with severe non-fatal lactic acidosis, and in the overall sample these concentrations were very low (3.2 mcg / ml live and 2.2 mcg / ml in deceased) to be considered MALA. In addition, such high lactate concentrations may be due to the situation of hypo perfusion and tissue hypoxia characteristic of the more severe stages of sepsis[4]. Likewise, renal failure present in most patients in the sample could partially explain lactic acidosis without the intervention of metformin in this process.

A previous study, which determined the role of metformin in acidosis of the septic patient, showed lower mortality in patients receiving metformin than in those not receiving this treatment[5]. These data agree with those showing higher serum metformin concentrations in the survivors, reducing the likelihood of MALA.

Given the above considerations, in our view the term MALA should not be used, since what is probably involved, mainly in the group of deceased patients, is lactic acidosis in patients with severe sepsis that coincidentally were receiving metformin.

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Conflicting interests

The authors declare no conflict of interest related to this article.

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Authors' reply

Respuesta de los autores

To the editor:

Referring to the letter of Cuero Pinto et al. regarding the factors associated with mortality due to metformin-associated lactic acidosis (MALA) in diabetic patients included in our study[1], we would like to point out the following:

1. In our study, patients did meet the criteria for MALA[2], in which detectable concentrations of the drug must be present in plasma, without minimum concentrations of metformin being needed for the diagnosis. This association is what we intended to study as a prognostic factor in the patients selected for our study.

2. In the design of our study, we stratified the sample by severity of lactic acidosis[3], to detect differences that may be masked in the data set. Therefore, our results may be due to the small number of patients included, as stated in the limitations section.

3. In the study cited, which shows the protective role of metformin treatment in patients with sepsis in relation to mortality[4], the drug concentrations in these patients were not measured, so they cannot strictly be considered as MALA . In particular, regarding whether high concentrations of metformin are a protective prognostic factor, we have already made clear that, according to our results, this claim is controversial. However, other authors, such as Boucaud-Maitre et al.[5], have observed a significant correlation between plasma metformin and lactate concentrations, suggesting that the accumulation of metformin may contribute to lactate hyperproduction leading to lactic acidosis, as occurs in attempted suicide without other associated risk factors.

4. Boucaud-Maitre et al.[5] observed renal failure as the main trigger of lactic acidosis, which in turn provokes the accumulation of metformin and causes hyperlactacidemia and decreased serum pH, not forgetting other concomitant pathological situations that occur with states of hypoxia and associated comorbidities, results which our findings support.

5. We understand that sepsis may be a confounding factor in establishing an association between drug concentrations, severity, and prognosis of lactic acidosis. Therefore, in the limitations of our work, we mentioned the absence of a control group which prevented us from comparing our results with other causes of lactic

acidosis, such as sepsis, in the absence of treatment with metformin.

In summary, we consider the MALA criteria well established in our series of patients and we believe that more studies are needed to determine the causal and prognostic role of metformin concentrations in patients with lactic acidosis, to be able to evaluate the contribution of other concomitant factors of a multifactorial entity.

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High-sensitivity troponin testing in the diagnosis of acute coronary syndrome in the emergency department

Troponina de elevada sensibilidad en el diagnóstico de síndrome coronario agudo en urgencias

To the editor:

We have read with interest the editorial by Alfonso et al. "Diagnosis of acute coronary syndrome in patients with chest pain in the emergency room: changes in view?"[1]. We agree to a great extent with the authors, but there are some aspects of their work that we would like to comment on.

Firstly, they refer in the text to "enzymatic determination"; in this regard we wish to clarify that troponin is a structural heart protein which, when bound to calcium, facilitates actin myosin interaction. It is currently the biomarker recommended in clinical guidelines, and should be determined in isolation, since the joint determination with creatine kinase does not add value[2]. Unlike other biomarkers, such as creatine kinase, troponin is not an enzyme, as it does not catalyse any biochemical reaction. In our view, we should refer to the "serial determination of biomarkers of myocardial injury" instead of "enzymatic determination".

Second, the authors commented that, in the new clinical guidelines, serial determination is recommended at 3 hours. This recommendation is applicable if high-sensitivity cardiac troponin determination methods are used[2]. These immunoassays, unlike previous methods, determine the 99th percentile of a healthy reference population with a coefficient of variation equal to or lower than 10% and also determine the exact troponin value in at least 50% of said population[3]. These methods are currently available in Europe but have not yet been approved in the United States and there is some controversy over their interpretation[4]. In our environment, its use is heterogeneous and conventional or high sensitivity methods[5] are used depending on each laboratory. This fact is relevant and must be taken into account when drawing up protocols of action, which as suggested by the authors, should be implemented.

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Author's reply

Respuesta de los autores

To the editor:

We sincerely appreciate the interest of García-Sarasola et al. in our editorial comment on the diagnosis of acute coronary syndrome in the emergency department[1]. Basically, we agree with all your appreciations. Firstly, we agree that it is preferable to use the term "myocardial necrosis markers" rather than the classic term "enzymatic determination" since troponins are cardiac proteins without enzymatic activity, and creatine kinase has lost much of its diagnostic relevance. In fact, classical enzymes are practically not mentioned in the latest guidelines, which only discuss the value of different troponin determinations[2,3].

In our editorial, we also highlighted the novelty introduced in the latest guidelines referring to repeat 1-hour determination of high-sensitivity troponins to rule out the diagnosis of acute coronary syndrome[1-3]. Precisely, this possibility is only contemplated when using high sensitivity troponins and is presented simply as an alternative to conventional serial determinations with longer waiting times. Finally, although we also agree that the use of high-sensitivity troponins is variable and its use has provoked controversy[3,4], in Spain there is a clear trend towards its progressive incorporation in most centers. Almost a decade ago we emphasized the

importance of making a critical approach to the use of computed tomography for the diagnosis of acute coronary syndrome in the emergency room5. Today, high-sensitivity troponins provide us with a new diagnostic tool of great utility provided that its use is framed within a global clinical approach of the patient and of protocols of action agreed, validated and periodically reviewed[2-4].

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History of the new unmanned aerial vehicles in health care

Reseña histórica sobre los nuevos vehículos aéreos no tripulados para uso sanitario

To the editor:

In the editorial published in EMERGENCIAS "Drones at the service of medical emergency systems: something more than a toy" by Francisco Javier Escalada Roig, where he refers to the study by Pardo Ríos et al. published in the same issue, the author comments on new advances which aeronautics offer for use in health care: so-called drones or more properly called unmanned aerial vehicles. We would just add a historical note; as we all know, history repeats itself and expectations about new devices already appeared a century ago when health aviation began.

These articles coincide with the next centenary of the date of the first flights to evacuate wounded soldiers at the end of World War I in the front of Serbia during 1917, organized by the head of the French aeronautical section Vitrat[1]. The current advance of drones is a giant step for aeronautics that is beginning to revolutionize air transport. It is to be hoped that this revolution will soon reach the health field.

A century ago Spaniards participated very actively in the beginning of a new health care activity "Health Aviation" with three historically relevant facts: the invention of the rotary wing apparatus for health purposes and its development by Juan de la Cierva and an American businessman, Harold Pitcairn; the celebration of the II International Congress of Sanitary Aviation in Madrid 1933; and the experience of evacuating patients by plane during the war in Morocco. The success of these actions was due to the enthusiastic participation of doctors, military staff and engineers who saw in this new means of transport the future of emergency evacuation and medical care. The first flight of a rotary wing apparatus for health purposes was made in Paris in 1929 involving the autogyro of De La Cierva, precursor of the current helicopter and to some extent of the so-called current drones[2].

As Mooy wrote in the first article on the usefulness of aviation for health care purposes in 1910[3] and emphasized at the First Congress of Sanitary Aviation held in Paris in 1929[4], the principal missions entrusted to this new aspect of aeronautics were the transport of sick people, health care material and the location of injured persons. And one of the main problems to be solved was the creation of legislation for this new activity. As we can see, today we are faced with the same challenges as a century ago.

It is necessary, as happened then, that Spanish doctors participate actively in the regulation and development of this new form of aerial health activity. The Spanish Society of Emergency Medicine (SEMES), as a representative of the group of emergency health professionals, should be involved in this new development.

I take the opportunity to suggest that EMERGENCIAS create a section for the publication of articles on historical topics of our specialty, to give more academic content to our "historic" claim for the specialty.

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Editor's reply

Respuesta del editor

I share with González Canomanuel his weakness for historical aspects. Undoubtedly, deepening the story goes together a better understanding of the current moment and allows us to design the future with greater arguments than that which analysis limited to today can provide. And this perspective also applies to Emergency Medicine. Although not recognized in Spain *de jure*, its existence *de facto* for decades (or for centuries or millennia, if we are lax in its definition) has indisputably generated episodes worthy of being collected, reported and studied.

EMERGENCIAS has always been sensitive to the importance of knowing our history, and all its sections are open to the contributions that scholars in this field wish to submit. In the reference section, González Canomanuel will see some examples of articles published in various sec-

tions of the Journal in which historical analysis or reflection is patent[1-10]. Therefore, without the need to create a specific section in the Journal, I encourage all colleagues with special sensitivity for the history of our specialty to address any aspect they consider of interest for our better self-knowledge, and whenever the quality of the final manuscript is good, you will find in the pages of EMERGENCIAS a warm welcome. And without a doubt, the gratitude of many of its readers.

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Triage is now in the Dictionary of the Royal Academy of the Spanish Language

Triaje ya está en el Diccionario de la Real Academia Española

There are things that are normalizing. For decades, emergency physicians, doctors in general and increasingly larger sections of the population use the word triage. This word, initially coined in French military medicine to designate the priority of attention for the wounded in the field of combat, has been extended to civil society. Thus, at present, it designates the prioritization of patients which is performed by the vast majority of hospital emergency departments in Spain[1-4] and emergency medical systems in catastrophic care and, more and more frequently, to order the demand for user attention in non-catastrophic situations[5,6]. What triage tries to do is ensure that patients with more serious or time-dependent processes are taken care of before the rest, regardless of when they request assistance.

Only two years ago, we had an open debate in the journal Revista with Joaquín Poch Broto, President of the Royal National Academy of Medicine, about the situation of the words triage and "urgenciólogo" in the Dictionary of the Spanish Royal Academy (DRAE)[7,8]. I note with satisfaction that triage has been incorporated into the latest edition of DRAE[9], so it is no longer necessary to write it in italics, a fact that has been adopted by EMERGENCIAS in the last few issues. Undoubtedly, persistent use has led to generalization of the word, and this has conditioned its acceptance.

I encourage you not to abandon the term "urgenciólogo", because it will surely be included in DRAE one day. It designates something clear and well-defined, not defined by any other word today. And so, without doubts and with conviction, we will achieve all our objectives. Sooner or later.

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