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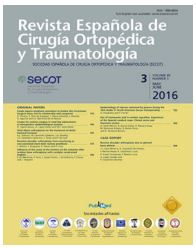

LETTER TO THE EDITOR

Letter to the Editor on ''Efficacy and safety of the topical application of tranexamic acid in primary cementless hip arthroplasty: Prospective, randomised, double-blind and controlled study''☆

Carta al director sobre «Eficacia y seguridad de la aplicación del ácido tranexámico tópico en la artroplastia primaria no cementada de cadera: estudio prospectivo, aleatorizado, doble ciego y controlado»

We carefully read the interesting article published in your journal on ''Efficacy and safety of the topical application of tranexamic acid in primary cementless hip arthroplasty: prospective, randomised, double-blind and controlled study'' by F.J. Tavares et al. where they assessed the efficacy and safety of the topical application of tranexamic acid (TXA), with its use also being considered for patients with a history of thromboembolism.[1]

Despite the interest and relevance of the study hypothesis, we would like to point out several observations on the methodology of this study which we think may be of use for a critical reading of it.

TXA dose: the patients in the TXA group received 1.5 g of the drug. We find it striking that the dose is relatively low when several meta-analyses exist to confirm its safety in higher doses (between 2 and 5 g). Bearing this point in mind, it is possible that the administration of a higher dose would have achieved more favourable outcomes than those detected, demonstrating once again the usefulness and safety of this drug for this indication.[2–4]

Perioperative fluid therapy control: patient haemoglobin and haematocrit are both analytical parameters of concentration. As a result and due to primary hip arthroplasty representing surgery with blood loss, the concentration of both parameters will be principally conditioned by volume replacement of the intravascular space. If no strict criteria is established for maintenance fluid therapy (normally with balanced crystalloids), and blood replacement (crystalloids and/or colloids) we run the risk of introducing an added factor of confusion, which may be excessive volume replacement by the anaesthesiologist, especially in those patients with a higher visual estimation of bleeding: the higher the visual estimation, the greater the volume replacement and higher risk of haematocrit haemodilution.

Calculation of bleeding: mathematical formulas are an ideal parameter for calculating perioperative bleeding.[5] Those used (Nadler et al. for estimation of the volume of patient bleeding,[6] and Good et al. for the estimation of bleeding),[7] assume that the patient's blood volume remains stable at the beginning and at the end of the measurement period, when in reality it cannot be considered stable until at least 5 days following surgery. According to the article we may suspect that final haematocrit is not determined for the formula until day 4, with consideration of mean stay and standard deviation also being included (6.62 ± 2.04 days 5.92 ± 1.58 days). We find it striking that the Good et al. formula, once the blood volume of red cells has been calculated, estimates the total blood volume by assuming that the haematocrit of lost blood is the same as the initial one. This is obviously incorrect. Choosing how to determine lost blood volume is of utmost importance and especially if we take into account that it is one of the variables which in multivariable analysis was proven to be associated with transfusion.

Adverse events: Another aspect which has come to our attention is the detection of adverse events. Although it is widely known that TXA is a safe drug, it is not exempt from adverse reactions, among which the most important are VTE and PE.[8,9] Although a lower number of events have not been detected in patients who received topical TXA it would appear recommendable to use this administration route in patients presenting with higher risk.[3,8] The adverse events of any drug are clearly related to plasma concentrations. In this sense, the plasma concentration of topically administered TXA is approximately 10 times lower than the concentration reached after intravenous administration.[10,11]

The text suggests that these complications were assessed by following purely clinical criteria as is commonly the case in the majority of hospitals in our environment. However, in the context of a clinical trial, it is essential to safeguard patient safety, and provide objectifiable data on the

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outcomes. We therefore believe it would have been of interest to determine the presence or absence of these events using something other than the clinical trial. For example a non-invasive, accessible and low cost ultrasound test could have been performed.

The authors also stated that 3 of their patients had died when data collection was made. We therefore wondered whether these deaths had a causal relationship with the administration of the drug or with the actual surgical procedure. Again, this is an important aspect for ensuring the safety of intervention.

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B. Barrachina[a], I. Iriarte[a], A. Albinarrate[a], A. Lopez-Picado[b,*]

[a] *Servicio de Anestesiología y Reanimación, Hospital Universitario Araba, Vitoria-Gasteiz, Álava, Spain*
[b] *Unidad de Investigación Clínica y Ensayos Clínicos, Instituto de Investigación Sanitaria del Hospital Clínico San Carlos, Hospital Clínico San Carlos, Madrid, Spain*

* Corresponding author.
E-mail address: amanda.lopezpicado@gmail.com (A. Lopez-Picado).