Pharmacologic preventive strategies for takotsubo stress cardiomyopathy. What does evidence tell us?

Estrategias farmacológicas de prevención contra la miocardiopatía de takotsubo. ¿Qué nos aportan las pruebas?

Mr. Director:

After reading the takotsubo stress cardiomyopathy (TSCM) case-report and review of the literature by De Boer and Booij,1 we would like to comment on the preventive aspects of this medical condition. The authors cautiously state that perioperative beta-blockade (BB) would probably provide protection in these patients. As diagnosis-rates steadily increase, anesthesiologists are bound to be faced with rising numbers of TSCM cases, and deeper insights into the natural history of this disease would be helpful in the pre-anesthesia consultation.

Prior to laparoscopic hemicolectomy, we evaluated a 55-year-old woman. She had a history of mild mitral and severe aortic regurgitation. Three years before, a TSCM episode triggered by an intense emotional event was recorded. She was discharged on acetylsalicylic acid, enalapril, bisoprolol and diazepam, but two months later bisoprolol had to be discontinued due to dizziness and exercise intolerance. We added clorazepate to the treatment in order to handle her emotional state, and also provided information reassuring her as to the chance of relapse. Enalapril was maintained up to 24h before surgery, but BB was dismissed. She was allotted an ASA III class and was included in an enhanced recovery program. Surgery was performed under a combined technique of subarachnoid and remifentanil–propofol based general anesthesia. No complications occurred, and within one-year follow-up no re-admittance was recorded.

Assessing individualized TSCM relapse risk is challenging. Long-term follow-up trials show that recurrence, globally low, significantly declines four years after the first episode; however, higher rates of patients continue suffering from chest pain of uncertain meaning.3 BB in our patient resulted in abolition of the compensatory response to aortic regurgitation, for that reason a decision was made not to re-establish this treatment. The three-year lapse since debut in our patient decreased the probability of recurrence; therefore, we were surely approaching a different scenario from that described by de Boer and Booij, but we must be aware that no drug can prevent TSCM.

The ultimate pathophysiology of TSCM is still to be elucidated, precluding consensus on prevention, but massive adrenergic release is the most widely accepted explanation for the myocardial microcirculation impairment and cell metabolism disruption associated with this disease. Thus, BB arises as the reasonable choice in the long-term treatment. Although there is rationale for BB continuation, cohorts repeatedly demonstrate that these drugs do not check debut nor relapse,2,3 and low-dose regimens do not attenuate the severity of presentation either.4 Two reasons explain this therapeutic failure. First, standard dosage of BB might provide insufficient protection against the magnitude of the adrenergic release observed in TSCM; and secondly, the excess of circulating catecholamines might disclose the underlying up-regulation phenomenon associated with chronic BB intake. The latter is thought to be the cause of recurrence after BB withdrawal, stressing the importance of maintaining this treatment throughout the perioperative period when previously established. Alpha- and beta-adrenergic blockade for acute coronary acute syndromes seem to be more beneficial on myocardial microcirculation than BB alone. This finding, also reproduced in animals under immobilization-induced stress, suggests that symptoms might be mitigated by double blockade. Dexmedetomidine, combining double adrenergic blockade with sedative proprieties, might provide a more suitable...
profile for improving microcirculation impairment. Although recommended for TSCM surgical cases,\(^2\) dexmedetomidine has not been tried in this setting.

Angiotensin II inhibitors might modulate the symptoms, though do not eliminate recurrence\(^3\); and the risk-modifying power of estrogen replacement remains debatable, as pre-existing vascular derangements are unlikely to be reversed by hormonal treatment.

Anesthesiologists deal with a range of medical conditions in which BB deleterious effects may outweigh the unproven benefits found in TSCM. We agree with the authors that physical or psychological stress triggers must be carefully avoided, but neither BB, nor other drugs should delude us into a false safety feeling. TSCM is a rare disease with a low recurrence rate, all of which precludes obtaining consistent evidence as to the best preventive approach, other than treatment of cardiovascular risk-factors and adequate management of co-morbidities. Valuable data from national and supranational registries are underway, but meanwhile evidence shows that no validated pharmacologic strategy has proven preventive in these cases.

**Bibliografía**


A. Pavón-Benito*, E. Pérez-Bergara, M. Dufur-Mendivil, M. Salvador-Bravo

**Servicio de Anestesiología y Reanimación, Complejo Hospitalario de Navarra, Spain**

*Corresponding author.

**E-mail address:** ruizpavon@yahoo.es (A. Pavón-Benito).

http://dx.doi.org/10.1016/j.redar.2014.05.018