We know that metaraminol is a sympathomimetic amine which acts on the \( \alpha_1 \)-adrenergic receptor with some stimulation of the \( \beta \)-adrenergic receptors. The combination of increased systemic vascular resistance and increased contractility results in an elevation in arterial pressure. However, the effect of metaraminol (or other sympathomimetics) in patients with Takotsubo cardiomyopathy may be less predictable due to the dysfunctional myocardial response to catecholamine stimulation. Indeed, there is evidence to suggest a paradoxical negative inotropic effect of sympathomimetic amines in these patients which appears to be dose-dependent. This finding was corroborated by Rathakrishnan and Lee, who also observed that augmenting already high concentrations of circulating catecholamines with exogenous compounds may cause accelerated deterioration. Limited evidence suggests that using agents which have no action on the \( \beta \)-adrenergic receptors may be safer in these patients.

This interesting case demonstrates that caution is advised when using sympathomimetic drugs in people with Takotsubo cardiomyopathy. Furthermore, avoidance of agents which act on the \( \beta \)-adrenergic receptors may be a safer option for these patients.

**Declaration of interest**

None declared.

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Optimizing preoperative haemoglobin with intravenous iron

Editor—The patient blood management approach is currently accepted by orthopaedic teams and there is a consensus for the need of blood-saving techniques in this surgery. I.V. iron is effective for correcting iron deficiency anaemia in patients undergoing orthopaedic surgery, but proper diagnosis of the iron deficit may have an influence on the effectiveness of corrective treatment and lead to more cost-effective and safer use in terms of adverse side-effects.

In an observational epidemiological study, we included all patients who had received treatment with i.v. iron sucrose, alone or associated with erythropoietin (rHuEPO), to optimize preoperative anaemia in major orthopaedic surgery. The indications for i.v. iron treatment were preoperative Hb \(< 13 \text{ g dl}^{-1}\) (male and female) and iron deficiency, which was established based on abnormal haematimetric and biochemical parameters values as shown in Table 1. If, after treatment with i.v. iron, Hb did not reach \(13 \text{ g dl}^{-1}\) or if the cause of anaemia was suspected of being a chronic condition, recombinant human erythropoietin (rHuEPO 40,000 UI) therapy was added.

Over the 5 yr study period, 412 patients received i.v. iron, which was given alone in 279 patients and combined with rHuEPO in 133. In both treatment groups, the highest Hb increase occurred in patients with the lowest Hb values on initial study.

As shown in Table 1, Hb increased by \(0.80 \text{ g dl}^{-1}\) in patients receiving i.v. iron and this increase correlated significantly with functional iron parameters (percentage of hypochromic erythrocytes, levels of soluble transferrin receptor), whereas ferritin levels and transferrin saturation percentage showed no correlation. In patients receiving i.v. iron plus rHuEPO Hb increased by \(1.47 \text{ g dl}^{-1}\) and it did not correlate with any functional iron parameter. The paradoxical relationship between Hb increase and serum ferritin levels (i.e. higher Hb increases with lower ferritin level concentrations) supports the notion that rHuEPO acts more in accordance with the i.v. iron administered than with the iron stored as measured by ferritin. It is probable and logical that a lower ferritin value would lead to a higher dose of iron being prescribed.

The most important finding from our study is the fact that the parameters often recommended by clinicians and guidelines, such as mean corpuscular volume, hypochromasia, and transferrin saturation, which serve to classify anaemia, were useless in establishing the iron status as a basis to indicate iron treatment, to guide dosing, and to determine the need for associated rHuEPO in patients of advanced age with joint disease. In our study, <25% of patients presented hypochromic erythrocytes and <20% showed microcytosis. Nonetheless, the functional parameters, such as the percentage of hypochromic red blood cells and the stTFR, were elevated in a higher percentage of patients; that is, a functional iron deficiency was documented in more than 60% of patients. Similarly, inflammation markers (C-reactive

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1 Cesario V, Loureiro MJ, Pereira H. Takotsubo cardiomyopathy in a cardiology department. Rev Port Cardiol 2012; 31: 603–8
4 Abe Y, Tamura A, Kadota J. Prolonged cardiogenic shock caused by the dysfunctional myocardial response to catecholamine stimulation. Indeed, there is evidence to suggest a paradoxical negative inotropic effect of sympathomimetic amines in these patients which appears to be dose-dependent. This finding was corroborated by Rathakrishnan and Lee, who also observed that augmenting already high concentrations of circulating catecholamines with exogenous compounds may cause accelerated deterioration. Limited evidence suggests that using agents which have no action on the β-adrenergic receptors may be safer in these patients.

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protein and erythrocyte sedimentation rate measurement) did not prove to be useful for assessing the Hb increase after i.v. iron administration.

In conclusion, despite the limitations of any observational study, and the need to be confirmed in a prospective trial, determination of functional status, other than transferrin saturation, seems to be of greater help to the clinician for indicating iron in this population, and provide a more reliable prediction of efficacy than other iron deficiency-related measures. Although we believe that it is necessary to determine ferritin concentration levels, because it provides information on the patient’s iron stores and excludes those with high levels before i.v. iron is administered, we suggest incorporating functional parameters in the preoperative workup as an aid to deciding the appropriateness of this treatment.

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Treatment of refractory post-dural puncture headache with low doses of the strong opioid piritramide

Editor—Epidural analgesia is considered to be the most effective method for pain relief during labour and delivery. Concomitantly, post-dural puncture headache (PDPH) due to inadvertent dural puncture is the most frequent major complication. In obstetric patients, PDPH hinders them from feeding and nursing their newborns. Therefore, an efficient, rapid, permanently available, and harmless treatment is needed.

When conservative treatment is ineffective, the performance of epidural blood patch (EBP) is often recommended. However, evidence of this procedure is still limited.1 In obstetric patients, the success rate of EBP with 34% is lower than in general.2 The patient is at risk of complications with every repetition.

We report two cases of severe PDPH after accidental dural puncture during labour epidural analgesia, a 28-yr-old para 2 (168 cm/65 kg) at 35 weeks of gestation and a 33-yr-old para 0 (165 cm/65 kg) at 39 weeks. The epidural catheter was placed in the loss of resistance to saline technique at L3–4 space using an 18 G Tuohy needle. After the first attempt, the procedure was successfully repeated and live infants were delivered vaginally. The first patient developed a dull frontal postural headache 5 h and the second 10 h after dural puncture. In the absence of neurological symptoms, PDPH was diagnosed. In both patients, PDPH was completely refractory to conservative treatment with ibuprofen (≤ 1200 mg), diclofenac (≤ 75 mg), acetaminophen (≤ 1500 mg), caffeine (≤ 400 mg), and theophylline (≤ 200 mg) and also volume substitution and bed rest. In one patient, an EBP decreased pain only temporarily; in the other patient, EBP was not performed because of elevated inflammatory parameters.

In both patients, two and three applications of small doses of the strong opioid piritramide (3.75 mg) 5 days after onset of PDPH immediately and completely relieved headache without disturbance of breastfeeding. Already the first application reduced pain intensity from 8/10 and 5/10 NRS (numeric rating scale 0–10) to 3/10 and 2/10 NRS, respectively. In one case, only one more application was necessary 15 h later and in the other patient, two more applications were administered after 17 and further 19 h. A follow-up after several days showed no recurrence of PDPH symptoms.

A Cochrane Review revealed only a limited evidence for the use of common drugs in PDPH.3 The use of strong opioids in PDPH has never been evaluated systematically. Particularly in the postpartum period, the use of strong opioids is controversially discussed because of potential CNS depression of mothers and newborns. However, short-term maternal use of opioids seems usually safe and infrequently hazardous for their babies.4

In our institution, the strong opioid piritramide is the opioid of choice for perioperative pain management. The potency ratio of morphine to piritramide is 1:0.7.5 Within 24 h, 15 mg (equipotent to 10 mg morphine) of piritramide is allowed to be administered i.v. (3.75 mg every 4–6 h) in a breastfeeding mother. To date, there are no reports of CNS depression of mothers or babies. Withdrawal in infants after cessation of administration has not been reported.

The mode of action of strong opioids in PDPH is still unknown. In preclinical studies, opioids were shown to act within the trigeminal system to inhibit neurogenic dural vasodilation and brainstem neuronal activity.6 As meningeal irritation and reflex vasodilatation of the meningeal vessels are considered as well-established pathophysiological mechanisms of PDPH, these results could explain the mode of action of strong opioids.

Our case reports demonstrate that strong opioids, not yet included in the guidelines, may represent a promising tool in the management of post-partal PDPH.

Declaration of interest

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