Receptor-specific Reversible Sedation: Dangers of Vascular Effects

To the Editor—The editorial by Dr. Talke\(^1\) enthuses about the future role in man of α\(_2\)-agonist-mediated sedation with easy reversibility after atipamezole administration. He rightly emphasizes the future role of "a new subtype-specific α\(_2\) agonist with sedative but not vasocostricter effects" (italics added).\(^2\) Scheinert \textit{et al.}\(^2\) briefly allude to the use of α\(_2\)-adrenoreceptor agonists and antagonists in veterinary practice. We would point out that α\(_2\)-adrenoreceptor agonists, such as xylazine, have been widely used in veterinary and anesthetic practice for 29 yr.; and detomidine,\(^3\) medetomidine, and atipamezole have been used for 10 yr. Some years ago we\(^4\) showed severe cardiovascular changes and bradycardia in horses and, during a similar time period, it has been known that in sheep there is a sudden profound decrease in arterial oxygen pressure (P\textsubscript{aO\textsubscript{2}}) after xylazine administration. Until recently, the explanation for this has been obscure. However, we\(^4\) and others\(^5\) have shown extensive pulmonary edema after xylazine sedation in sheep. In our animals, P\textsubscript{aO\textsubscript{2}}, breathing air decreased from 97.9 ± 6.7 mmHg ± SEM to 58.1 ± 5.2 mmHg ± SEM immediately after xylazine administration. All our animals had extensive pulmonary edema and microvascular congestion with erythrocytes extravasated into the alveolar space.

We interpreted this as a consequence of pulmonary venospasm, there being no evidence of acute inflammation in the lung, no sign of platelet emboli, and no evidence of free radical release. There are wide species differences in the effect of xylazine on pulmonary function, but it is worth bearing in mind the potency of the vascular effects of some of these α\(_2\)-agonist sedatives in humans and animals. The different receptor subtypes in the cardiovascular and central nervous systems must obviously be carefully investigated before we can enthuse about the inclusion of new α\(_2\)-receptor agents in human clinical practice.

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In Reply.—I thank Drs Jones and Taylor for their interest in and comments about my editorial.1 They reinforce my point that currently available non-subtype-selective α2 agonists have sedative and hemodynamic effects, and that, at high doses, these hemodynamic effects may cause undesirable side effects. In addition to the cardiovascular and pulmonary effects discussed by Drs Jones and Taylor, at high doses, these compounds may have deleterious effects on vital organ blood flow in animals and humans. When α2 agonists are used for sedative purposes, their peripheral vasoconstrictive effects seem to cause most of the undesirable side effects, such as the ones described by Drs Jones and Taylor. Fortunately, it appears that the centrally mediated sedative/sympatholytic effects and the peripherally mediated vasoconstrictive effects are mediated by different α2 receptor subtypes. To provide the desired therapeutic effect (sedation) without side effects (vasoconstriction) is precisely why subtype-specific α2 agonists may, in the future, provide the bases for a reversible intravenous anesthetic technique in humans. However, before my enthusiasm for the potential role of the use of α2 agonists in a reversible intravenous anesthetic technique can become reality, new drugs must be developed, undergo rigorous preclinical and clinical testing, and be evaluated by experts in appropriate regulatory agencies, as is common with all new drugs. Meanwhile, continuing research work in this area will lead to better understanding of these compounds, help us to avoid serious side effects, and improve the anesthetic care of animals and humans.

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Janos Balassa and Rudolf Eisenmenger: Forgotten Pioneers of Resuscitation

To the Editor.—The review of Juvin and Desmonts1 is excellent, especially with respect to French contributions to internal cardiac massage. However, two pioneers are mentioned.

Firstly, Janos Balassa (1814–1868) should be mentioned, who, in 1858, successfully performed cricothomy followed by chest compressions during a case of asphyxia from laryngitis.2,3

Secondly, Rudolf Eisenmenger (1871–1946) published, in 1903, a device for suction and pressure on the abdomen (and lower chest) to promote breathing and circulation.4 He was the first to propose active compression–decompression cardiopulmonary resuscitation (ACD-CPR) and a device (Lautenschläger, Munich, Germany) to do so, which was later named Biomotor.6 With his device at least one successful resuscitation in cardiac arrest is documented.7 Animal experiments in 1929 showed the device to generate not only blood pressure, but also blood flow, as evidenced by carbon dioxide exhalation and transport of intravenously injected dye to all parts of the body.8 Eisenmenger worked on and published information about ACD-CPR from 1903 until 1942.9 He thus upheld external cardiac resuscitation in the "dark age" of artificial resuscitation.

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