Oxygen Sensing in the Ductus Arteriosus: Endothelin Still a Player

To the Editor:

In a recent issue of Circulation Research, Hong et al1 provided additional data in support of a mitochondrial mechanism for oxygen sensing in the ductus arteriosus. While commending the authors on the advance in this area, I find objectionable their hasty dismissal of an alternative scheme implicating endothelin in the same process. Far from being a concept exclusively originating from our work, as implied in the article, this position is espoused by diverse groups.2

In taking their conclusion to the fore, Hong et al1 quoted 3 publications that warrant a comment. The first one by Michelakis et al,3 being based on experiments with the isolated human ductus, negates a role for endothelin because the combined inhibition of its synthesis and action (with phosphoramidon and BQ123, respectively) is reportedly not followed by curtailment of the oxygen contraction. Furthermore, in the same article, oxygen does not increase the yield of the peptide. Regrettably, however, in reaching the former conclusion, the authors compared the oxygen response of an untreated vessel with that of a vessel being exposed not only to the endothelin inhibitors but also to drugs (ie, meclofenamate, L-NAME) interfering with potent endogenous relaxants, such as prostaglandin E2 and nitric oxide. In other words, the action of endothelin inhibitors was assessed on a vessel manifesting an enhanced contractile drive for oxygen, incidentally documented by the authors themselves,3 although using still the untreated vessel as a reference. Hardly a condition to observe an inhibition, how the 2 mechanisms may eventually dovetail in promoting ductus closure. This is our position1 and, in fact, while validating the endothelin function, we have found evidence of an alternative, hitherto uncharacterized, oxygen-sensing mechanism2 that could well represent the mitochondrial function being investigated by Hong et al.1

Disclosures

None.

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