Ibudilast: A Non-selective PDE Inhibitor with Multiple Actions on Blood Cells and the Vascular Wall

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ABSTRACT

Ibudilast (3-isobutyryl-2-isopropylpyrazolo[1,5-a]pyridine) is a nonselective inhibitor of cyclic nucleotide phosphodiesterase (PDE). It is widely used in Japan for improving prognosis and relieving symptoms in patients suffering from ischemic stroke or bronchial asthma. These clinical applications are based on the properties of ibudilast that inhibit platelet aggregation, improve cerebral blood flow and attenuate allergic reactions. The inhibition of platelet aggregation and vasodilatation by ibudilast may be due to synergistic elevation of intracellular cyclic nucleotides and release of nitric oxide (NO) or prostacyclin from endothelium, rather than direct inhibition of PDE5 or PDE3. Another important property of ibudilast is its antiinflammatory activity possibly associated with potent inhibition of PDE4. Combined with its relaxing effects on bronchial smooth muscle, antiinflammatory activity of ibudilast could favorably influence pathophysiology of asthma by antagonizing chemical mediators triggering asthmatic attacks. Ibudilast was also reported to significantly attenuate inflammatory cell infiltration in the lumbar spinal cord in an animal model of encephalomyelitis. Future investigations should include effects of ibudilast on inflammatory reactions between endothelium and blood cells, which may initiate the development of atherosclerosis.