

Neonatal and paediatric intensive care

Advertisement

From Miss S. Arenas-Lopez

Re: "Neonatal and paediatric intensive care" (*Hosp Pharm*, February 2003, pp66–71). The article reviews the role of the pharmacist in this complex discipline of neonatal and paediatric intensive care and gives a general overview on current services and therapies.

For the past three years, working at Guy's Hospital PTCU, I have acquired some experience in this field and I have also completed an MSc studying the use of clonidine in PICU. I would like to add some comments to this article and correct a misleading statement.

The authors stated that the mode of action of clonidine is by stimulating the opiate receptors in the central nervous system. This is incorrect and none of the references stated by the authors support the statement.

Clonidine hydrochloride is a partial agonist at α_2 -receptors, both within the central nervous system and in the periphery, being more specific for α_2 -receptors than for α_1 -receptors. Within the central nervous system, clonidine acts at all central α_2 -receptors, stimulation of which is associated with decreased neuronal excitability. High serum concentration of clonidine may stimulate central α_1 -receptors enhancing neuronal excitability.¹ Stimulation of central α_2 -receptors by clonidine has been reported to cause hypotension, bradycardia, sedation, analgesia, hypothermia, and changes in motor activity and conditioned behaviour. The cardiovascular effects of clonidine are predominantly mediated by stimulation of central postsynaptic α_2 -receptors. Stimulation of peripheral presynaptic α_2 -receptors (on postganglionic noradrenergic or cholinergic neurons) contributes to reduce saliva flow, reduced intestinal motor activity and gastric acid secretion and bradycardia, as well as endocrine-metabolic effects such as inhibition of insulin secretion from the pancreatic β -cell. Clonidine also binds to imidazoline receptors. However, the main contribution to the cardiovascular action of clonidine is via α_2 -receptors.²

Clonidine is rapidly and well absorbed following oral administration, with bioavailability reaching about 100 per cent in adults, although no data is available on its oral bioavailability in children. It is a lipid-soluble drug, widely distributed throughout most tissues with an apparent volume of distribution of 2.1L/kg. It is moderately bound to plasma protein (between 20 and 40 per cent), probably albumin. Approximately 40 per cent of an administered dose undergoes oxidative metabolism in the liver leading to inactive metabolites while the remainder (60 per cent) is excreted unchanged by the kidney. The elimination half-life of clonidine is 20–25 hours in adults with normal renal function, but is longer in patients with renal impairment.³ In studies performed in children, clonidine was administered for sedation through different routes (eg, epidurally, intravenously, rectally) and the elimination half-life observed was shorter by approximately eight hours with a smaller volume of distribution (0.9L/kg).⁴

The authors also state that an overdose of clonidine may be reversed with naloxone. Such a use is

controversial and not the first-line approach, and therefore, expert advice should be sought from poisons information centres.²

Sara Arenas-Lopez

Senior paediatric pharmacist
Guy's Hospital, London

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Mrs Bolton and Ms Khoo reply:

We thank Miss Arenas-Lopez for her letter. We have since reviewed the article and would like to correct some of the points made regarding mode of action of clonidine and the use of naloxone in clonidine overdose.

Clonidine's mode of action is as a selective agonist at centrally located α_2 adrenoceptors which results in a reduction in central sympathetic activity, along with pronounced sedation and analgesia. The article stated that it acts on opiate receptors; this is not accurate.

Although naloxone has been suggested as an antidote for clonidine reversal, naloxone in doses of up to 100mcg/kilogram intravenously was ineffective in reversing symptoms and signs of clonidine overdose in five paediatric patients, contrary to successful use of the antagonist in previous reports.¹ In a retrospective analysis of 47 children with clonidine poisoning, only three out of 19 given naloxone showed definite improvement; it was concluded that naloxone is, at best, an inconsistent antidote for clonidine poisoning.²

Omonefe Bolton and Ghi Pei Khoo

Senior paediatric pharmacists
St George's Healthcare NHS Trust, London

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