Clonidine hydrochloride is well established in paediatric practice being first described as an epidural additive over 30 years ago. The APA poll suggests that about 50% of practitioners use caudal clonidine as an additive with approximately 10% also adding clonidine for peripheral nerve blocks. Almost 40% do not use clonidine as an additive. In our institution clonidine is routinely used with caudal and paravertebral anaesthetic techniques to prolong block duration. We administer clonidine added to levobupivacaine for continuous epidural analgesia postoperatively but it is not added to our peripheral nerve blocks or infusions for post-operative peripheral nerve block catheters.

Clonidine has very high lipid solubility and readily penetrates the central nervous system. It is metabolised in the liver to inactive metabolites with 65% of the dose being excreted unchanged in the urine, average elimination half life is approximately 8 hours. The action of the drug peaks approximately 10 minutes after intravenous administration lasting for 3-7 hours. Due to its renal elimination the half life is markedly increased in renal impairment. Clonidine has several sites of action. It stimulates alpha 2 adrenoceptors presynaptically decreasing noradrenaline release from central and peripheral sympathetic nerve terminals. It also acts postjunctionally on the dorsal horn neurons of the spinal cord inhibiting release of substance P. Clonidine has also been shown to act on cholinergic, purinergic and serotonergic pain systems to produce analgesia. Thus the rationale for central administration of clondine appears to be sound. In addition to its spinal level of action it also acts at supraspinal sites in the locus coeruleus enhancing descending inhibitory tracts to the dorsal horn. Radioligand studies confirm this area to be a major site for the sedative and analgesic actions of clonidine. Animal studies do suggest that a part of the action of clonidine may be mediated peripherally. Several studies in humans support this notion showing superior analgesia with for example intrarticular clonidine being more effective than clonidine injected subcutaneously for knee arthroscopy[1]. This action of clonidine may be mediated through action at the site of injury and may not apply when injected at a distance from the painful insult.

Examining the evidence for our current use of clonidine, it has been the subject of several meta-analyses and randomised controlled trials. These have confirmed its ability to prolong the duration of central blockade[2]. Complications associated with its use appear to be dose dependent , such as hypotension, bradycardia and sedation. The above meta-analysis found a dose of 2mcg/kg clonidine (with a limit of 150mcg) to be effective with a minimal increase in complications. Studies suggest that caudal clonidine is more efficacious than iv clonidine[3] with reduced postoperative pain scores best seen in those with caudal clonidine, however there is an effect of iv clonidine as shown by Hansen et al. in 2004[4] where in 46 children iv clonidine was found to be as effective as the caudal additive with a trend to favour caudal clonidine.

Data regarding the addition of clonidine to peripheral nerve blocks appears to be somewhat conflicting. A qualitative review by McCartney et al. in 2007 analysing 27 studies (1385 patients) found conflicting results on whether peripheral clonidine was beneficial[5]. Almost half of the studies reviewed found no benefit to peripheral clonidine and there was a suggestion that any benefit was found best with shorter to intermediate acting local anaesthetics and less so with longer acting agents such as bupivicaine. A meta-analysis by Popping et al. (1054 patients, 573 receiving clonidine) found that clonidine extended duration to first postoperative analgesia by approximately 2 hours[6]. In this meta-analysis NNH was approximately 10 for hypotension and bradycardia. This data was extracted on adult patients who did not undergo general anaesthesia limiting its application to the paediatric population. Dose responsiveness could not be well established and it

could not be ruled out that the clonidine effect was due to systemic absorption. There has been a recent metanalysis by Lonnqvist et al. published in Paediatric Anaesthesia this year examining peripheral clonidine or dexmedetomidine as an adjunct to peripheral nerve blocks in children[7]. Their meta-analysis combined data from 5 randomised controlled studies (total 283 children) and found prolongation of time to first analgesic prolonged by approximately 6 hours. This is at significant variance from data in the adult literature which may reflect increased systemic absorption in the paediatric population. The positive result was present even when dexmedetomidine was excluded from the analysis.

The available data does suggest there may be some benefit to adding clonidine to peripheral nerve blocks however it is not clear which local anaesthetics, blocks or doses are optimal for prolongation of analgesia. This warrants further robust high quality study. In view of the high lipid solubility, large scale studies examining intravenous and peripherally administered clonidine to establish whether the effect is related purely to a systemic action of the clonidine or a local effect as this has not yet been established and perineural safety cannot be absolutely confirmed. Without clear patient benefit its use in peripheral nerve blocks at the present time cannot be recommended routinely.

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