Role of Preoperative Blockade in Pheochromocytoma–Paraganglioma: A Clinician's Perspective

Pheochromocytoma–paraganglioma (PPGL) produces excessive catecholamines, which lead to peripheral vasoconstriction and hypertension. Intraoperative tumour handling causes wide fluctuations in blood pressure, with intraoperative surges and post-surgery hypotension. Non-selective alpha-blocker (NSAB), namely phenoxybenzamine, was described in 1967 to reduce the blood pressure fluctuations and enable preoperative volume re-expansion, bringing in the concept of preoperative blocking.[1] Subsequently, selective alpha-blockers (SAB) such as doxazosin, prazosin, and calcium channel blockers (nicardipine) were used.

The choice of one drug over another is backed by sparse data in the form of observational studies and there is only one randomised controlled trial (PRESCRIPT trial) comparing phenoxybenzamine and doxazosin. Though the percentage time outside the target blood pressure (primary endpoint) was similar in both arms, the intraoperative hemodynamic instability score (secondary endpoint) was lesser with phenoxybenzamine.[2] In the meta-analysis (included one RCT and seven observational studies) comparing NSAB and SAB published in the current issue, the authors deduced that NSAB offers an advantage in the form of lesser intraoperative vasodilator requirements. Another recent meta-analysis (included 1 RCT and 10 observational studies) also concluded NSAB arm had a lesser intraoperative vasodilator requirement and had lower maximum intraoperative systolic blood pressures. Notably, both meta-analyses observed comparable (NSAB vs. SAB) intraoperative and postoperative hypotension risk and overall morbidity.[3]

What additional information do these meta-analyses provide beyond that described in the PRESCRIPT trial?

Meta-analysis is considered superior to RCT in the evidence pyramid, as it analyses a larger sample size with the inclusion of different populations. However, the results of meta-analyses need to be interpreted with caution. The pre-requisites for interpreting a meta-analysis are to ensure homogenous data and good-quality studies.[4] The inclusion of observational studies may lead to bias related to confounding factors and may exaggerate the treatment effect.[5] Both the authors of the meta-analyses addressing the efficacy of NSAB and SAB acknowledge the latter limitation of their analyses.

The meta-analyses echo the findings of the PRESCRIPT trial. From the clinician's purview, even though the vasodilator requirements (secondary endpoints) were lesser for the phenoxybenzamine arm, the duration outside the target blood pressure was similar for both groups. It then translates that good intraoperative anaesthetic techniques can maintain hemodynamic stability, irrespective of the type of alpha-blocker used for preoperative blocking.

A pilot RCT comparing amlodipine with prazosin showed that the time outside the target blood pressure (primary endpoint) was significantly greater in the prazosin arm than in the amlodipine arm.[6] Furthermore, extensive studies to confirm these pilot observations and pharmacological effects of L-type calcium channel blockers on PPGL need to be carried out.

What is the way forward? There is a need for well-planned, prospective, and randomised trials. Only then, such a meta-analysis will provide impactful results that may be practice-changing.

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