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Author manuscript

*Endocr Pract.* Author manuscript; available in PMC 2019 April 23.

Published in final edited form as:

*Endocr Pract.* 2019 January ; 25(1): 106–108. doi:10.4158/EP-2018-0455.

## Why Take the Risk? We Only Live Once – The Dangers Associated with Neglecting a Preoperative Alpha Adrenoceptor Blockade in Pheochromocytoma Patients

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### Keywords

Pheochromocytoma; paraganglioma; alpha adrenoceptor blockers

Pheochromocytomas (PHEOs) are rare neuroendocrine tumors that arise from the chromaffin cells of the adrenal medulla, while their extra-adrenal chromaffin counterparts of the sympathetic ganglia are known as paraganglioma's (PGLs). PHEO/PGLs oversecrete catecholamines, which can surge to enormous levels and result in paroxysmal hypertension, diaphoresis, pallor, and tachycardia (1, 2). Surgery remains the only curative, therapeutic option for PHEO/PGLs; however, resection bears high perioperative risks and complications (3, 4).

Numerous observational, retrospective studies have reviewed perioperative morbidity, mortality, and risks associated with surgical resection of a PHEO/PGL (4–11). Recently, Groeben et al have published a consecutive case series of 276 patients who underwent surgical excision of a PHEO/PGL. Of their 276 patients, 110 were prescribed a preoperative alpha adrenoceptor blockade, while 166 were not. Results revealed no difference in maximal intraoperative systolic pressure, excessive hypertensive episodes, or major complications between the two populations (5). In accordance with their findings, Groeben et al proposed altering the current standard practice of preoperative care – an alpha adrenoceptor blocker to prevent perioperative cardiovascular complications (1). Additionally, the report warned of the significant side effects associated with alpha adrenoceptor blockade administration, including vertigo, malaise, headache, gastrointestinal distress, and postoperative hypotension and tachycardia (5). However, Isaacs and Lee hypothesized that medicinal side effects are significantly easier to control than the potentially devastating intraoperative complications to an unblocked surgical candidate from excess catecholamine release (11), and postoperative

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**Conflicts of Interest:** All Authors declare there are no conflicts of interest

hypotension secondary to an alpha adrenoceptor blockade has long been recognized, but is adequately controlled with hydration and if necessary, the administration of vasopressors. Furthermore, in a multicenter, retrospective analysis, Conzo et al discovered that when treated with preoperative doxazosin, only seven of their 48 patients experienced a perioperative hypertensive crisis, and just four patients experienced postoperative hypotension. While Conzo et al acknowledged that doxazosin did not prevent all intraoperative hypertensive crises; they credited the medication with limiting the duration of operative blood pressures greater than 180/90 mm Hg, and preventing major cardiovascular complications, which in turn allowed for low morbidity (6). Similarly, Livingston et al reported that preoperative phenoxybenzamine was a significant factor in achieving hemodynamic stability (8), and after Weingarten et al studied the relationship between preoperative hormonal levels and postoperative volume overload resulting in hypotension following surgical excision, they also recommended a preoperative alpha adrenoceptor blockade be given to all patients undergoing a PHEO/PGL resection (7).

While an alpha adrenoceptor blockade is instrumental in achieving adequate blood pressure control in the operating room, its foremost goal is avoidance of a sudden release of catecholamines during daily psychological and physical stressors, as well as from various medications and minor procedures like dental work (12, 13). Inappropriately blocked PHEO/PGL patients present to surgery with at least one sign or symptom associated with excess catecholamine release, which can escalate aforementioned cardiovascular and other organ-specific complications (14). While it is imperative adrenoceptor blockade be administered, it is just as crucial that the correct medication be prescribed. Beta adrenoceptor blockers can be added to the patients regimen following catecholamine or alpha adrenoceptor-induced tachycardia (2); however, they must only be given after the initiation of an alpha adrenoceptor blocker. In a multi-institutional retrospective cohort study, Luiz et al discovered that over a third of patients were not treated according to US Endocrine Society practice guidelines (14). Of those patients, greater than 50% were not given any pharmacological blockade, and 11% of the patients were given a beta adrenoceptor blockade as initial therapy, which can precipitate a catecholamine-induced hypertensive crisis instead of protect the patient from one (14). During anesthesia and intraoperative tumor manipulation, a physician is at the ready to counteract the detrimental effects of a hypertensive crisis; however, an alpha and beta adrenoceptor blockade can act as a safeguard when the patient is *not* in the operating room under the care of an experienced surgical staff.

We also recognize the presence of extenuating circumstances, which may prevent an idealistic plan for tumor removal. The rule of surgical divergence describes PHEO/PGL patients undergoing emergency procedures without a proper blockade or prior to PHEO/PGL excision (15). During these critical scenarios, physicians must remain vigilant and attempt to protect the patient from the potentially catastrophic consequences of circulating catecholamines with administration of an alpha adrenoceptor blockade throughout surgery, and with persistent blood pressure monitoring and correction when necessary. We also acknowledge that while the evidence used in the US Endocrine Society guideline is based purely on observational studies, their recommendations are founded on robust evidence favoring a preoperative alpha adrenoceptor blockade (1). Prospective studies identifying an appropriate population to forego adrenoceptor blockade administration do not exist.

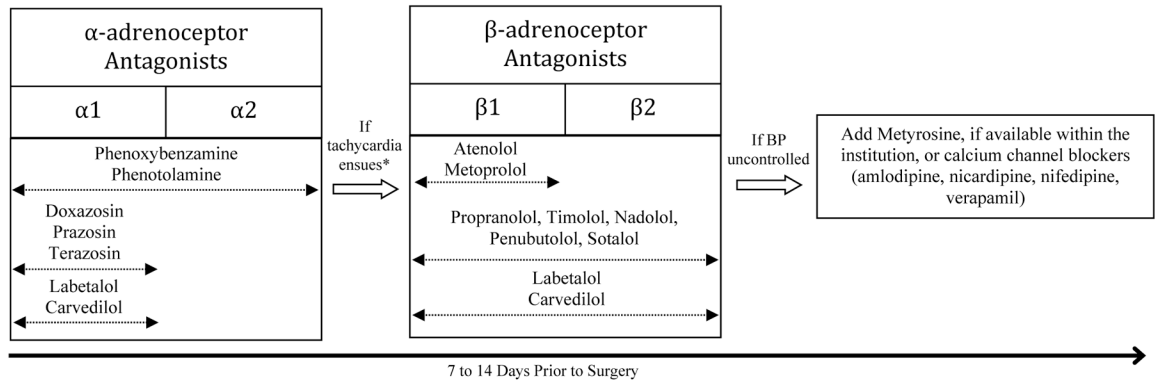
Therefore, to ensure the safety, protection, and well-being of patients, prolonged circulating catecholamines must be carefully, adequately, and appropriately managed with the current first line of medical care – an alpha adrenoceptor blockade. It is our experience and opinion that this current approach will ensure the Hippocratic oath “primum non nocere” to its best standards and values.

## Acknowledgements:

This work was supported by the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development at the National Institutes of Health, Bethesda, Maryland, USA

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**Figure 1.**  
Preferred Blockade Administration for Preoperative PHEO/PGL Patients

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