

# Comparison of phenoxybenzamine and doxazosin in perioperative management of patients with pheochromocytoma

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## Abstract

**Background:** Adrenalectomy with preoperative pharmacological preparation is strongly recommended in patients diagnosed with pheochromocytoma, in order to prevent perioperative complications.

**Aim:** To compare phenoxybenzamine (PhB) and doxazosin (DOX) in terms of perioperative haemodynamic status in patients with pheochromocytoma, who have been prepared for adrenalectomy.

**Methods:** Retrospective analysis of 44 patients with pheochromocytoma (aged 16–80 years, 29 females) who underwent adrenalectomy. Patients were divided into two groups: 35 patients on DOX and nine patients on PhB.

**Results:** Mean time of preparation for surgery was 38.8 days in the DOX group and 18.3 days in the PhB group ( $p = 0.04$ ). No statistically significant differences between the DOX and PhB groups in intraoperative blood pressure (BP) fluctuations were found:  $< 170/100$  mm Hg (34% vs. 44%, respectively,  $p = 0.42$ ),  $\geq 200/110$  mm Hg (40% vs. 22%, respectively,  $p = 0.28$ ). Mean greatest intraoperative systolic BP ( $195 \pm 53$  vs.  $166 \pm 42$  mm Hg,  $p = 0.21$ ) and diastolic BP ( $98 \pm 20$  vs.  $89 \pm 46$  mm Hg,  $p = 0.21$ ), and mean lowest intraoperative systolic BP ( $87 \pm 13$  vs.  $79 \pm 17$  mm Hg,  $p = 0.25$ ) and diastolic BP ( $49 \pm 8$  vs.  $46 \pm 12$  mm Hg,  $p = 0.60$ ) were not different between the DOX and PhB groups, respectively. Sodium nitroprusside was administered in 30% DOX vs. 11% PhB patients ( $p = 0.25$ ). Laparoscopic surgery was conducted in 97% DOX vs. 89% PhB patients ( $p = 0.64$ ). Postoperative BP drop below 90/60 mm Hg was noted in 48% of the DOX vs. 43% of the PhB group ( $p = 0.56$ ). Negative correlation was found between the length of DOX administration with maximal intraoperative systolic BP ( $r = -0.45$ ,  $p = 0.006$ ) and diastolic BP ( $r = -0.39$ ,  $p = 0.019$ ).

**Conclusions:** There are no clinically relevant differences between patients with pheochromocytoma, who have been prepared for adrenalectomy with DOX or PhB.

**Key words:** pheochromocytoma, blood pressure, adrenalectomy, doxazosin, phenoxybenzamine, alpha-adrenolytics

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## INTRODUCTION

Pheochromocytoma is a rare catecholamine-producing neuroendocrine tumour associated with high haemodynamic risk and mortality when left untreated [1]. Its management may lead to setbacks due to cardiovascular complications, e.g.

hypertension, tachycardia, dysrhythmias, hyperglycaemia, intravascular volume depletion, and others [2]. Patients treated surgically are at increased cardiac risk, especially during the intraoperative period [3]. The approach to diagnosis and surgical treatment is well described, while preoperative

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management is still controversial [4]. Recommendations strongly suggest preoperative blockade to prevent perioperative cardiovascular complications by using alpha-adrenergic receptor blockers (A-adrenolytics) as the first choice and calcium channel blockers as the second for 7–14 days prior to surgery, with or without beta-adrenergic blocking agents (B-adrenolytics) [5–7]. Alpha-blockade may be accomplished using drugs such as phenoxybenzamine (PhB) or doxazosin (DOX), each with its own pros and cons [8]. PhB blocks alpha-adrenergic receptors non-selectively, in contrast to DOX, which is a specific alpha-1 inhibitor [9]. PhB has some adverse side effects such as orthostatic hypotension, fatigue, nasal stuffiness, and tachycardia. DOX, on the other hand, does not cause baroreceptor reflex because it does not block the presynaptic alpha-2 receptors, which regulate noradrenalin release at adrenergic nerve endings [10]. PhB is the drug of choice for treating pheochromocytoma in many medical centres. In Poland, however, the availability of the drug is limited. This is why DOX has become the first-line medication in preoperative preparation of patients with pheochromocytoma.

The aim of this study was to compare the results of preoperative preparation for pheochromocytoma resection between patients with DOX vs. PhB administration in terms of perioperative blood pressure (BP) stability.

## METHODS

### Patients

A retrospective analysis was conducted using the data of 44 patients diagnosed with pheochromocytoma, who had undergone adrenalectomy in the period 2010 to 2016 at the Department of General and Endocrine Surgery, Medical University of Warsaw. Patients were qualified to the study based on histopathology report. Enrolled patients were divided into two groups: with administration of DOX ( $n = 35$ ) and PhB ( $n = 9$ ). A study flowchart is presented in Figure 1.

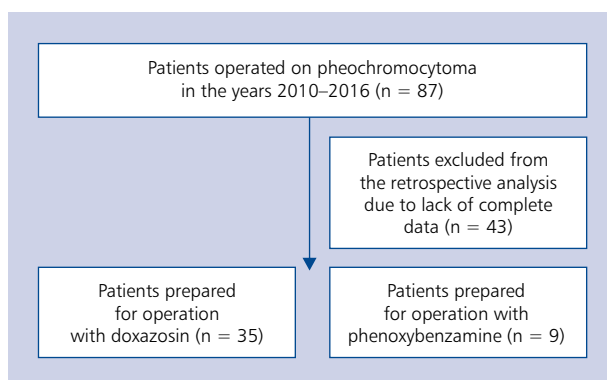


Figure 1. Study flowchart

### Study design

Collected data included preoperative patient characteristics (age, sex, body mass index, clinical manifestations), tumour characteristics (laterality, maximal dimension), two samples of 24-h urine metanephrines (24-HUM), preoperative treatment (drug administration with BP control), intraoperative characteristics (surgery technique of adrenalectomy, BP control, sodium nitroprusside requirement), and postoperative BP control. The characteristics of the study groups are shown in Table 1.

### Biochemical measurements

Urine metanephrine measurement was done by the spectrophotometric method [11]. The medication interfering with the measurements, e.g. sotolol-, labetalol-, and catecholamine-containing drugs, were withdrawn before urine collection.

### Preoperative interventions

The patients were prepared for surgery with increasing doses of DOX or PhB. The maximal doses per day were 1 mg to 12 mg of DOX and 10 mg to 60 mg of PhB. The doses were increased according to BP and heart rate (HR) control. The target BP and HR measurements while seated were below 130/80 mm Hg and 70–80 bpm, respectively. If required, the patients continued the treatment with other hypertensive drugs such as angiotensin-converting-enzyme inhibitors/angiotensin receptor blockers or calcium channel blockers.

All patients were given antihypertensive treatment in the evening one day before surgery. In the morning of the operation day the patients were left without antihypertensive medication.

All patients were prepared for surgery with intravenous (IV) 0.9% saline infusion 1–2 L in the evening before surgery and in the morning of the surgery day. B-adrenolytics were given in case of tachycardia > 80–90 bpm.

### Intraoperative interventions

Intra-arterial beat-to-beat BP measurements were done. Data were obtained by averaging for 30-s readings. The mean intraoperative BP was calculated from the induction of general anaesthesia until the end of stitching the wound after surgery.

The greatest intraoperative BP was the maximal measurement of BP between the induction of general anaesthesia until the end of stitching the wound after surgery. The lowest intraoperative BP was the minimal measurement of BP between the induction of general anaesthesia until the end of stitching the wound after surgery.

Hypotension was defined as sudden BP drop below 90/60 mm Hg and was managed with IV 0.9% saline infusion. According to institutional procedures, sodium nitroprusside was administered when a sudden BP increase by at least 30% of baseline was observed. B-adrenolytics were administered in cases of sudden HR increase.

**Table 1.** Demographic characteristic of the groups

Parameter	DOX (n = 35)	PhB (n = 9)	p
Age (years)	53 ± 14	50 ± 16	0.68
Males	12 (34%)	3 (33%)	0.64
BMI [kg/m <sup>2</sup> ]	27 ± 6	24 ± 2	0.47
Left-side tumour	11 (35%)	5 (56%)	0.24
Maximal tumour dimension [cm]	4.2 ± 1.8	4.8 ± 2.4	0.62
Time of alpha-adrenolytics administration before adrenalectomy [days]	38.8 ± 25.7	18.3 ± 10.5	0.04
Beta-adrenolytics:			
before operation	16 (46%)	2 (22%)	0.19
after operation	11 (31%)	1 (11%)	0.22
ACEI/ARB:			
before operation	3 (9%)	2 (22%)	0.24
after operation	1 (3%)	1 (11%)	0.28
Amlodipine:			
before operation	3 (9%)	2 (22%)	0.24
after operation	1 (3%)	0 (0%)	0.61
Laparoscopy	34 (97%)	8 (89%)	0.64
Laparoscopy converted to open surgery	1 (3%)	1 (11%)	0.37
Hypertension	24 (69%)	5 (56%)	0.63
Diabetes	8 (23%)	1 (11%)	0.42
Hyperlipidaemia	15 (43%)	5 (56%)	0.38

Values are presented as mean ± standard deviation or number (%); ACEI — angiotensin converting enzyme inhibitors; ARB — angiotensin receptor blockers; BMI — body mass index; DOX — group with doxazosin administration; PhB — group with phenoxybenzamine administration

### Postoperative interventions

All patients after surgery were monitored within an intensive care unit (ICU) for 12 h after surgery. BP and HR were measured every 30 min. The mean values were calculated from the whole period of ICU observation. All patients were administered IV 0.9% saline infusions.

Postoperatively, DOX or PhB were withdrawn. Other hypertensive drugs were given according to the patient's requirements.

### Outcome analyses

- The comparison between the DOX and PhB groups in terms of clinical characteristics and laboratory evaluation.
- The analysis of correlations between maximal and minimal intraoperative and minimal postoperative BP values with length of drug administration, maximal A-adrenolytics doses, maximal tumour dimension, and 24-HUM measurements in both groups.
- The intraoperative analysis of BP fluctuations assessed according to systolic BP (SBP)/diastolic BP (DBP) in three groups: < 170/100 mm Hg, 170/100–199/109 mm Hg, and ≥ 200/110 mm Hg.

### Statistical analyses

Statistica software package v.12 (StatSoft, Tulsa, OK) was used for statistical analysis. The quantitative data results were expressed as mean ± standard deviation. To quantify differences between both groups, the Mann-Whitney U test and Fisher's exact test were used. Spearman's rank test was used for correlations of ranked, quantitative variables. P < 0.05 was chosen as statistically significant.

## RESULTS

### Preoperative evaluation and interventions

Demographic characteristics of the groups are demonstrated in Table 1. Differences in presented parameters between DOX and PhB groups were not statistically significant except for longer time of A-adrenolytic administration before adrenalectomy in DOX group than in PhB. Tumour-associated symptoms were observed in 37% and 56% in the DOX and PhB groups, respectively, without statistical difference between groups (Table 2).

The doses of drugs in both groups are presented in Table 3. The maximal DOX dose was 12 mg, while PhB was 60 mg. Among our patients 34% of the DOX group reached

**Table 2.** Clinical manifestations; p = not significant

Symptoms	DOX	PhB
One or more	13 (37%)	5 (56%)
Sweats	13 (37%)	5 (56%)
Palpitations	15 (44%)	5 (56%)
Tremor	3 (9%)	1 (11%)
Headache	11 (31%)	4 (44%)
Dizziness	4 (11%)	1 (11%)
Pallor	7 (20%)	2 (22%)
Agitation	8 (23%)	1 (11%)

Values are presented as number (%); DOX — group with doxazosin administration; PhB — group with phenoxybenzamine administration

**Table 3.** Alpha adrenolytics administration

Maximal doses [mg]			
	DOX	PhB	
≤ 4	12 (34.3%)	10	1 (11.1%)
5–9	19 (54.3%)	20	7 (77.8%)
≥ 10	4 (11.4%)	60	1 (11.1%)

Values are presented as number (%); DOX — group with doxazosin administration; PhB — group with phenoxybenzamine administration

**Table 4.** 24-hour urine metanephrines measurements

	DOX (n = 35)	PhB (n = 9)	p
24 HUM 1 [ $\mu\text{g}/24\text{ h}$ ]	2344 ± 1897	1250 ± 356	NS
24 HUM 2 [ $\mu\text{g}/24\text{ h}$ ]	2067 ± 1988	2350 ± 1021	NS

Values are presented as mean ± standard deviation; 24-HUM 1 — 24-h urine metanephrines 1<sup>st</sup> measurement; 24-HUM 2 — 24-h urine metanephrines 2<sup>nd</sup> measurement; 24-h urine metanephrines measured by spectrophotometry (normal range 100–1000  $\mu\text{g}/24\text{ h}$ ); DOX — group with doxazosin administration; NS — not significant; PhB — group with phenoxybenzamine administration;

the target BP value with ≤ 4 mg/day and only 11% required a dose ≥ 10 mg. In the PhB group the highest dose of 60 mg required 11% of patients to properly control BP before surgery.

The measurements of 24-HUM showed no statistically significant differences between groups (Table 4).

### Intraoperative evaluation and interventions

The main method of adrenalectomy in this study group was laparoscopic surgery in 97% vs. 89% of patients in the DOX and PhB groups, respectively. One patient from each group had the operation converted from laparoscopic to open surgery due to tumour removal difficulty. Usage of sodium nitroprusside was without statistical difference between groups (Table 5).

**Table 5.** Intraoperative blood pressure (BP) fluctuations and intraoperative usage of sodium nitroprusside

	DOX	PhB	p
<b>SBP/DBP [mm Hg]</b>			
< 170/100	12 (34.3%)	4 (44.5%)	0.42
170/100–199/109	9 (25.7%)	3 (33.3%)	0.47
≥ 200/110	14 (40.0%)	2 (22.2%)	0.28
Usage of SN	9 (30.0%)	1 (11.1%)	0.25
<b>Greatest intraoperative BP [mm Hg]</b>			
Systolic	195.3 ± 52.7	166.1 ± 41.7	0.21
Diastolic	98.3 ± 20.0	89.4 ± 46.5	0.21
<b>Lowest intraoperative BP [mm Hg]</b>			
Systolic	86.9 ± 13.5	78.9 ± 17.5	0.25
Diastolic	49.0 ± 8.2	46.1 ± 12.4	0.61
<b>Mean intraoperative BP [mm Hg]</b>			
Systolic	123.0 ± 17.1	118.3 ± 15.9	0.68
Diastolic	69.3 ± 8.8	66.2 ± 7.1	0.34

Values are presented as number of patients (%) and mean ± standard deviation; DBP — diastolic blood pressure; DOX — group on doxazosin; SBP — systolic blood pressure; SN — sodium nitroprusside; PhB — group on phenoxybenzamine

No statistically significant differences between groups were found in terms of intraoperative BP fluctuations: highest and lowest intraoperative BP, analysis in subgroups: < 170/100 mm Hg, 170/100–199/109 mm Hg, and ≥ 200/110 mm Hg. No difference was also detected between mean SBP and DBP between groups (Table 5).

We found in the DOX group significant correlations between the length of DOX administration with intraoperative maximal SBP ( $r = -0.45$ ,  $p = 0.006$ ) and maximal intraoperative DBP ( $r = -0.39$ ,  $p = 0.019$ ) — the shorter the time of preparation the higher the BP.

A negative correlation was also detected between mean postoperative SBP and length of DOX administration ( $r = -0.35$ ,  $p = 0.04$ ).

We did not find any correlations between the maximal dose of either drug and other analysed parameters.

Among PhB patients no statistically significant correlations were found between maximal and minimal intraoperative and minimal postoperative BP values and length of drug administration, maximal tumour dimension, or 24-HUM measurements.

### Postoperative evaluation and interventions

The data are described in Table 6. There was no difference between groups in the minimal and maximal SBP noted in 12-h postoperative BP control and in postoperative BP drop below 90/60 mm Hg as well as mean SBP and DBP. None of the patients required BP-increasing drugs after surgery, apart from 0.9% saline infusion.

**Table 6.** Postoperative blood pressure (BP) measurements

BP	DOX	PhB	p
Mean SBP [mm Hg]	119.3 ± 21.1	115.9 ± 16.4	0.82
Mean DBP [mm Hg]	68.5 ± 12.1	66.8 ± 9.0	0.66
Minimal SBP [mm Hg]	99.4 ± 12.2	103.3 ± 16.6	0.47
Maximal SBP [mm Hg]	135.3 ± 30.1	127.9 ± 22.8	0.22
Postoperative BP drop below 90/60 [mm Hg]	17 (48.4%)	4 (42.9%)	0.09

Values are presented as number (%) and mean ± standard deviation; DBP — diastolic blood pressure; DOX — group on doxazosin; SBP — systolic blood pressure; PhB — group on phenoxybenzamine

## DISCUSSION

Surgical excision is the recommended method of pheochromocytoma treatment [12–14]. However, patients are at risk of haemodynamic instability before, during, and after surgery [12]. Therefore, appropriate perioperative management is warranted to prevent unnecessary complications [13]. We compared the effects of DOX and PhB in preparation for surgery. No differences were found in terms of intraoperative BP fluctuations or in postoperative BP control.

There are few studies that compare DOX and PhB in preparation pheochromocytoma for surgery, but data are equivocal. Prys-Roberts and Farndon [9] carried out a retrospective analysis on the safety and efficacy of DOX vs. PhB in operated pheochromocytoma patients and found that a lower diastolic arterial BP accompanied the administration of DOX preoperatively and intraoperatively. Weingarten et al. [15] analysed results of studies in two large United States medical centres comparing two preoperative medical management strategies for pheochromocytoma resection. At the Mayo Clinic, PhB was more likely to be used (98%), while Cleveland Clinic patients were treated more frequently with selective alpha-1 blockade (65%; doxazosin, terazosin, or prazosin). According to BP fluctuations, Cleveland Clinic patients had a greater maximal SBP intraoperatively (209 vs. 187 mm Hg,  $p = 0.01$ ). However, phenylephrine was administered more often at the Mayo Clinic (56 vs. 27%,  $p = 0.01$ ), which could have helped maintain intraoperative BP. During postoperative observations in both studies, no significant differences were found. Weingarten et al. [15] showed that management with PhB can lead to better results in the control of intraoperative BP; however, the use of PhB was associated with longer-lasting intraoperative hypotension. The mean minimal SBP we noted in 12-h postoperative BP control showed no difference between DOX and PhB patients. In another study, Agrawal et al. [16] prospectively compared the results of preoperative preparation for adrenalectomy with administration of PhB vs. prazosin and showed no significant differences in postoperative hypotensive episodes. The

minimum median SBP, however, was significantly higher in the prazosin group (71 vs. 78 mm Hg). Agrawal found PhB to be a better treatment option in achieving intraoperative haemodynamic stability. Hypertensive episodes (defined as SBP 160 mm Hg) and severe transient hypertensive crises were significantly more frequent in patients with prazosin administration. Median maximum SBP was also significantly higher in this group; 233 mm Hg compared to 181 mm Hg in PhB. Moreover, Kocak et al. [17] found no significant differences in intra- and postoperative haemodynamic status compared within three groups of patients preoperatively prepared with PhB, prazosin, or DOX. Kocak's results showed that preoperative management with administration of any of these preoperative medications is safe [17].

In our study, we found a negative correlation between the length of DOX administration and intraoperative maximal BP, which suggests that patients prepared for adrenalectomy with DOX may benefit from treatment prolongation. In both groups we did not find any significant correlations between maximal doses of drugs and maximal intraoperative SBP, DBP, or minimal postoperative SBP. We presented 14 (40%) cases in the DOX group and two (22%) cases in the PhB group, with intraoperative BP  $\geq 200$  mm Hg, whereas Li's study [13] presented with two (2%) and 10 (14%) cases, respectively. Their data showed that the intraoperative BP of the DOX group was smoothly controlled, and no hypotensive shock was present after surgery. Meanwhile 14% of PhB patients showed radical fluctuations. There was no significant difference in postoperative management.

Among our patients 34% in the DOX group reached satisfactory BP control with a dose equal to or lower than 4 mg, in comparison to 11% of patients in the PhB group on 10 mg. In Li's et al. study [13], which clearly emphasises the advantages of DOX [13], the same drug requirement was noted in 94% of patients with DOX and 7% of patients with PhB.

In our study 59% of the patients were clinically silent, i.e. without typical spells, and 34% presented also without hypertension, whereas in the cross-sectional study executed by Krane [18] on 32 pheochromocytomas diagnosed at the Henry Ford Hospital in Detroit, 11 (34%) of the cases were clinically unsuspected with atypical or asymptomatic presentation.

There were a few limitations of this study: its retrospective character, the fact that it was a single-centre study, and the relatively small number of patients.

## CONCLUSIONS

Patients with pheochromocytoma can be successfully prepared to adrenalectomy with DOX and PhB without any difference in intraoperative and postoperative BP control and additional pharmacological interventions.

Future studies should focus on confirming this observation in a larger prospective study.



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**Conflict of interest:** none declared

### References

- van der Horst-Schrivers ANA, Kerstens MN, Wolffenbuttel BHR. Preoperative pharmacological management of pheochromocytoma. *Neth J Med.* 2006; 64(8): 290–295, indexed in Pubmed: [16990692](#).
- Domi R, Laho H. Management of pheochromocytoma: old ideas and new drugs. *Niger J Clin Pract.* 2012; 15(3): 253–257, doi: [10.4103/1119-3077.100616](#), indexed in Pubmed: [22960956](#).
- Ramakrishna H. Pheochromocytoma resection: Current concepts in anesthetic management. *J Anaesthesiol Clin Pharmacol.* 2015; 31(3): 317–323, doi: [10.4103/0970-9185.161665](#), indexed in Pubmed: [26330708](#).
- Lentschener C, Gaujoux S, Tesniere A, et al. Point of controversy: perioperative care of patients undergoing pheochromocytoma removal-time for a reappraisal? *Eur J Endocrinol.* 2011; 165(3): 365–373, doi: [10.1530/EJE-11-0162](#), indexed in Pubmed: [21646289](#).
- Lenders JWM, Duh QY, Eisenhofer G, et al. Endocrine Society. Pheochromocytoma and paraganglioma: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab.* 2014; 99(6): 1915–1942, doi: [10.1210/jc.2014-1498](#), indexed in Pubmed: [24893135](#).
- Bednarczuk T, Bolanowski M, Sworcak K, et al. Adrenal incidentaloma in adults - management recommendations by the Polish Society of Endocrinology. *Endokrynol Pol.* 2016; 67(2): 234–258, doi: [10.5603/EP.a2016.0039](#), indexed in Pubmed: [27082051](#).
- Mazza A, Armigliato M, Marzola MC, et al. Anti-hypertensive treatment in pheochromocytoma and paraganglioma: current management and therapeutic features. *Endocrine.* 2014; 45(3): 469–478, doi: [10.1007/s12020-013-0007-y](#), indexed in Pubmed: [23817839](#).
- Pacak K. Preoperative management of the pheochromocytoma patient. *J Clin Endocrinol Metab.* 2007; 92(11): 4069–4079, doi: [10.1210/jc.2007-1720](#), indexed in Pubmed: [17989126](#).
- Prys-Roberts C, Farndon JR. Efficacy and safety of doxazosin for perioperative management of patients with pheochromocytoma. *World J Surg.* 2002; 26(8): 1037–1042, doi: [10.1007/s00268-002-6667-z](#), indexed in Pubmed: [12192533](#).
- Zhu Yu, He Hc, Su Tw, et al. Selective 1-adrenoceptor antagonist (controlled release tablets) in preoperative management of pheochromocytoma. *Endocrine.* 2010; 38(2): 254–259, doi: [10.1007/s12020-010-9381-x](#), indexed in Pubmed: [21046486](#).
- Pisano JJ. A simple analysis for normetanephrine and metanephrine in urine. *Clin Chim Acta.* 1960; 5: 406–414, indexed in Pubmed: [14433251](#).
- Mannelli M. Management and treatment of pheochromocytomas and paragangliomas. *Ann N Y Acad Sci.* 2006; 1073: 405–416, doi: [10.1196/annals.1353.044](#), indexed in Pubmed: [17102109](#).
- Li J, Yang CH. Improvement of preoperative management in patients with adrenal pheochromocytoma. *Int J Clin Exp Med.* 2014; 7(12): 5541–5546, indexed in Pubmed: [25664068](#).
- Conzo G, Musella M, Corcione F, et al. Laparoscopic adrenalectomy, a safe procedure for pheochromocytoma. A retrospective review of clinical series. *Int J Surg.* 2013; 11(2): 152–156, doi: [10.1016/j.ijssu.2012.12.007](#), indexed in Pubmed: [23267853](#).
- Weingarten TN, Cata JP, O'Hara JF, et al. Comparison of two preoperative medical management strategies for laparoscopic resection of pheochromocytoma. *Urology.* 2010; 76(2): 508.e6–508.11, doi: [10.1016/j.urology.2010.03.032](#), indexed in Pubmed: [20546874](#).
- Agrawal R, Mishra SK, Bhatia E, et al. Prospective study to compare peri-operative hemodynamic alterations following preparation for pheochromocytoma surgery by phenoxybenzamine or prazosin. *World J Surg.* 2014; 38(3): 716–723, doi: [10.1007/s00268-013-2325-x](#), indexed in Pubmed: [24233658](#).
- Kocak S, Aydintug S, Canakci N. Alpha blockade in preoperative preparation of patients with pheochromocytomas. *Int Surg.* 2002; 87(3): 191–194, indexed in Pubmed: [12403097](#).
- Krane NK. Clinically unsuspected pheochromocytomas. Experience at Henry Ford Hospital and a review of the literature. *Arch Intern Med.* 1986; 146(1): 54–57, indexed in Pubmed: [3942465](#).

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# Porównanie doksazosyny i fenoksybenzaminy w przygotowaniu do leczenia operacyjnego guza chromochłonnego

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## Streszczenie

**Wstęp:** Główną trudnością w przygotowaniu pacjenta z guzem chromochłonnym do adrenalektomii jest stabilizacja układu sercowo-naczyniowego w trakcie oraz po operacji. Dlatego też farmakologiczne przygotowanie chorego stanowi nadal wyzwanie dla klinicystów. Odpowiednia podaż leków ma za zadanie zapobiec niepożądanym skutkom wzrostów i spadków ciśnienia śród- oraz pooperacyjnych.

**Cel:** Celem pracy było porównanie skuteczności leczenia doksazosyną (DOX) i fenoksybenzaminą (PhB) w prewencji niestabilności hemodynamicznej u pacjentów przygotowywanych do operacji guza chromochłonnego.

**Metody:** Retrospektywną analizą objęto 44 chorych (16–80 lat, 29 kobiet) operowanych z powodu guza chromochłonnego, w tym 35 pacjentów leczonych DOX oraz 9 osób stosujących PhB.

**Wyniki:** Średni czas przygotowania farmakologicznego do operacji w grupie DOX wynosił 38,8 dnia vs. 18,3 dnia w grupie PhB ( $p = 0,04$ ). Nie odnotowano istotnych statystycznie różnic między DOX i PhB w śródoperacyjnym pomiarze ciśnienia tętniczego (BP) w zakresach  $< 170/100$  mm Hg (34% vs. 44%,  $p = 0,42$ ) oraz  $\geq 200/110$  mm Hg (40% vs. 22%,  $p = 0,28$ ); w zakresie średniego najwyższego skurczowego BP ( $195 \pm 53$  vs.  $166 \pm 42$ ,  $p = 0,21$ ) i rozkurczowego BP ( $98 \pm 20$  vs.  $89 \pm 46$ ,  $p = 0,21$ ); średniego najniższego skurczowego BP ( $87 \pm 13$  vs.  $79 \pm 17$ ,  $p = 0,25$ ) i rozkurczowego BP ( $49 \pm 8$  vs.  $46 \pm 12$ ,  $p = 0,60$ ). Z powodu wzrostu ciśnienia nitroprusydek sodu stosowano u 30% pacjentów z grupy DOX i u 11% osób z grupy PhB ( $p = 0,25$ ). Adrenalektomię drogą laparoskopową wykonano u 97% chorych z grupy DOX i u 89% pacjentów z grupy PhB ( $p = 0,64$ ). Odnotowano pooperacyjną hipotensję  $< 90/60$  mm Hg u 48% chorych z grupy DOX i u 43% osób z grupy PhB ( $p = 0,56$ ). Ujemną, statystycznie istotną korelację stwierdzono między długością przyjmowania DOX a najwyższym śródoperacyjnym skurczowym BP ( $r = -0,45$ ;  $p = 0,006$ ) oraz rozkurczowym BP ( $r = -0,39$ ;  $p = 0,019$ ).

**Wnioski:** Nie zaobserwowano istotnych klinicznie różnic między wynikami chorych przygotowywanych do operacji za pomocą DOX oraz PhB.

**Słowa kluczowe:** guz chromochłonny, ciśnienie tętnicze, adrenalektomia, doksazosyna, fenoksybenzamina, alfa-adrenolityki

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