Systematic Review and Meta-analysis

Pre-Operative Selective vs Non-Selective α-Blockade in Pheochromocytoma–Paraganglioma Patients Undergoing Surgery: A Meta-Analysis

Sanjay K. Yadav, Goonj Johri[1], Chandan K. Jha[2], Sanjeet Kumar Jaiswal[3], Saket Shekhar[4], Vivek V. Kumar, Saroj K. Mishra[5]

Department of Surgery, NSCB Medical College, Jabalpur, Madhya Pradesh, India, [1]Department of Breast Surgery, Wythenshawe Hospital and Nightingale Breast Centre, Manchester University Foundation Trust, United Kingdom, Departments of [2]Surgery and [4]Biostatistics, All India Institute of Medical Sciences, Patna, Bihar, India, [3]Department of Endocrinology, KEM Hospital, Mumbai, Maharashtra, India, [5]Department of Endocrine Surgery, SGPGIMS, Lucknow, Uttar Pradesh, India

Abstract

The main objective of this systematic review and meta-analysis was to review, assess and report on the studies that have evaluated selective alpha blockade (SAB) vs. non-selective alpha blockade (NSAB) therapy in patients undergoing surgery for pheochromocytomas and paragangliomas (PPGL). We performed a systematic search of electronic databases. A meta-analysis was conducted to examine the effectiveness of the two blockades. RevMan 5.3 was used for the meta-analysis. Of the eight articles that met the inclusion criteria, there was only one randomized control trial. Meta-analysis showed that there was no significant difference between the groups SAB and NSAB with regard to intra-operative systolic blood pressure (SBP) >160 mm Hg (relative risk (RR) 0.95 [95% CI 0.57, 1.56] *P* = 0·83) and intra-operative vasopressor requirement (RR 1.10 [95% CI 0.96, 1.26] *P* = 0·16). Meta-analysis revealed that there was a significant difference between the groups (SAB vs NSAB) with respect to post-operative vasopressor requirement (RR 1.66 [95% CI 1.0, 2.74] *P* = 0·05). There was no significant difference between the groups with respect to post-operative complications (RR 0.84 [95% CI 0.58, 1.22] *P* = 0·36). In conclusion, as patients blocked selectively may have a higher incidence of vasodilator requirement intra-operatively, NSAB offers some haemodynamic advantage over SAB. However, NSAB's real clinical benefit cannot be ascertained with the current studies as this difference did not result in any significant advantage over SAB with regard to morbidity or mortality.

Keywords: Non-selective alpha-blockers, paraganglioma, pheochromocytoma, selective alpha-blockers

Abstract based on this research was presented as an oral presentation at the Royal Australasian College of Surgeons Annual Scientific Congress 2021, Melbourne, Australia.

Introduction

Pheochromocytomas and paragangliomas (PPGLs) are catecholamine-secreting tumours originating from chromaffin cells of the adrenal medulla and paraganglia.[1] Surgical resection is the only curative option for PPGLs. However, manipulation of the tumour during surgery may result in life-threatening cardiovascular events.[2] For prevention of these life-threatening events, the endocrine society has recommended that all patients with a hormonally functional PPGL should undergo pre-operative blockade (α-adrenergic receptor blockers as the first choice).[3] There are two types of α-blockers - selective and non-selective. Non-selective alpha-adrenergic blockers, e.g., phenoxybenzamine (PBZ) cause vasodilation by blocking both alpha-1 and alpha-2 receptors. However, PBZ causes non-competitive and irreversible alpha blockade and can lead to post-operative hypotension.[4,5] On the other hand, selective alpha-blockers such as doxazosin, terazosin and prazosin are competitive and short-acting α1-receptor blockers. The short-acting effect

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Address for correspondence: Dr. Sanjay K. Yadav, Assistant Professor of Surgery, Netaji Subhash Chandra Bose Medical College, Jabalpur, Madhya Pradesh, India. E-mail: sky1508@gmail.com

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decreases the risk of post-operative hypotension but as a result of competitive property, there is more risk of intra-operative haemodynamic instability (HDI).[4,5]

The main objective of this systematic review and meta-analysis was to review, assess and report on the studies that have evaluated selective alpha blockade (SAB) vs. non-selective alpha blockade (NSAB) therapy in patients undergoing surgery for PPGL with regard to perioperative haemodynamic stability and mortality.

Methods

A protocol was developed a priori by the reviewers and was registered at PROSPERO database, identifier: CRD42020177486.

Search Strategy: The first (GJ) and second (SKY) authors designed a search protocol to identify evidence relevant to this review. We systematically searched the following electronic databases: PubMed, EMBASE, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews from inception till 30 September 2020.

We also searched the reference lists of included studies and previous reviews in this field. The first step of the screening process was carried out by two reviewers (SKY and GJ) independently, which involved reading the titles and the abstracts using broad criteria. Each study was coded as eligible, ineligible or doubtful. The full text was reviewed for articles that were designated as 'eligible' or 'doubtful' by either reviewer. All disagreements were resolved via discussion amongst authors through online consultation.

Inclusion criteria:

1. Study designs: Clinical trials, prospective cohort studies, observational studies and retrospective studies (Preliminary search by the reviewers did not result in any trials and very few prospective studies. Hence retrospective studies were also included)
2. Participants: Patients with PPGL undergoing surgery and receiving pre-operative alpha blockade
3. Intervention: SAB
4. Comparison: NSAB
5. Outcome: Perioperative HDI and perioperative mortality.

Exclusion criteria:

1. Study designs: Reviews, meta-analysis, case reports and case series (patients equal to or less than eight in any arm), studies whose primary aim was something other than to compare outcome differences between SAB and NSAB
2. Participants: Patients not undergoing surgery and not receiving pre-operative alpha blockade
3. Intervention/comparison: Studies that have used only one type of alpha blockade and not compared the outcome between two groups
4. Outcome: Studies that have not reported the outcome in terms of haemodynamic stability and perioperative mortality.

Risk of bias assessment: The Downs and Black assessment tool was used to assess the methodological quality of the included studies by two reviewers (SKY and SKJ).[6] Any disagreement was resolved by a third reviewer (GJ).

Data Extraction, Analysis and Synthesis:
Data extraction was carried out by the second author (SKY) and independently adjudicated by one other reviewer (GJ) using a pilot data extraction form developed to address the research question. Disagreements were resolved by discussion among the reviewers. The data that were extracted included the study design, method of the alpha blockade, number of patients included, the demographic and clinical details of the patients, primary perioperative outcome HDI systolic blood pressure (SBP) >160 mm Hg) and additional outcomes such as maximum intra-operative SBP and diastolic blood pressure (DBP) between the two groups, lowest intra-operative SBP and DBP between the two groups, the minimum and maximum heart beat rate (HBR) between the two groups, perioperative complication directly related to catecholamine crisis (atrial fibrillation/flutter, acute heart failure, mortality, etc.) and use of vasodilators or inotropes.

Results of the included studies were grouped based on the different study designs. Then, based on the pre-operative blockade approach (SAB vs NSAB), the data were aggregated and analysed in the different study designs. Qualitative analysis was carried out to present what has been done in the field and identify gaps in the literature for future research plans.

Where feasible, a meta-analysis was conducted to estimate a pooled weighted relative risk (RR). Pooling was planned a priori when statistical heterogeneity, assessed by the $I2$ statistics, was <50%.[7] RevMan 5.3 was used for the meta-analysis.

Results

The literature search

Our preliminary database search yielded 39 records and a hand search of relevant articles, and previous systematic reviews added 1 more record. After the removal of duplicates, 39 records were identified for the first step of the screening process. Through our initial screening of titles and abstracts, 28 records were excluded [Figure 1].

Of the 10 articles that met the inclusion criteria, one was randomized control trial, one prospective case-control study and the remaining eight were retrospective studies.[8-17] All 10 studies included in this review scored from 10 to 20 (out of 31) on the risk of bias assessment tool; most of the studies scored low on the power criterion as there was less number of patients included. On reporting and selection bias, all the studies scored an average or above average. Eight of the studies failed to reach an average score on confounding bias, with the exception being Agarwal *et al.*[8] and Buitenwerf *et al.*,[9] which scored 3 and 5, respectively. Table 1 summarizes the results of the risk of bias assessment.

Qualitative review of included studies

Table 2 summarizes the study characteristics. Agrawal *et al.*[8] conducted a prospective case-control study in India which included 15 patients in SAB and 17 patients in the NSAB group. The authors concluded that NSAB was superior to SAB in controlling intra-operative haemodynamic fluctuations as patients in the SAB group had significantly more intra-operative episodes of transient hypertension (SBP >160 mm Hg) and hypertensive urgency (blood pressure (BP) [180/110 mm Hg]). However, no significant differences were found between the study groups for changes in HBR, post-operative BP alterations, the occurrence of arrhythmias and time taken to achieve haemodynamic stability or post-operative mortality. Buitenwerf *et al.*[9] conducted a randomized controlled trial (RCT). The study had 66 patients in the NSAB group and 68 in the SAB group. In this study too SBP >160 mm Hg was not statistically different between the two groups. The authors also calculated a haemodynamic instability (HI) score which

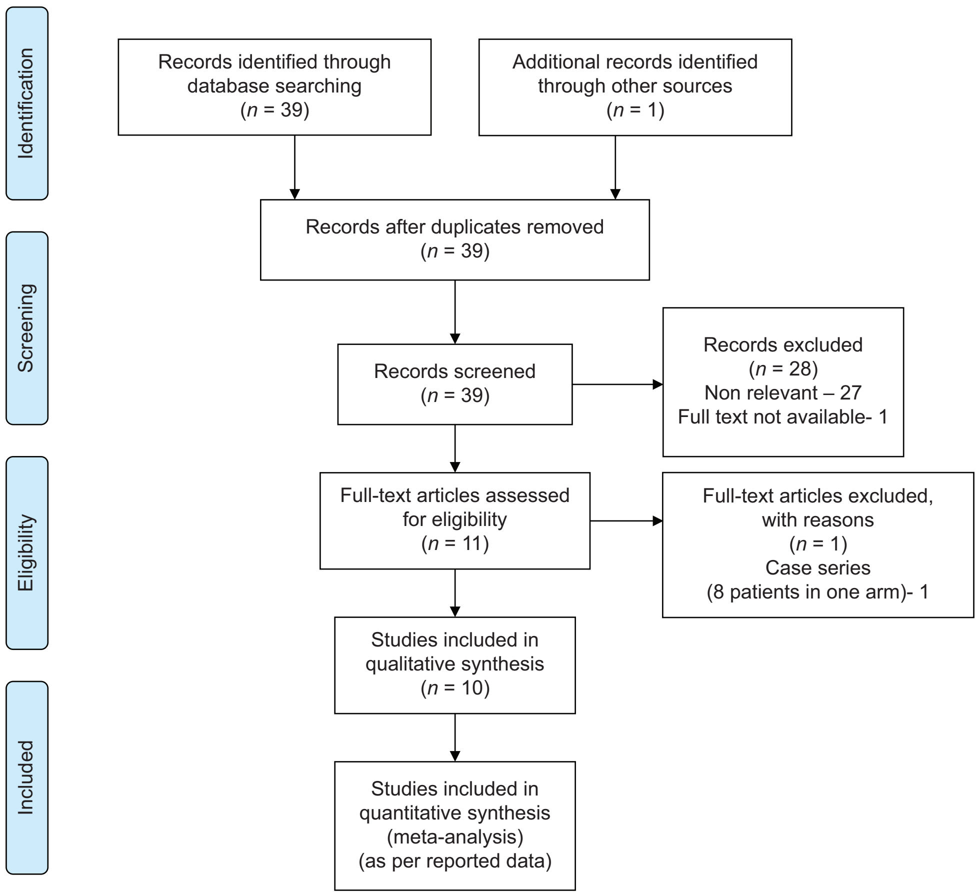

Figure 1: Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram

Table 1: Results of the risk of bias assessment using the Downs and Black assessment tool

Study	Reporting (10)	External validity (3)	Bias (7)	Confounding (6)	Power (5)	Total (31)
Agrawal *et al.*[8]	8	0	5	3	0	16
Buitenwerf *et al.*[9]	8	1	5	5	1	20
C. Liu *et al.*[10]	7	0	3	2	0	12
Keirnan *et al.*[11]	5	0	3	2	0	10
Malec *et al.*[12]	6	0	3	1	0	10
Randle *et al.*[13]	5	0	3	2	0	10
Li *et al.* [14]	5	0	3	2	0	10
Zhu *et al.*[15]	5	0	3	2	0	10
Kong *et al.*	6	0	3	2	0	11
Bruynzeel *et al.*	5	0	3	2	0	10

Downs and Black score ranges were given corresponding quality levels: excellent (26-28); good (20-25); fair (15-19); and poor (≤14).” Published in: Age-related macular degeneration and low-vision rehabilitation: a systematic review

Table 2: Study characteristics

Author, year, country of origin	Study design	Arms	Sample Size	Main finding	Comment
Agarwal *et al*.[8] India, 2013	Prospective non-randomized case control	2	SAB- 13 NSAB-14	Patients prepared with SAB had significantly more intra-operative episodes of transient hypertension (SBP 160 mm Hg) and hypertensive urgency (BP [180/110 mm Hg]). Conclusion: NSAB was found superior to SAB in having fewer intra-operative haemodynamic fluctuations.	NSAB superior over SAB in controlling intra-operative HDI
Buitenwerf *et al*.[9] Netherlands, 2019	Randomized controlled open-label trial	2	SAB-68 NSAB- 66	Authors calculated a HI score which consists of three intra-operative components: haemodynamic variables (i.e., BP and heart rate), cumulative dosage of vasoactive medication and fluid therapy. The HI score was significantly worse in doxazosin group (50.0 [35.3-63.8]) as compared to PBZ group (38.0 [28.8-58.0]) Conclusion: PBZ was more effective in preventing intra-operative HDI, but it could not be established whether this was associated with a better clinical outcome.	NSAB superior over SAB in controlling intra-operative HDI
C Liu *et al*.[10] China, 2017	Retrospective	2	SAB-149 NSAB-377	Patients in the NSAB group showed a more significant decline in post-operative SBP than the SAB group (P=0.041). No other significant difference between the two groups. Conclusion: Authors did not find any significant difference in intra-operative HDI, post-operative recovery and post-operative complications between groups	No difference between two groups
Kiernan *et al*.[11] USA, 2014	Retrospective	2	SAB-16 NSAB-71	SAB were associated with an increased number of episodes of SBP >200 mm Hg (RR 20.9). There were no differences in other HDI measurements or post-operative outcomes among the blockade groups. Conclusion: Selective blockade was associated with significantly more episodes of intra-operative hypertension but no perioperative adverse outcomes	NSAB superior over SAB in controlling intra-operative HDI
Malec *et al*.[12] Poland, 2017	Retrospective	2	SAB-35 NSAB-9	No statistically significant differences between the SAB and NSAB groups in intra-operative BP fluctuations were found. Mean greatest intra-operative SBP and mean lowest intra-operative SBP and DBP were not different between the groups. Conclusion: There are no clinically relevant differences between SAB and NSAB	No difference between two groups
Randle *et al*.[13] USA, 2016	Retrospective	2	SAB-18, NSAB-34	No significant difference in overall intra-operative haemodynamics between patients blocked selectively and non-selectively. However, post-operatively, patients blocked selectively were more likely to require additional support with vasopressor infusions in the PACU or ICU admission	No difference in intra-operative HDI. But post-operatively patients in SAB group required vasopressor support
Li J *et al*.[14] China, 2014	Retrospective	2	SAB-85, NSAB-70	In doxazosin group, two patients had radical fluctuations in SBP during surgery, as compared to PBZ in which 10 patients had radical fluctuations. No hypertensive crisis and hypotensive shock appeared after surgery in both groups. Compared with PBZ, doxazosin has better haemodynamic control.	SAB superior over NSAB in controlling intra-operative HDI
Zhu *et al*.[15] China, 2010	Retrospective	2	SAB-36, NSAB-31	Systolic arterial pressures both before and after induction of anaesthesia were all significantly higher in the SAB patients than in the NSAB. The fluctuation of systolic arterial pressure during operation was more stable in SAB group than in NSAB group	SAB superior over NSAB in controlling intra-operative HDI
Kong *et al*.	Retrospective propensity matched	2	SAB-89, NSAB-89	NSAB had lower time weighted average-SBP >160 and lower highest SBP during surgery than SAB. Post-operative outcomes did not differ significantly between the two groups.	NSAB superior over SAB in controlling intra-operative hypertension
Bruynzeel *et al*.	Retrospective	2	SAB-42, NSAB-31	There was no significant difference in BP fluctuations intra-operatively with respect to both hypertensive and hypotensive episodes. No relation was found between the SAB or NSAB dosage and intra-operative BP fluctuations or post-operative hypotension.	No difference between two groups

consisted of three intra-operative components: haemodynamic variables (i.e., BP and heart rate), a cumulative dosage of vasoactive medication and fluid therapy. The HI score was significantly worse in the SAB group (50.0 [35.3–63.8]) as compared to the PBZ group (38.0 [28.8–58.0]). Kiernan *et al.*[11] too evaluated HI score in a retrospective study involving 91 patients (NSAB 71, SAB 16). HI score was significantly poor in the SAB group. However, this did not result in increased perioperative cardiovascular morbidity or mortality in the SAB group in both studies. Malec *et al*.[12] evaluated 44 patients undergoing adrenalectomy for PPGL (NSAB 9, SAB 35). No statistically significant differences between the SAB and NSAB groups in intra-operative BP fluctuations were found: <170/100 mm Hg (34% vs. 44%, respectively), ≥200/110 mm Hg (40% vs. 22%). Mean greatest intra-operative SBP (195 ± 53 vs. 166 ± 42 mm Hg) and DBP (98 ± 20 vs. 89 ± 46 mm Hg), and mean lowest intra-operative SBP (87 ± 13 vs. 79 ± 17 mm Hg) and DBP (49 ± 8 vs. 46 ± 12 mm Hg) were not different between the SAB and NSAB groups, respectively. Perioperative morbidity and mortality were the same.

Randle *et al.*[13] retrospectively identified 52 (SAB 18, NSAB 34) patients undergoing unilateral laparoscopic adrenalectomy for pheochromocytoma (PCC). They found no significant difference in the overall intra-operative haemodynamic between patients blocked selectively and non-selectively. However, post-operatively, patients blocked selectively were more likely to require additional support with vasopressor infusions in the post-anaesthesia care unit (PACU) or intensive care unit (ICU) admission. There was no significant difference in perioperative complications.

Liu *et al.*[10] did a retrospective review in which 149 patients received SAB and 377 patients NSAB. In this study, intra-operative BP fluctuation was more in the NSAB group (4.4%) as compared to the SAB group (3.4%) but it was not significant. The average mean post-operative SBP was 123 mm Hg (± 21) in the SAB group, and 107 mm Hg (± 23) in the NSAB group. Overall, patients in the NSAB group had significantly more obvious decline than in SAB.

Zhu *et al.*[15] evaluated 67 patients, 36 in SAB and 31 in the NSAB group. In contrast to previous studies, they found that systolic arterial pressures both before and after induction of anaesthesia were all significantly higher in the doxazosin patients than in the PBZ group. After the tumour was removed, the lowest systolic arterial pressure was significantly higher in the doxazosin group than in the PBZ group. They did not provide post-operative outcome data.

Li *et al.*[14] retrospectively analysed data of 155 patients (NSAB 70, SAB 85). They reported that in the doxazosin group, two patients had radical fluctuations in SBP during surgery, as compared to PBZ in which 10 patients had radical fluctuations. No hypertensive crisis and hypotensive shock appeared after surgery in both groups. Compared with PBZ, doxazosin has better haemodynamic control. Kong *et al.*[16] performed a retrospective propensity-matched analysis involving 89 patients in each NSAB and SAB group. They reported that NSAB was superior in controlling intra-operative hypertension. Bruynzeel *et al.*[17] did not find any difference in the two groups in their retrospective analysis.

Four studies[8,9,11,16] concluded that NSAB was better over SAB in controlling intra-operative HDI. While two studies[14,15] reported SAB to be superior over NSAB in controlling intra-operative instability. Four other studies[10,12,13,17] did not find any difference.

Meta-analysis

Intra-operative SBP >160 mm Hg

Four studies evaluated the proportion of patients whose SBP went above 160 mm Hg during surgery. A total of 201 patients were in the SAB group and 159 in the NSAB group. There was no significant difference between the groups (RR 0.95 [95% CI 0.57, 1.56] $P = 0{\cdot}83$) [Figure 2]. Statistical heterogeneity was detected between the two groups ($I^2 = 79\%$, $P = 0{\cdot}003$) and so a random-effects model was employed.

Intra-operative SBP >200 mm Hg

Four studies evaluated the proportion of patients whose SBP went above 200 mm Hg during surgery. A total of 151 patients were in the SAB group and 127 in the NSAB group. There was no significant difference between the groups (RR 1.31 [95% CI 0.69, 4.42] $P = 0{\cdot}66$) [Figure 3]. Statistical heterogeneity was detected between the two groups ($I^2 = 75\%$, $P = 0{\cdot}008$) and so a random-effects model was employed.

Intra-operative HR (>120/min): Only two studies provided data on intra-operative HBR. Agrawal *et al.*[8] defined tachycardia as HR >120/min and Buitenwerf *et al.*[9] defined it as HR >100/min. Hence meta-analysis could not be performed.

Intra-operative mean SBP and DBP: Most studies reported mean and only a few reported median. Median SBP and DBP give a better idea than mean hence meta-analysis was not performed.

Intra-operative vasopressor and vasodilator support

Four studies evaluated the proportion of patients requiring vasopressor and vasodilator support during surgery. A total of 115 patients were in the SAB group and 185 in the NSAB group. There was no significant difference between the groups with respect to intra-operative vasopressor requirement (RR 1.10 [95% CI 0.96, 1.26] $P = 0{\cdot}16$) [Figure 4]. Statistical heterogeneity was not detected between the two groups ($I^2 = 0\%$, $P = 0{\cdot}78$). A random-effects model was employed. However, there was a significant difference between the groups with respect to intra-operative vasodilator requirement (RR 1.36 [95% CI 1.13, 1.62] $P = 0{\cdot}0008$) [Figure 5]. Statistical heterogeneity was not detected between the two groups ($I^2 = 0\%$, $P = 0{\cdot}67$). A random-effects model was employed.

Post-operative vasopressor support

Three studies evaluated the proportion of patients requiring vasopressor support in the post-operative period. A total of 47 patients were in the SAB group and 119 in the NSAB group. There was no significant difference between the groups with respect to post-operative vasopressor requirement (RR 1.66 [95% CI 1.0, 2.74]

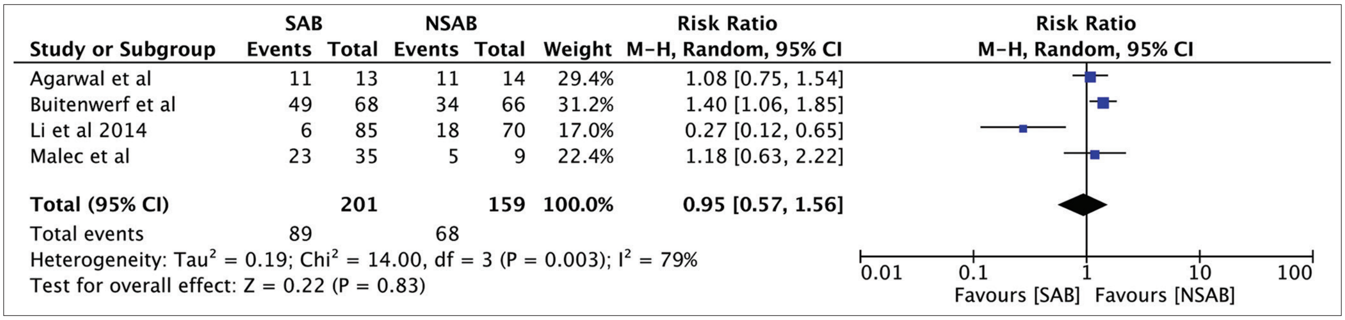

Figure 2: Forest plot for SBP > 160 mmHg comparing SAB and NSAB

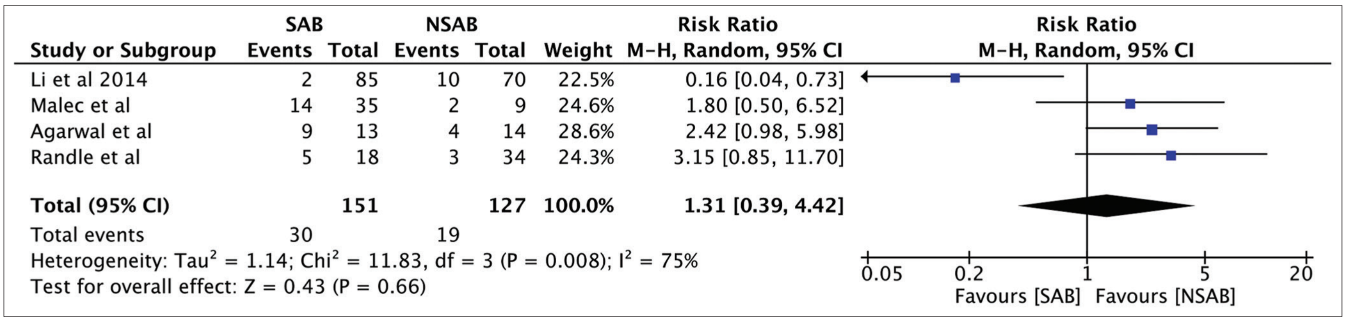

Figure 3: Forest plot for SBP > 200 mm Hg comparing SAB and NSAB

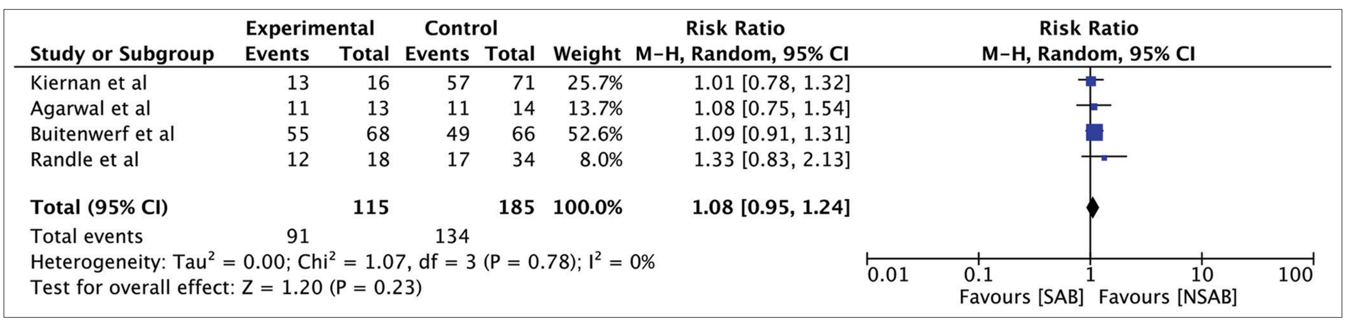

Figure 4: Forest plot for intra-operative vasopressor requirement comparing SAB and NSAB

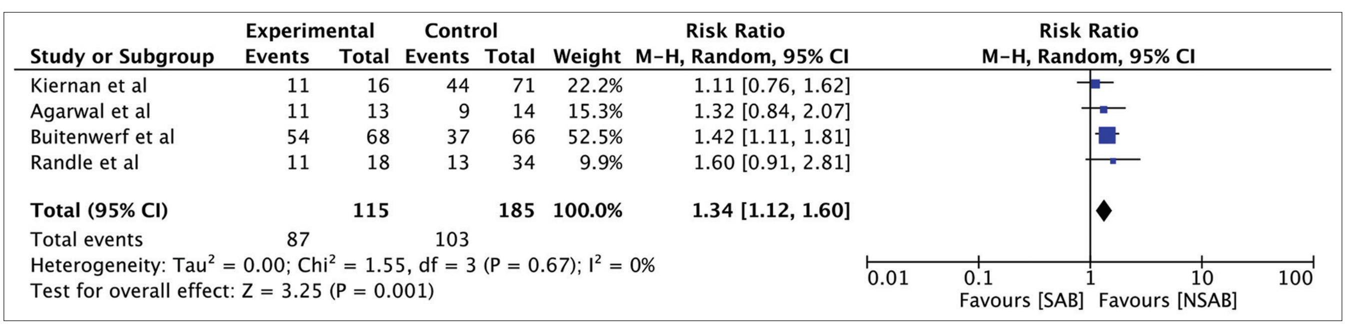

Figure 5: Forest plot for intra-operative vasodilator requirement comparing SAB and NSAB

P = 0·05) [Figure 6]. Statistical heterogeneity was not detected between the two groups (I^2 = 0%, P = 0·62). A random-effects model was employed. We did not include only RCT by Buitenwerf *et al.*[9] in this meta-analysis, as they have defined post-operative hypotension as a mean arterial BP <60 mm Hg. While others had different endpoints (SBP <80 mm Hg).

Post-operative complications

Five studies reported on the post-operative cardiovascular event. A total of 268 patients were in the SAB group and 530 in the NSAB group. There was no significant difference between the groups with respect to post-operative cardiovascular events (RR 0.84 [95% CI 0.58, 1.22] P = 0·36) [Figure 7]. Statistical heterogeneity was not detected between the two

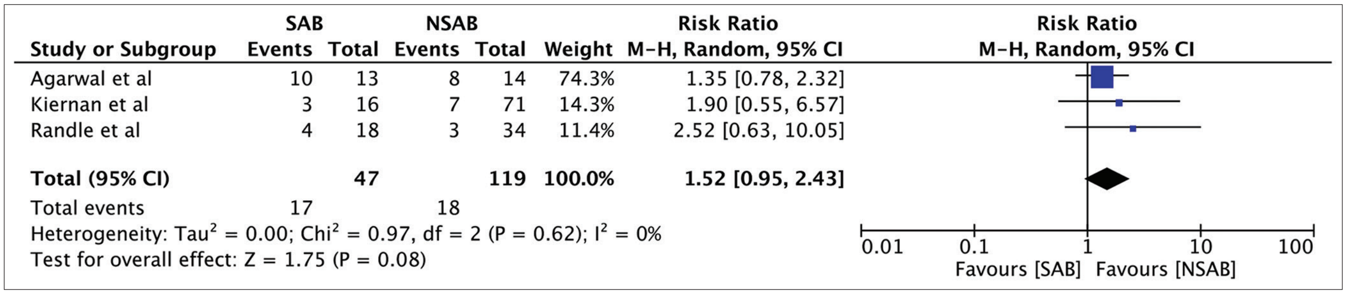

Figure 6: Forest plot for post-operative vasopressor requirement comparing SAB and NSAB

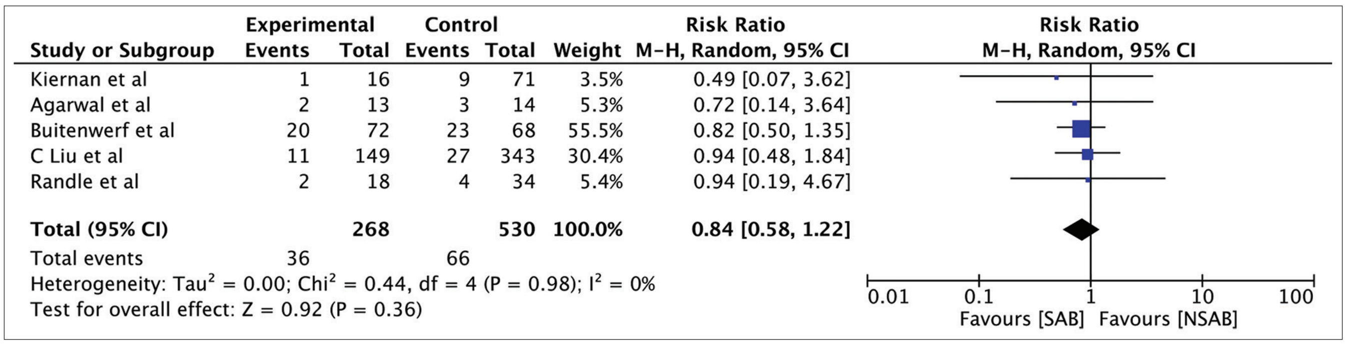

Figure 7: Forest plot for post-operative cardiovascular events comparing SAB and NSAB

groups (I^2 = 0%, *P* = 0·98). A random-effects model was employed.

Discussion

A qualitative review of the included studies showed four studies concluded NSAB to be superior over SAB in offering intra-operative haemodynamic advantage while two studies concluded vice versa. When we performed a meta-analysis, pooled estimates did not reveal any significant intra-operative haemodynamic advantage of NSAB over SAB except for the requirement of vasodilators favouring NSAB. However, due to the lack of any RCTs, we could not come to any conclusions with regard to the preferred mode of the blockade, which can result in lower morbidity and mortality.

Although surgical resection is the definitive treatment of PPGLs, the importance of pre-operative optimization in reducing perioperative morbidity and mortality cannot be overemphasized.[18] This primarily entails control of hypertension and expansion of vascular volume. Hypertension is primarily caused by alpha-1-mediated vasoconstriction and beta-1-mediated tachycardia and inotropy.[19] Pre-operative alpha-blockade, along with fluid and salt intake, is recommended by the Endocrine Society Clinical Guidelines Subcommittee for patients undergoing PCC and paraganglioma (PGL) resection.[20]

There is no consensus, however, over the preferred alpha-blocker (selective vs. non-selective) to be used. PBZ causes irreversible inactivation of both alpha- 1 and 2 receptors by forming covalent bonds with the receptor molecule. For its effect to be reversed, new receptors need to be formed which may take up to 24–48 h after stopping the drug. This implies better control of intra-operative haemodynamics but a higher incidence of post-operative hypotension requiring vasopressor infusion. Selective alpha-1 blockers (prazosin, doxazocin and terazosin) preferentially antagonize alpha-1 receptors resulting in vasodilatation and hypotension, which is not sustained due to the reversible nature of blockade. This review also showed that patients blocked with SAB had a higher incidence of intra-operative SBP >160 mm Hg and heart rate (although not statistically significant) as compared to NSAB.

Proponents for and against the use of NSAB over SAB and vice versa exist but there is no conclusive evidence to prove[19,20] or disprove[21] either school of thought due to the unavailability of high-quality data and RCTs. Interestingly, a more interesting question is whether the alpha blockade is required at all.[22,23] A recent multicentre retrospective study showed that the cardiovascular complication rate was 5·9% (90 of 1517) in patients with pre-operative α-receptor blockade and 0·9% (3 of 343) among patients without α-receptor blockade.[23] However, most of the patients without an α-receptor blockade were from a single centre in this study, and this puts a question whether the two groups of patients from this centre were different in their characteristics.[23] On the other hand, most evidence points towards decreased intra- and post-operative cardiovascular complications after some form of an alpha blockade.[1] In this meta-analysis also, parameters like SBP >160 mm Hg, SBP >200 mm Hg, intra-operative vasopressor requirement and cardiovascular events were similar between the two groups. The findings of this meta-analysis are in agreement with van der Zee and de Boer[24] who did not identify a difference in overall HDI based on the type of pre-operative blockade and no clear superior alpha blockade strategy exists. This information is important for many clinicians as PBZ is difficult to procure in many parts of the world and is costly as well. Hence, in the absence of superiority of SAB or NSAB over one another, secondary considerations such as availability, convenience, patient tolerance and cost factors should be given important considerations before prescribing them. Our findings are different from Zawadzka *et al.*[25] where authors reported that NSAB was superior to SAB in preventing intra-operative BP fluctuations. The only similar finding is a requirement of intra-operative vasodilator drug, which was more in the SAB group. We could not conclude if one drug was superior over the other drug, as we believe that while a systematic review on the topic is warranted to summarize the existing evidence. However, a conclusion based on a meta-analysis combining a heterogeneity of different study types (one RCT, one prospective study and eight retrospective studies) examining slightly different endpoints can be misleading.

The current review has many limitations, the major one being the lack of RCTs or prospective studies, which are considered most ideal for a meta-analysis. Another major limitation is the high risk of bias in the included studies. English-only reports and publication bias are other limitations, we did not assess for publication bias in this review due to the small number of studies included. Direct comparisons between studies were often limited because of the following reasons:

(1) the variety of haemodynamic variables used, (2) lack of uniform variables, (3) the use of cointerventions such as other antihypertensive drugs, (4) variable response rates and post-operative complications resulting in potential selection bias and (5) target BP will vary between centres and even individual anaesthetists, hence variations in the use of vasoactive agents is difficult to interpret. This will hold true in any retrospective study. Similarly, studies did not report regarding pre-operative symptoms such as light-headedness, nasal stuffiness or fatigue, often reported by patients on the alpha blockade and hence this aspect could not be analysed.

Conclusion

As patients blocked selectively may have a higher incidence of vasodilator requirement intra-operatively, NSAB offers some haemodynamic advantage over SAB. However, NSAB's real clinical benefit cannot be ascertained with the current studies as this difference did not result in any significant advantage over SAB with regard to morbidity or mortality. A multicentre RCT may help in answering this question definitively and any future prospective randomized trial should include assessment of pre-operative adverse reactions/symptoms, defined BP targets for which vasodilators or vasopressors are required and an arm with no alpha blockade. In the absence of superiority of SAB or NSAB over one another, secondary considerations such as availability, convenience, patient tolerance and cost factors should be given important considerations before prescribing them and we recommend any of the available drugs can be used for alpha blockade if it is planned.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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