CURRENT STATUS REVIEWS

Pudendal Nerve Block in Hemorrhoid Surgery: A Systematic Review and Meta-analysis

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BACKGROUND: Postoperative pain represents an important issue in traditional hemorrhoidectomy. Optimal pain control is mandatory, especially in a surgical day care setting.

OBJECTIVE: The aim of this study was to investigate the use of pudendal nerve block in patients undergoing hemorrhoidectomy.

DATA SOURCES: PubMed, Google Scholar, Cochrane Library, and Web of Science databases were searched up to December 2020.

STUDY SELECTION: Randomized trials evaluating the pudendal nerve block effect in patients undergoing hemorrhoidectomy were selected.

INTERVENTIONS: Hemorrhoidectomy under general or spinal anesthesia with or without pudendal nerve block was performed.

MAIN OUTCOME MEASURES: Opioid consumption, pain on the visual analogue scale, length of hospital stay, and readmission rate were the main outcomes of interest and were plotted by using a random-effects model.

RESULTS: The literature search revealed 749 articles, of which 14 were deemed eligible. A total of 1214 patients were included, of whom 565 received the pudendal nerve block. After hemorrhoidectomy, patients in the pudendal nerve block group received opioids less frequently (relative risk, 0.364; 95% CI, 0.292–0.454, $p < 0.001$) and in a lower cumulative dose (standardized mean difference, –0.935; 95% CI, –1.280 to –0.591, $p < 0.001$). Moreover, these patients experienced less pain at 24 hours (standardized mean difference, –1.862; 95% CI, –2.495 to –1.228, $p < 0.001$), had a shorter length of hospital stay (standardized mean difference, –0.742; 95% CI, –1.145 to –0.338, $p < 0.001$), and had a lower readmission rate (relative risk, 0.239; 95% CI, 0.062–0.916, $p = 0.037$). Sensitivity analysis excluded the occurrence of publication bias on the primary end point, and the overall evidence quality was judged "high."

LIMITATIONS: Occurrence of publication bias among some secondary end points and heterogeneity are the main limitations of this study.

CONCLUSIONS: This systematic review and meta-analysis show significant advantages of pudendal nerve block use. A reduction in opioid consumption, postoperative pain, complications, and length of stay can be demonstrated. Despite the limitations, pudendal nerve block in patients undergoing hemorrhoidectomy should be considered.

KEY WORDS: Analgesia; Hemorrhoidectomy; Nerve block; Pain; Pudendal; Surgery.

Hemorrhoids is the third most common outpatient GI diagnosis with nearly 4 million office and emergency department visits in the United States annually,[1] and, although rarely serious, hemorrhoids often have a significant negative impact on the quality of life. Medical therapy with phlebotonics, topical ointments, and dietary modification, as well as noninvasive office-based procedures such as rubber band ligation or infrared coagulation are usually effective at early stages, but advanced disease often requires surgery.[2,3] Excisional hemorrhoidectomy is one of the oldest and most widely used techniques.[4]

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To date, it is considered the most effective, but also the most painful method in comparison with more recently developed, less invasive techniques, such as stapled hemorrhoidectomy or Doppler-guided dearterialization.[5,6]

Optimal pain control is mandatory, in particular, when patients are treated in a day care surgery setting,[7,8] which is increasingly advocated in many countries[9,10] to reduce health care costs.[11] One important perspective in the management of posthemorrhoidectomy pain is the application of a multimodal pain control strategy. The PROSPECT (PROcedure-SPECific post-operative pain managemenT) Working Group[12,13] emitted Grade A recommendations for pain management after hemorrhoid surgery including beyond conventional oral analgesics, oral diosmin, metronidazole, laxatives, topical application of lidocaine, glyceryl trinitrate, cholestyramine ointments, and infiltration with long-acting local anesthetics. A recent evidence-based review has concluded that pudendal nerve block (PNB) is effective in controlling postoperative pain after colorectal surgical procedures.[14] Likewise, PROSPECT recommendations stated that PNB was preferred over the simpler but apparently less effective perianal infiltration.[12,13] Indeed, perianal anesthesia can be effective up to 6 hours,[15–18] whereas PNB has been demonstrated to last longer.[12,19] Pudendal nerve block with or without general anesthesia may also be preferred to spinal anesthesia thanks to its longer analgesic duration and lower rate of complications.[20] Several randomized trials have been published on PNB, but, to date, only 1 systematic review with no meta-analysis has been published.[14]

The aim of this systematic review and meta-analysis was to investigate the effect of PNB use on postoperative outcomes in patients undergoing hemorrhoidectomy.

MATERIALS AND METHODS

This systematic review and meta-analysis were written according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[21] No ethical approval or informed consent was required.

Search Strategy

A literature search of PubMed, Google Scholar, Cochrane Library, and Web of Science databases was performed by 2 researchers (F.M., J.G., December 1, 2020). The combination of terms for the literature search was: (“pudend*”OR”ischiorectal”)AND(“block*”OR”anesthesia”OR”anaesthesia”) AND(“hemorrhoids”OR”hemorrhoid”OR”haemorrhoids” OR”haemorrhoid”OR”hemorrhoidectomy”OR”haemorrhoidectomy”OR”surgery”). No year restriction was applied.

Eligibility Criteria

Studies deemed eligible for inclusion were randomized controlled trials involving patients undergoing hemorrhoidectomy and comparing PNB with any other treatment. We excluded studies involving perianal blocks, in the case of nonhemorrhoidal disease or studies with a sample size of <10 patients. Additional eligible studies were searched for in the reference list of full-text evaluated articles. Language restrictions were set to include English, Spanish, Italian, German, and French.

Data Collection and Outcomes

Study characteristics were collected, and disagreements were resolved by discussion. For each study found in the literature search, title, abstract, authors, years, and journal were analyzed and independently reviewed by 3 (F.M., J.G., M.D.G.) researchers. Articles not matching the topic and those nonrandomized or published in a language different than mentioned earlier were excluded. Subsequently, potential eligible studies were evaluated in full text to determine the inclusion in qualitative and quantitative analyses.

For each eligible study title, authors, years, journal, inclusion and exclusion criteria, type of randomization, blinding procedure, PNB technique, type of local anesthetics, number of patients, opioid consumption, data on postoperative pain, operative time, length of recovery room stay, urinary retention, nausea and vomiting, satisfaction rate, time to return to work, length of hospital stay, and readmission rates were extracted.

Postoperative opioid consumption was considered the primary end point. Among secondary end points, postoperative pain on a visual analogue scale (VAS), intraoperative additional opioid need, operative time, postoperative complications (urinary retention, nausea/vomiting), length of hospital stay, readmission, and satisfaction rate were considered. Opioid consumption was defined either as the amount of opioids needed or the number of patients requiring opioids according to the provided data. Pain on the VAS was defined as the perceived pain on a 0 to 10 scale at rest, during walking, sitting, or first bowel movements.

Quality Assessment

The risk of bias and study quality were independently reviewed by 2 researchers (F.M., M.D.G.) according to the Cochrane Collaboration tool for assessing risk of bias.[22] The overall quality of evidence was graded according to the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach.[23] Risk of bias, inconsistency, indirectness, imprecision, and publication bias were 5 factors attributed to the selected studies that could reduce by 1 or 2 the initial quality of evidence.

Statistical Methods

As effect estimate, we computed the standardized mean difference (SMD) or the relative risk (RR) between groups (PNB vs no PNB) for each study and its 95% CI. In the case of missing data, mean and SD were estimated from the median, range, and interquartile values.[24,25] The overall measure of effect was estimated by applying the random-effects model.[26] The Higgins I^2 index[27] was computed to assess the percentage of total cross-study variation due to heterogeneity. I^2 values >50% were considered to indicate the presence of heterogeneity.[27,28] The sensitivity analysis was performed by iteratively recalculating the pooled mean difference estimate after the time of exclusion of each study. Small-study effect, which indicated that the chance of a smaller study being published was increased if it showed a stronger effect, was assessed by means of the Egger test. The funnel plot was performed to assess the occurrence of publication bias.[29] Subgroup analyses were performed according to specific clinical questions (ie, general or spinal anesthesia, PNB technique), and the adjusted indirect comparison "Bucher method" was applied to estimate OR.[30] Statistical analysis was performed on MedCalc Statistical Software version 19.5.1 (MedCalc Software Ltd, Ostend, Belgium; https://www.medcalc.org; 2020).

RESULTS

Literature Search

Literature search on PubMed, Google Scholar, Cochrane Library, and Web of Science revealed 749 articles. Two hundred eleven duplicates were removed, and 497 articles were excluded because they did not match the main topic. Forty-one articles were evaluated in full text, and only 1 study was found within the references screening. Fifteen articles were further excluded as nonrandomized: 7 involved perianal blocks, 3 reported duplicate data, and 2 excluded articles were written in Persian (Fig. 1). Fourteen randomized trials with a total of 1214 patients were included in the present meta-analysis.[31–44]

Study Characteristics

All included randomized trials provided data on study design and methods (Table 1). Inclusion criteria were well defined by all studies, whereas 4 did not specify the exclusion criteria.[32,33,39,40] Seven studies were double-blinded,[31,32,34,36,40,41,44] one was single-blinded[35] and the other did not qualify for either.

The PNB procedure was achieved in 4 studies under nerve stimulation[34–36,40] and in one[44] under ultrasound guidance; anatomic landmarks were used in the remaining 9 studies.[31–34,37–39,41–43] Ten studies reported a PNB,[33–40,42,44] whereas 4 used a different denomination to perform the pudendal nerve branches block (3 ischiorectal block[31,41,43] and 1 posterior perineal block[32]). The type of anesthetics

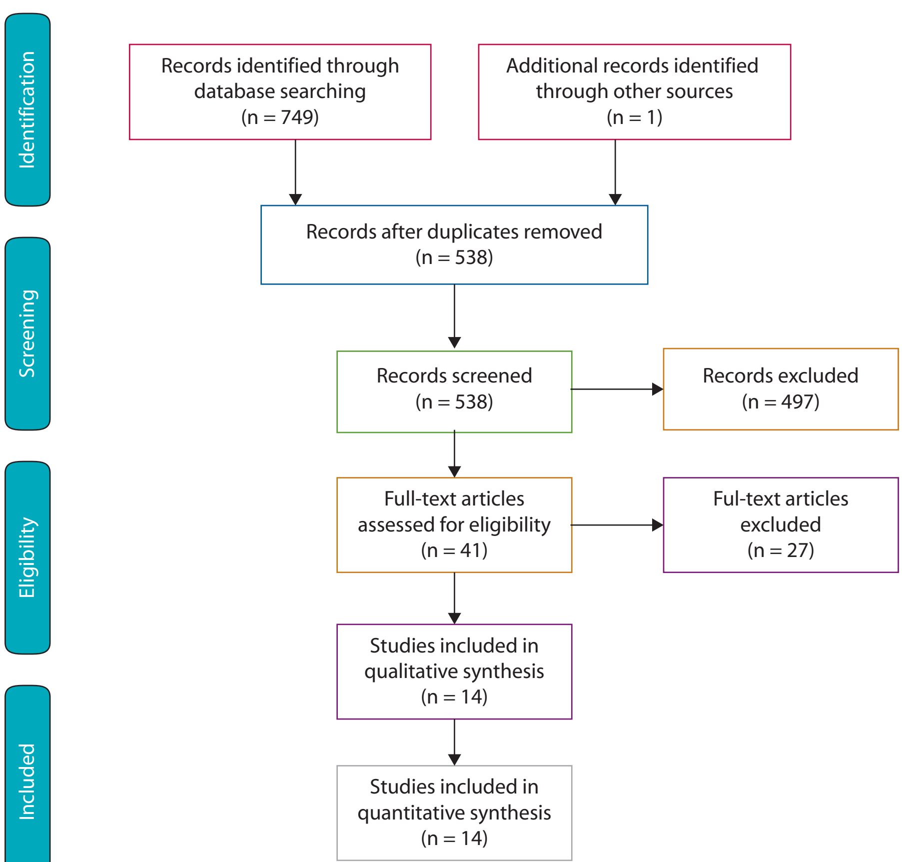


FIGURE 1. Flow chart of the literature search according to the PRISMA guidelines.

TABLE 1. Characteristics of included studies

Study	Inclusion criteria and procedures	Exclusion criteria	Type of randomization and groups	Blinding	PNB technique	Local anesthetic (total)	Quality assessment
Luck 2000[31]	Hemorrhoids grade II (after failed rubber band ligation or sclerotherapy) Grade III–IV (open hemorrhoidectomy)	ASA grade 4 or 5 Chronic renal failure, coagulopathy, symptoms of bladder neck obstruction, or inadequate social support after surgery	GA + PNB + LA GA + LA 1:1 ratio, sealed, opaque envelope	Double Patients and nursing staff blinded to which treatment arm	Anatomic landmarks	Bupivacaine 0.33% and lidocaine 0.17%. 60 mL	Good
Brunat 2003[32]	Hemorrhoids grade IV ASA grade 1 and 2 (open hemorrhoidectomy)	Not reported	GA + PNB GA 1:1 ratio	Double Patients and investigator blinded to which treatment arm	Anatomic landmarks	Ropivacaine 0.75%. 40 mL	Good
Kim 2005[33]	Hemorrhoids grade II–IV (open hemorrhoidectomy)	Not reported	PNB + LA SP 1:1 ratio.	Not reported	Anatomic landmarks	Bupivacaine 0.5%. 10–15 mL	Fair
Naja 2005[34]	Hemorrhoids grade II–IV (open hemorrhoidectomy)	Chronic renal failure, coagulopathy, symptoms of bladder neck obstruction, patients for whom it was not possible to conduct a telephone follow-up	GA + PNB GA GA + placebo PNB 1:1:1 ratio, sealed opaque envelope technique based on computer-generated random numbers	Double Placebo (saline or local anesthetic mixture) prepared by an independent nurse outside the operating room. Randomization code was not broken before the end of the study. Patients, data collection nurses, surgeons, and anesthesiologists were blinded to which treatment arm	Under nerve stimulation control	Each 20 mL of the local anesthetic mixture: 6 mL lidocaine 2%, 6 mL lidocaine 2% with adrenaline 5 μg·mL^{-1}, 5 mL bupivacaine 0.5%, 1 mL fentanyl 50 μg·mL^{-1}, and 2 mL clonidine 75 μg·mL^{-1}. Total dose: 0.7 mL/kg	Good
Naja 2006[35]	Hemorrhoids grade II–IV (open hemorrhoidectomy)	Chronic renal failure, coagulopathy, symptoms of bladder neck obstruction, patients for whom it was not possible to conduct a telephone follow-up	Sedation + PNB GA 1:1 ratio, computer-generated numbers table	Single Postoperative data collection performed by a trained research nurse who was blinded to patient group allocation	Under nerve stimulation control	Each 20 mL of the local anesthetic mixture: 6 mL lidocaine 2%, 6 mL lidocaine 2% with adrenaline 5 μg·mL^{-1}, 5 mL bupivacaine 0.5%, 1 mL fentanyl 50 μg·mL^{-1}, and 2 mL clonidine 75 μg·mL^{-1}. Total dose: 0.7 mL/kg	Good
Adly 2009[36]	Hemorrhoids grade II–IV (open hemorrhoidectomy)	ASA grade 4 and 5 and pregnant women	GA + PNB GA GA + placebo PNB 1:1:1 ratio. Sealed opaque envelope technique	Double Patients and investigators blinded	Under nerve stimulation control	Lidocaine 2%, bupivacaine 5%, fentanyl, clonidine. Total dose: 0.7 mL/kg	Good

(Continued)

TABLE 1. Continued

Study	Inclusion criteria and procedures	Exclusion criteria	Type of randomization and groups	Blinding	PNB technique	Local anesthetic (total)	Quality assessment
Santos 2009[37]	Hemorrhoids grade III–IV (closed hemorrhoidectomy)	Age <12 years old, hemorrhoids grade I and II, grade III or IV associated with other disease (fistula, fissure, etc)	SP + PNB SP 1:1 ratio, closed envelope technique just before the surgical intervention	Not reported	Anatomic landmarks	Ropivacaine 0.5%. 20 mL	Good
Castellví 2009[38]	Hemorrhoids grade III–IV (open hemorrhoidectomy)	Previous anal surgery, concomitant anal diseases (fissure, fistula, incontinence, and inflammatory bowel disease), anticoagulants or analgesics, hypersensitivity to local anesthetics	GA + PNB with diathermy SP with diathermy GA + PNB with Ligasure SP with Ligasure 1:1:1:1 ratio. Computer-generated list of randomization, allocation with sealed opaque envelope	Not reported	Anatomic landmarks	Ropivacaine 0.75%. 20 mL	Good
Tepetes 2010[39]	Hemorrhoids grade III–IV (open hemorrhoidectomy)	Not reported	PNB + LA LA 1:1 ratio.	Not reported	Anatomic landmarks	Lidocaine 1%. 40 mL.	Fair
Imbelloni 2012[40]	Patients undergoing hemorrhoidectomy	Not reported	SP + PNB SP 1:1 ratio, computer-generated list	Double Patients and investigators blinded	Under nerve stimulation control	Levobupivacaine enantiomeric excess 0.25%. 40 mL	Good
Rajabi 2012[41]	Hemorrhoids grade II-III-IV (open hemorrhoidectomy)	Hemorrhoids grade I, history of cardiovascular diseases	GA + PNB GA GA + placebo PNB 1:1:1 ratio, random envelope opening	Double Patient and data collectors blinded to group allocation	Anatomic landmarks	Bupivacaine 0.25%. 40 mL	Good
Aldabbas 2014[42]	Anal surgical procedures (only hemorrhoids reported)	ASA ≥2	SP + PNB GA + PNB SP GA 1:1:1:1 ratio.	Not reported	Anatomic landmarks	Lidocaine 2%, bupivacaine 2.5%	Fair
Nadri 2018[43]	Hemorrhoids grade IV ASA grade 1 and 2 (hemorrhoidectomy)	Age <18 or >64 years old. BMI ≥30 kg/m^2, cardiovascular disease, allergy to local anesthetic, emergency surgery, ASA grade 3 and 4, blood clotting alterations, anticoagulation therapy, patients who cannot accept anesthetics	PNB SP 1:1 ratio, randomized block design	Not reported	Anatomic landmarks	Bupivacaine 0.5%. 3 mL	Good
Di Giuseppe 2020[44]	Hemorrhoids grade II–IV (open hemorrhoidectomy)	Age <18 years old, pregnancy, allergy to local anesthetics	SP + PNB SP 1:1 ratio on a dedicated software	Double Patients and ward personnel (data collectors) were not informed about the treatment arm.	Ultrasound guided	Ropivacaine 0.75%. 20 mL	Good

GA = general anesthesia; LA = local anesthesia; PNB = pudendal nerve block; SP = spinal anesthesia.

TABLE 2. Postoperative pain values

Study	Groups	No. of patients	Pain within 6 h, mean (SD)	Pain at 12 h, mean (SD)	Pain at 24 h, mean (SD)	Pain at 48 h, mean (SD)
Luck 2000[31]	GA + PNB + LA	10	2.1 (0.34)[a]	–	2.5 (0.34)[a]	–
	GA + LA	10	3.9 (0.57)		5.1 (0.6)	
Brunat G 2003[32]	GA + PNB	25	0.75 (1.33) [a]	3.3 (2.7)	1.5 (1.6) [a]	–
	GA	27	3.85 (1.7)	4.4 (1.9)	2.0 (1.7)	
Kim J 2005[33]	PNB + LA	81	–	–	2.7 (2.1) [a]	–
	SP	82			5.2 (2.2)	
Naja Z 2005[34]	GA + PNB	30	2 (0.9)[a,b,c]	2 (0.8) [a,b,c]	2.4 (0.7) [a,b,c]	2.4 (0.6)[a,b,c]
	GA	30	5.7 (0.3)[c]	5.6 (0.4)[c]	5.5 (0.5)[c]	6.3 (0.6)[c]
	GA + placebo PNB	30	5 (0.4)[b]	4.9 (0.4)[b]	5 (0.4)[b]	6.3 (0.4)[b]
Naja Z 2006[35]	Sedation + PNB	35	2.6 (0.8)[a]	2.4 (0.6) [a]	2.8 (0.6) [a]	3.1 (0.6) [a]
	GA	37	5.6 (0.4)	5.6 (0.4)	5.5 (0.4)	6.0 (0.5)
Adly S 2009[36]	GA + PNB	20	–	1.05 (0.82)[a,b,c]	3.05 (1.19)[b,c]	–
	GA	20		2.75 (1.12)[c]	5.7 (1.42)[a,c]	
	GA + placebo PNB	20		1.9 (0.97)[b]	5.55 (1.64)[b]	
Santos 2009[37]	SP + PNB	20	1.30 (2.1)	0.16 (0.5)[a]	–	–
	SP	20	1.55 (1.43)	1.75 (1.48)		
Castellví 2009[38]	GA + PNB	38	2[a]	–	1.84[a]	–
	SP	36	5.06		4	
Tepetes 2010[39]	PNB + LA	60	2.2 (0.86)[a]	–	1.9 (0.86)	–
	LA	60	5.1 (1.08)		2.3 (1.08)	
Imbelloni 2012[40]	SP + PNB	100	0.25 (0.75)[a]	0.25 (0.75)[a]	1.18 (1.89)[a]	–
	SP	100	4.65 (2.29)	3.90 (2.08)	3.97 (1.93)	
Rajabi 2012[41]	GA + PNB	30	–	4.2 (2.1)[a,b,c]	–	–
	GA	30		8.5 (1.3)[c]		
	GA + placebo PNB	30		8.1 (0.9)[b]		
Aldabbas 2014[42]	SP/GA + PNB	58	2.44 (2.69)[a]	–	2.37 (2.82) [a]	2.19 (2.06)[a]
	SP/GA	56	4.14 (3.34)		3.78 (2.82)	3.67 (2.81)
Nadri 2018[43]	PNB	35	0.16 (0.81) [a]	0.91 (0.92)[a]	0.31 (0.63)[a]	–
	SP	35	3.09 (0.78)	2.06 (1.03)	1.11 (0.83)	
Di Giuseppe 2020[44]	SP + PNB	23	2.8 (2.4)[a]	3.4 (3.1)	1.4 (1.4) [a]	1.0 (1.6)
	SP	26	4.6 (3.7)	4.7 (3.6)	3.1 (2.4)	2.1 (2.0)

Values are presented as mean (SD) or as absolute number with percentage.
GA = general anesthesia; LA = local anesthesia; PNB = pudendal nerve block; SP = spinal anesthesia.
[a] Indicates a statistically significant difference.
[b,c] Indicate differences between groups.

was highly variable: 8 studies used long-acting local anesthetics (bupivacaine or ropivacaine) at different volumes and concentrations,[32,33,37,38,40,41,43,44] 5 used mixtures combining short- and long-acting local anesthetics,[31,34–36,42] and only 1 study used a short-acting anesthetic (lidocaine).[39] The surgical technique was open hemorrhoidectomy in 10 studies[31–36,38,39,41,44] (of which one used Ligasure or diathermy[38] and 1 used scalpel only[39]), closed hemorrhoidectomy in one,[37] and not specified in 3.[40,42,43] Control groups varied among the trials because some studies compared PNB against placebo PNB[34,36,41] or no PNB[31,32,37,39,40,42,44] and others used different types of anesthesia.[33,35,38,43]

Patient demographics and baseline characteristics were provided by all included studies.[31–44] Five studies reported the operative time[32,34,35,38,39] and 2 reported the intraoperative additional opioid need.[32,39] Three studies reported the administration of intraoperative fluids.[32,33,40]

Postoperatively, pain values or opioid consumption were provided by all studies included.[31–44] Three of them reported the duration of PNBs, defined as the time point of perceived pain after surgery[33,42] or the time point of first analgesic administration.[41] Twelve studies reported opioid consumption in the early postoperative period[31–36,38–40,42–44] at different time points (Table 2). Within the first postoperative hours, 3 studies provided data on pain[31,32,43]: three at 2 hours,[31,32,38] two at 4 hours,[31,32] seven at 6 hours,[34,35,37,38,40,43,44] three at 8 hours,[32,39,42] nine at 12 hours,[32,34–37,40,41,43,44] one at 16[42] and 18[42] hours, twelve at 24 hours,[31–36,38–40,42–44] two at 36 hours,[34,35] and four at 48 hours.[34,35,42,44] The 2 studies by Naja et al[34,35] also reported the pain at 3, 4, 5, and 6 days postoperatively and its duration during walking and sitting. Two studies reported pain during the first bowel movement[34,38] and 2 studies considered the time to first bowel movement.[32,40] Kim et al[31] described the strongest pain value on the VAS without providing the time point. Based on results from the other studies, pain can be accounted for between the 12th and the 36th hour after surgery, and it was plotted at 24 hours for the analysis. Pain on the VAS was reported by 3 studies[36,40,42] as raw data on diverse scales that had to be converted to VAS.[45] One study[38] reported the mean without SD and another study[39] reported the mean with ranges, thus requiring a SD estimation.[24,25,46]

Ten studies[33–41,44] reported the postoperative complications, 8 reported the length of hospital stay,[31,32,34–36,38,39,44] and 4 reported the satisfaction score[32,34,35,40] and unplanned hospital admission rate (Table 3).[31,34,35,44]

Quality Assessment and Risk of Bias

The risk of bias assessment is reported in Figure 2. Overall, the occurrence of selection, allocation, attrition, reporting, or other biases was judged very low. However, selection and detection biases should be considered relevant (Fig. 3). According to the GRADE approach,[23] the most common limitations were the lack of blinding and the incomplete accounting of patients and outcome events. Nevertheless, because these limitations were present in a minority of studies, this risk of bias was not considered relevant enough to rate down by 1, so that the overall evidence quality was judged "high."

The sensitivity analysis revealed that no study strongly influenced the results, and the Egger test[29] did not reveal the occurrence of the small-study effect. Among our analyses, I^2 values[27,28] ranged from 0% to 98%. In particular, the I^2 values were lower than 50% in regard to operative time, postoperative opioid need and consumption, urinary retention, nausea and vomiting, and rehospitalization rates, thus excluding the occurrence of publication bias. However, I^2 values were positive regarding the duration of PNB; the postoperative pain on the VAS at 6, 12, 24, and 48 hours; the length of stay; and the satisfaction score. However, the occurrence of publication bias was considered irrelevant on the primary end point, where the I^2 test resulted <50% and the funnel plot did not show any violation of the symmetry (Fig. 4).

Primary and Secondary Outcomes

A total of 1214 patients was included, of whom 565 received PNB and 649 did not receive PNB during the hemorrhoidectomy. All studies reported similar age and comorbidities among groups.

Regarding the primary end point, the overall difference in opioid consumption was 7.2 mg of morphine-equivalents (SMD, −0.935; 95% CI, −1.280 to −0.591, $p < 0.001$, $I^2 = 0\%$)[31,32,43] and the difference in the number of patients requiring opioids was 22% vs 65% in favor of the PNB group (RR, 0.364; 95% CI, 0.292–0.454, $p < 0.001$, $I^2 = 20.8\%$; Fig. 5).[33–36,38–40,42,44]

Regarding postoperative pain, the results were in favor of PNB use in all cases. In particular, at 6 hours, the overall mean difference on the VAS was 3.0 (SMD, −2.521; 95% CI, −3.420 to −1.622, $p < 0.001$, $I^2 = 96.1\%$),[31,32,34,35,37–40,43,44] at 12 hours the overall mean difference was 3.1 (SMD, −2.303; 95% CI, −3.271 to −1.336, $p < 0.001$, $I^2 = 95.9\%$),[32,34–37,40,41,43,44] at 24 hours the overall mean difference was 2.1 (SMD, −1.862, 95% CI, −2.495 to −1.228, $p < 0.001$, $I^2 = 94.9\%$),[31–36,38–40,42–44] and at 48 hours the overall mean difference was 2.5 (SMD, −3.337; 95% CI, −5.927 to −0.747, $p = 0.012$, $I^2 = 98.4\%$; Fig. 6).[34,35,42,44] Naja et al[34,35] reported reduced pain in patients who received PNB at 3 days (SMD, −5.776; 95% CI, −8.222 to −3.330, $p < 0.001$, $I^2 = 91.5\%$), at 4 days (SMD, −5.344; 95% CI, −7.535 to −3.154, $p < 0.001$, $I^2 = 90.6\%$), at 5 days (SMD, −4.900; 95% CI, −6.296 to −3.503, $p < 0.001$, $I^2 = 79.9\%$), at 6 days (SMD, −4.520; 95% CI, −5.110 to −3.931, $p < 0.001$, $I^2 = 0\%$), during walking (SMD, −0.830; 95% CI, −1.160 to −0.500, $p < 0.001$, $I^2 = 0\%$), and sitting (SMD, −0.794; 95% CI, −1.154 to −0.434, $p<0.001$, $I^2 = 16.3\%$). Moreover, lower pain was reported during the first bowel movements (SMD, −1.889; 95% CI, −2.975 to −0.803, $p = 0.001$).[34,38]

Rescue doses of opioids were needed intraoperatively in 30% vs 62% of patients in the study by Tepetes et al.[39] Similarly, Brunat et al[32] reported lower opioid consumption in the PNB groups compared with the control group (60 ± 80 mg vs 300 ± 150 mg of morphine-equivalents). The reported operative time was 40.6 ± 15.7 vs 42.5 ± 13.9 minutes and similar among groups (SMD, 0.123; 95% CI, −0.139 to 0.385, $p = 0.358$, $I^2 = 43.5\%$).[32,34,35,38,39] No difference in fluid administration was reported among PNB and control groups.[32,33,40]

Postoperative complications occurred less frequently in the PNB group. Urinary retention occurred in 10 of 342 (2.9%) patients vs 93 of 398 (23.4%) patients in the PNB and control groups (RR, 0.159; 95% CI, 0.089–0.285, $p < 0.001$, $I^2 = 0\%$).[31–39,44] Combined nausea/vomiting was reported in 5 of 308 (1.6%) patients vs 60 of 390 (15.4%) patients in the PNB and the control groups (RR, 0.224; 95% CI, 0.101–0.495, $p < 0.001$, $I^2 = 0\%$; Fig. 7).[31,32,34–38,40,41]

The mean length of hospital stay was shorter in the PNB group: 17.4 vs 29.5 hours (SMD, −0.742; 95% CI, −1.145 to −0.338, $p < 0.001$, $I^2 = 79.3\%$).[31,32,34–36,38,39,44] After discharge, 1 of 100 (1%) patients in the PNB group vs 14 of 131 (10.7%) control patients required a readmission (RR, 0.239; 95% CI, 0.062–0.916, $p=0.037$, $I^2 = 0\%$).[31,34,35,44] Finally, patients with PNB were more frequently satisfied after hemorrhoidectomy: 173 of 190 (91.1%) vs 69 of 224 (30.8%) (RR, 2.746; 95% CI, 1.459–5.171, $p = 0.002$, $I^2 = 90.9\%$).[32,34,35,40]

Subgroup Analyses

When performing PNB with anatomic landmarks, 47 of 237 (19.8%) and 143 of 233 (61.4%) patients required opioids in the PNB and control groups (RR, 0.336; 95% CI, 0.228–0.496, $p < 0.001$, $I^2 = 41.3\%$), pain at 6 hours (SMD, −2.056; 95% CI, −3.054 to −1.058, $p < 0.001$, $I^2 = 94.9\%$) and at 24 hours (SMD, −1.033; 95% CI, −1.520 to −0.546, $p < 0.001$, $I^2 = 86.4\%$) was lower in the PNB group. Urinary retention occurred in 9 of 234 (3.8%) and 75 of 235 (32.1%) patients (RR, 0.145; 95% CI, 0.077–0.275,

TABLE 3. Postoperative outcomes

Study	Groups	No. of patients	Operative time, mean (SD), min	Urinary retention, n (%)	Vomiting, n (%)	Nausea, n (%)	PNB duration, mean (SD), h	Opioid needed at 24 h, n (%) or mean ± SD	Recovery room, mean (SD), min	Satisfied with the treatment, n (%)	Return to work, mean (SD), days	Length of stay, mean (SD), h	Readmission, n (%)
Luck 2000[31]	GA + PNB + LA	10	–	0	1 (10)		–	45 mg	–	–	–	5 (r 3–25)	1 (10.0)
	GA + LA	10		1 (10)	1 (10)			95 mg				7.5 (r 4–24)	2 (20.0)
Brunat 2003[32]	GA + PNB	25	30 (15)	0	0	0	–	18 ± 16[a]	79 (39)[a]	25 (100)[a]	–	60 (24)	–
	GA	27	35 (10)	0	0	0		33 ± 20	123 (36)	17 (68)		61 (31)	
Kim 2005[33]	PNB + LA	81	–	6 (7.4)[a]	–	–	9.1 (3.8) [a]	16 (19.8) [a]	–	–	–	–	–
	SP	82		57 (69.5)			3.1 (1.4)	45 (54.9)					
Naja 2005[34]	GA + PNB	30	66 (18.6)	0	0	3 (10.0)	–	6 (20.0) [a,b,c]	60 (21.0)	27 (90.0) [a,b,c]	6.6 (2.9)[a]	21 (10.4)[a]	0
	GA	30	60 (15.0)	3 (10)	2 (6.7)	4 (13.3)		13 (43.3)[b]	72 (26.4)	11 (36.7)[b]	14.1 (7.5)[b]	30 (14.0)[b]	5 (16.7)
	GA + placebo PNB	30	60 (18.6)	3 (10)	3 (10.0)	4 (13.3)		11 (36.7)[c]	72 (28.2)	15 (50.0)[c]	14.3 (7.2)[c]	28 (14.2)[c]	2 (6.7)
Naja 2006[35]	Sedation + PNB	35	63 (18)	0[a]	1 (2.7)		–	6 (17.1)[a]	46 (18)[a]	30 (85.7)[a]	7.2 (3.4)[a]	6.9 (11.0)[a]	0
	GA	37	61 (15)	8 (21.6)	5 (13.5)			15 (40.5)	74 (27)	9 (24.3)	13.8 (1.7)	29.8 (14.3)	3 (8.1)
Adly 2009[36]	GA + PNB	20	–	0	2 (10.0)	4 (20.0)	–	0[a,b,c]	–	–	–	27.6 (8.8) [a,b,c]	–
	GA	20		2 (10.0)	5 (25.0)	6 (30.0)		12 (60.0)[b]				48.0 (17.4)[b]	
	GA + placebo PNB	20		2 (10.0)	6 (30.0)	7 (35.0)		16 (80.0)[c]				45.6 (18.9)[c]	
Santos 2009[37]	SP + PNB	20	–	0[a]	0	0	–	–	–	–	–	–	–
	SP	20		9 (45.0)	1 (5.0)	0							
Castellví 2009[38]	GA + PNB diathermy	18	22 (r 16–35)	1 (5.5)	1 (5.5)	–	–	0[a,c]	–	–	–	9.0 (6.9) [a,c]	–
	GA + PNB Ligasure	20	13 (r 8–14)	1 (5.0)	0			1 (5.0)[b]				6.9 (4.0)[b]	
	SP diathermy	19	20 (r 15–32)	4 (21.1)	4 (21.1)			9 (47.4)[c]				17.4 (8.9)[c]	
	SP Ligasure	17	11 (r 7-13)	2 (11.8)	3 (17.6)			9 (52.9)[b]				16.6 (9.1)[b]	
Tepetes 2010[39]	PNB + LA	60	31.8	1 (1.7)	–	–	–	8 (13.3)[a]	–	–	–	3.6 (10.7)[a]	–
	LA	60	31.8	2 (3.3)				27 (45.0)				8.4 (13.1)	
Imbelloni 2012[40]	SP + PNB	100	–	–	0 [a]		–	34 (34)[a]	–	91 (100)[a]	–	–	–
	SP	100			25 (25)			100 (100)		17 (17)			
Rajabi 2012[41]	GA + PNB	30	–	–	0	4 (13.3)	9.3 (2.7) [a,b,c]	–	–	–	–	–	–
	GA	30			3 (10.0)	8 (26.7)	3.1 (1.5)[b]						
	GA + placebo PNB	30			2 (6.7)	8 (26.7)	3.3 (1.8)[c]						
Aldabbas 2014[42]	SP + PNB	29	-	-	-	-	25.4[a,b]	9 (31.0)[a,b]		-	-	-	-
	GA + PNB	29					19.5[c]	13 (44.8)[c]					
	SP	28					2.5[b]	25 (89.3)[b]					
	GA	28					0.5[c]	28 (100)[c]					
Nadri 2018[43]	PNB	35	–	–	–	–	–	97.5 mg	–	–	–	–	–
	SP	35						210 mg					
Di Giuseppe 2020[44]	SP + PNB	23	–	1 (4.3)	–	–	–	5 (21.7)	–	–	–	28.8 (28.8)[a]	0
	SP	26		0				10 (38.4)				43.2 (43.2)	2 (7.7)

Values are presented as mean ± SD or as absolute number with percentage.

GA = general anesthesia; LA = local anesthesia; PNB = pudendal nerve block; r = range; SP = spinal anesthesia.

[a] Indicates a statistically significant difference.

[b] and [c] indicate differences between groups.

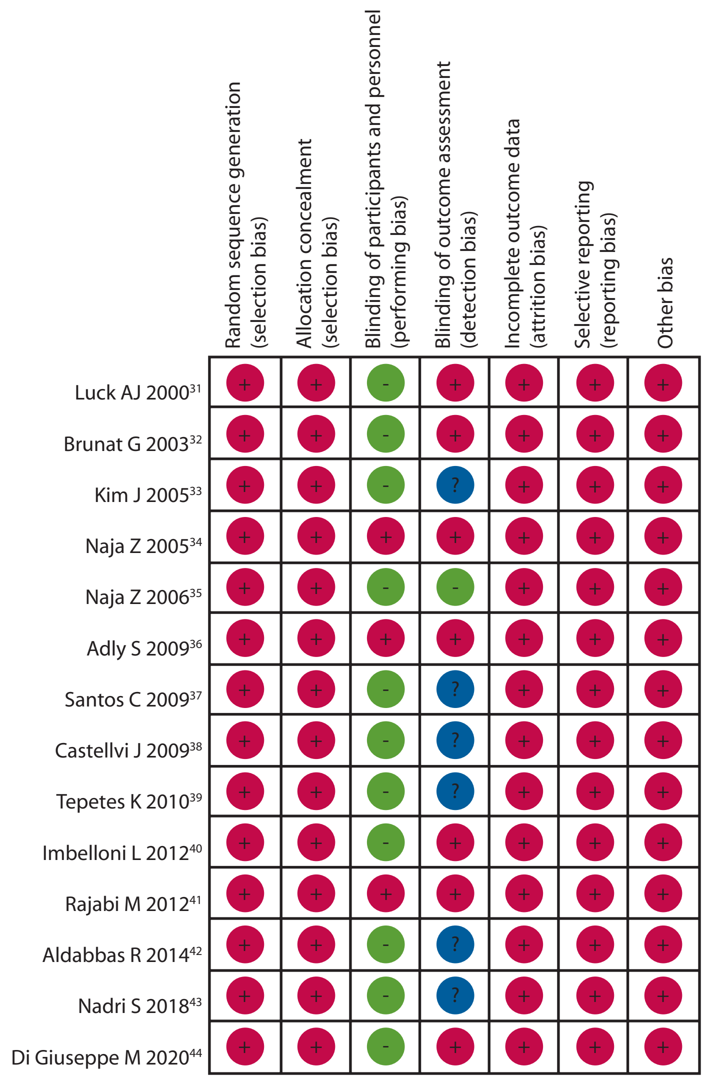


FIGURE 2. Risk of bias among the included studies.

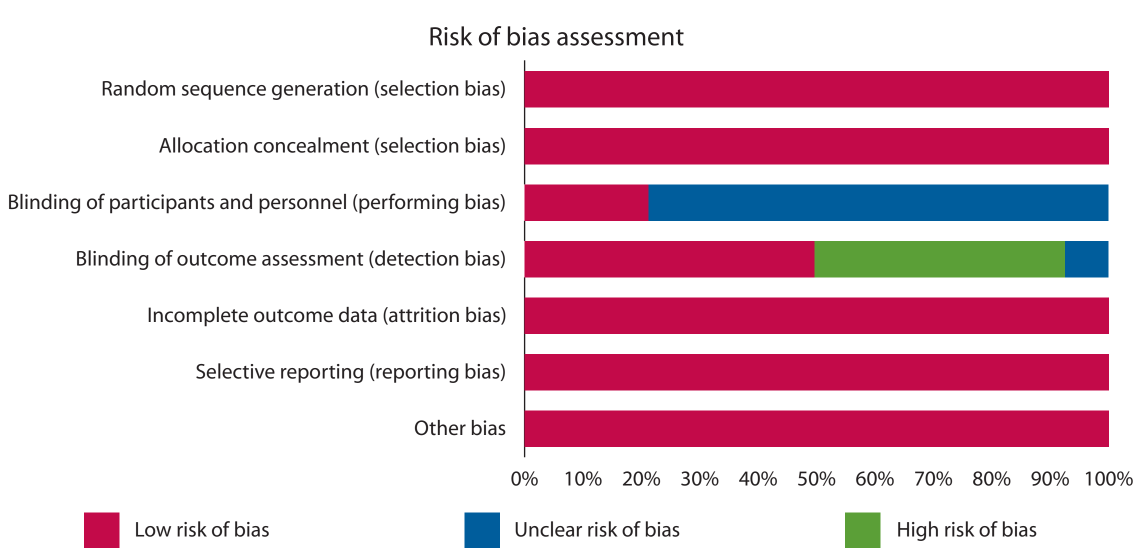
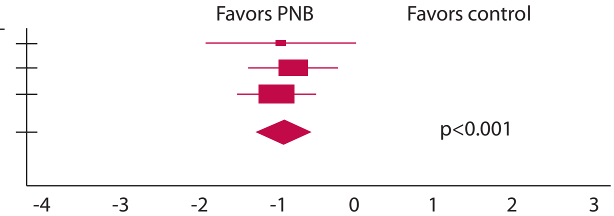


FIGURE 3. Risk of bias assessment.

Opioids quantity (mg)

	Total	SMD	95% CI	
Luck AJ 2000[31]	20	-0.966	-1.921	-0.011
Brunat G 2003[32]	52	-0.812	-1.384	-0.240
Nadri S 2018[43]	70	-1.022	-1.524	-0.520
Total (random effects)	142	-0.935	-1.280	-0.591

Test for heterogeneity: Significance level p=0.857, I^2 (inconsistency): 0%



Opioids consumption (n)

	Total	Relative Risk	95% CI	
Kim J 2005[33]	162	0.356	0.220	0.575
Naja Z 2005[34]	90	0.500	0.229	1.091
Naja Z 2006[35]	72	0.423	0.185	0.966
Adly S 2009[36]	60	0.034	0.002	0.534
Castellvi J 2009[38]	74	0.053	0.007	0.374
Trpetes K 2010[39]	120	0.296	0.147	0.599
Imbelloni LE 2013[40]	200	0.343	0.262	0.450
Aldabbas R 2014[42]	114	0.401	0.287	0.560
Di Giuseppe M 2020[44]	49	0.565	0.225	1.412
Total (random effects)	941	0.364	0.292	0.545

Test for heterogeneity: Significance level p=0.258, I^2 (inconsistency): 20.79%

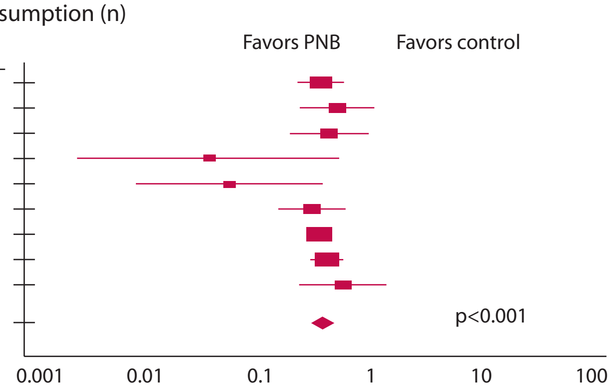


FIGURE 4. Funnel plot on the primary end point. PNB = pudendal nerve block.

p = 0.476, I^2 = 0%) and nausea/vomiting in 2 of 123 (1.6%) and 14 of 153 (9.2%) patients (RR, 0.268; 95% CI, 0.074–0.967, p = 0.675, I^2 = 0%) in the PNB and control groups. When PNB under nerve stimulation was performed, 46 of 185 (24.9%) and 167 of 237 (70.5%) patients required opioids in the PNB and control groups (RR, 0.367; 95% CI, 0.243–0.553, $p < 0.001$, I^2 = 28.5%), patients experienced less pain at 6 hours (SMD, −4.271; 95% CI, −6.308 to −2.234, $p < 0.001$, I^2 = 95.8%) and at 24 hours (SMD, −3.376; 95% CI, −5.242 to −1.510, $p < 0.001$, I^2 = 97.2%). Urinary retention occurred in 0 of 85 (0%) and 18 of 137 (13.1%) patients (RR, 0.126; 95% CI, 0.024–0.649, p = 0.817, I^2 = 0%) and nausea/vomiting in 3 of 185 (1.6%) and 46 of 237 (19.4%) patients (RR, 0.170; 95% CI, 0.046–0.633, p = 0.217, I^2 = 32.6%) in the PNB and control groups. No difference in terms of efficacy was estimated according to the PNB technique applied on opioid consumption (OR, 0.607; 95% CI, 0.056–6.637), urinary retention (OR, 1.037; 95% CI, 0.125–8.622), and nausea/vomiting (OR, 1.683; 95% CI, 0.252–11.233), whereas PNB under nerve stimulation seemed to be more effective on pain at 6 hours (SMD, −2.215; 95% CI, −4.392 to −0.038) and at 24 hours (SMD, −2.343; 95% CI, −4.124 to −0.562) than the one with anatomic landmarks.

Finally, opioid consumption did not vary among subgroups according to the type of local anesthetics (mixture vs long acting: OR, 1.915; 95% CI, 0.231–15.880) or type of anesthesia (general vs spinal: OR, 0.473; 95% CI, 0.001–657.635). No noteworthy difference on postoperative pain at 6 and 24 hours or complications were noted among groups according to the anesthetics used or the type of anesthesia.

DISCUSSION

Our systematic review and meta-analysis showed that the use of PNB in patients undergoing hemorrhoidectomy reduces opioid consumption, postoperative pain, complications, length of hospital stay, and readmissions. This is the first meta-analysis on this subject that is based mostly on good-quality randomized trials and provides level Ia evidence to support a wider use of PNB during hemorrhoidectomy.

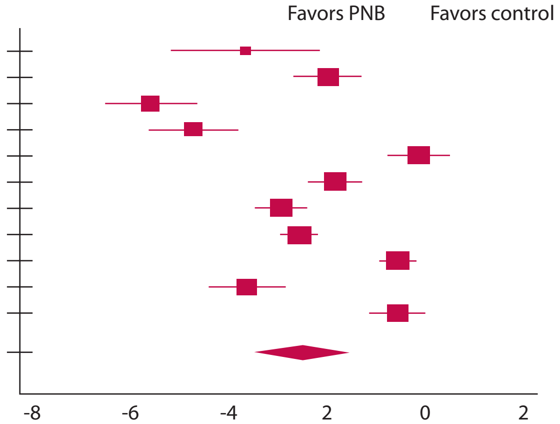
Better pain control with PNB was undisputable in the early postoperative period but was also reported for up to 5 days[34,35] and during sitting and walking. Time to first bowel movement was similar[32,40] in patients receiving or not receiving the PNB, but the first bowel movement was less painful.[34,38] The differences in the duration of effectiveness could be explained by the local anesthesia action on peripheral and central hyperalgesia mechanisms, which is described to reduce postoperative pain beyond the period of direct action.[47] Even PNB may not fully cover the whole duration of postoperative pain, which usually lasts 7 to 10 days after hemorrhoidectomy, but it facilitates same-day patient discharge and assumedly decreases health care costs.[35,39,44,48,49]

Complications related to the PNB procedure such as intravenous injection of the anesthetic, permanent nerve lesions, hematoma, abscesses or phlegmons were never reported in our literature search,[14,40,44,50] although this may

Pain within 6 hours on the visual analog scale (VAS)

	Total	SMD	95% CI	
Luck AJ 2000[31]	20	-3.673	-5.189	-2.157
Brunat G 2003[32]	52	-1.991	-2.666	-1.316
Naja Z 2005[34]	90	-5.608	-6.549	-4.668
Naja Z 2006[35]	72	-4.733	-5.647	-3.819
Santos C 2009[37]	40	-0.136	-0.765	-0.492
Castellvi J 2009[38]	74	-1.840	-2.389	-1.291
Tepetes K 2010[39]	120	-2.952	-3.473	-2.431
Imbelloni LE 2012[40]	200	-2.573	-2.949	-2.196
Aldabbas R 2014[42]	114	-0.558	-0.934	-0.182
Nadri S 2017[43]	70	-3.644	-4.419	-2.869
Di Giuseppe M 2020[44]	49	-0.561	-1.139	-0.0173
Total (random effects)	901	-2.521	-3.420	-1.622

Test for heterogeneity: Significance level p=0.001, I^2 (inconsistency): 96.13%



Pain at 24 hours on the visual analog scale (VAS)

	Total	SMD	95% CI	
Luck AJ 2000[31]	20	-5.106	-7.026	-3.186
Burnut G 2003[32]	52	-0.298	-0.850	-0.254
Kim J 2005[33]	163	-1.157	-1.490	-0.824
Naja Z 2005[34]	90	-5.168	-6.051	-4.285
Naja Z 2006[35]	72	-5.267	-6.259	-4.276
Adly S 2009[36]	60	-1.777	-2.408	-1.146
Castellvi J 2009[38]	74	-1.426	-1.941	-0.911
Tepetes K 2010[39]	120	-0.407	-0.770	-0.0441
Imbelloni LE 2012[40]	200	-1.455	-1.768	-1.142
Aldabbas R 2014[42]	114	-0.497	-0.871	-0.122
Nadri S 2018[43]	70	-1.074	-1.579	-0.568
Di Giuseppe M 2020[44]	49	-0.838	-1.430	-0.247
Total (random effects)	1084	-1.862	-2.495	-1.228

Test for heterogeneity: Significance level p=0.001, I^2 (inconsistency): 94.93%

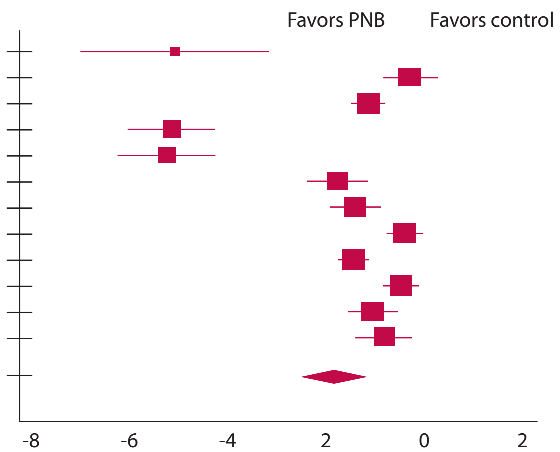


FIGURE 5. Forest plot showing the postoperative opioid consumption and need. PNB = pudendal nerve block; SMD = standardized mean difference.

have been subject to reporting bias. Pudendal nerve block obviously requires adequate training and expertise. This meta-analysis confirmed not only a very favorable safety profile for PNB, but also significantly lower rates of nausea and vomiting. Pudendal nerve block also decreased the rate of urinary retention, a relatively frequent complication after hemorrhoid surgery that may hinder outpatient treatment. Perioperative fluid administration could not explain the lower incidence of urinary retention in the patients receiving PNB because there were no differences between groups in the studies that reported these data.[32,33,40] Combined with a better pain control, the lower complication rate resulted in reduced hospital stay and readmission rates. It is no surprise that patients treated in the PNB group were more satisfied.

Three different guidance techniques for PNB were reported in the studies included. The method based on nerve stimulation seemed to be more effective on pain control than the method using anatomical landmarks, although opioid consumption and postoperative complications were similar. A comparison with the ultrasound-guided technique was not performed because it was only described by Di Giuseppe et al.[44] One advantage of nerve stimulation or ultrasound guidance should be the lower dose of local anesthetic needed, which is also expected to reduce rare complications such as sciatic nerve block.[51] There is no strong evidence supporting one PNB technique over another, and it is likely that the best results can be obtained by the PNB technique with which the operator is more familiar. Similarly, we were unable to draw any conclusions regarding the variation of efficacy according to the type and technique of hemorrhoidectomy performed.

Our meta-analysis was unable to draw any conclusions about differences when using a single long-acting rather than a combination with short-acting anesthetics. In our opinion, PNB should always include a long-acting anesthetic, such as ropivacaine known for its optimal safety profile,[52,53] but not necessarily epinephrine, which does not seem to add significant advantages at a risk of systemic complications.[54] Regarding type of anesthesia, both spinal and general are equally acceptable in combination

Operative time

	Total	SMD	95% CI	
Brunat G 2003[32]	52	-0.389	-0.944	0.165
Naja Z 2005[34]	90	0.340	-0.103	0.784
Naja Z 2006[35]	80	0.120	-0.322	0.561
Castellvi J 2009[38]	74	0.472	0.006	0.937
Tepetes K 2010[39]	120	0.000	0.359	0.359
Total (random effects)	416	0.123	-0.139	0.385

Test for heterogeneity: Significance level p=0.131, I^2 (inconsistency): 43.54%

Length of hospital stay

	Total	SMD	95% CI	
Luck AJ 2000[31]	20	-0.176	-1.078	-0.726
Brunat G 2003[32]	52	-0.035	-0.584	-0.514
Naja Z 2005[34]	90	-0.643	-1.093	-0.192
Naja Z 2006[35]	72	-1.774	-2.325	-1.223
Adly S 2009[36]	40	-1.216	-1.801	-0.631
Castellvi J 2009[38]	74	-1.219	-1.720	-0.719
Tepetes K 2010[39]	120	-0.399	-0.762	-0.036
Di Giuseppe M 2020[44]	49	-0.381	-0.953	-0.191
Total (random effects)	537	-0.742	-1.145	-0.338

Test for heterogeneity: Significance level p=0.001, I^2 (inconsistency): 79.35%

Postoperative urinary retention

	Total	SMD	95% CI	
Luck AJ 2000[31]	20	0.333	0.015	7.323
Kim J 2005[33]	163	0.107	0.049	0.233
Naja Z 2005[34]	90	0.151	0.009	2.601
Naja Z 2006[35]	52	0.0621	0.004	1.037
Adly S 2009[36]	60	0.217	0.012	3.842
Santos C 2003[37]	40	0.0526	0.003	0.847
Castellvi J 2009[38]	74	0.316	0.068	1.464
Tepetes K 2010[39]	120	0.500	0.047	5.368
Di Giuseppe M 2020[44]	49	3.375	0.144	79.002
Total (random effects)	740	0.159	0.089	0.285

Test for heterogeneity: Significance level p=0.467, I^2 (inconsistency): 0%

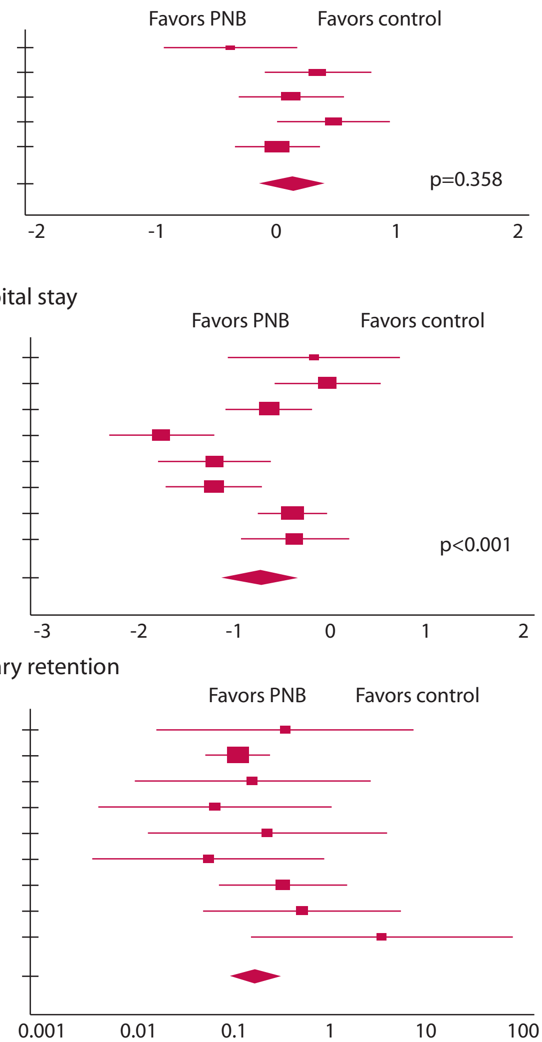


FIGURE 6. Forest plot of postoperative pain at 6 and 24 hours. PNB = pudendal nerve block; SMD = standardized mean difference.

with PNB and can be chosen according to surgeons', anesthesiologists', and patients' preference and experience.

This meta-analysis has some limitations. The most relevant are related to publication bias and heterogeneity. Although the I^2 value was 21% and 0% on the primary end point, its results were positive among some secondary end points: duration of PNB, postoperative pain, length of stay, and satisfaction. However, an intrinsic limitation of the Higgins I^2 index is the difficulty to decide whether relevant heterogeneity is present, or the effect is clinically important,[27] so that its interpretation depends heavily on clinical and methodological diversity among studies. In this meta-analysis, all studies shared the same clinical question and were methodologically appropriate and comparable; therefore, a significant clinical impact of the PNB, rather than heterogeneity effect, can be argued. Demographics, inclusion and exclusion criteria, and hemorrhoid grades were similar in all studies, as well as type of intervention, except for 1 study reporting on closed hemorrhoidectomy.[37] Heterogeneity was also present for the PNB technique, control arms, and type of anesthesia and anesthetics. Heterogeneous study designs make it difficult to draw meaningful conclusions about the efficacy of PNB because the comparator is not the same. However, accurate subgroup analyses performed according to the PNB technique, anesthetics mixture, or type of anesthesia did not show noteworthy differences compared with the main analysis. The language restriction may represent another limitation, but only 2 studies were excluded and the effect of excluding non-English trials is generally negligible.[55] Another limitation is represented by missing data; it was necessary to estimate the effect by converting into mean and SD.[24,25,45,46] Even if the estimated effect may not exactly reflect the original data, it was approximated because the differences among groups were flattened to reduce the estimation-based bias.

FIGURE 7. Forest plot showing results on operative time, length of hospital stay, and urinary retention.

CONCLUSIONS

This systematic literature review and meta-analysis shows statistically significant advantages of PNB use in patients undergoing hemorrhoidectomy. In particular, a reduction in terms of opioid consumption, postoperative pain, complications, and length of hospital stay and a higher satisfaction can be demonstrated. Despite limitations, PNB should be considered in all patients undergoing hemorrhoidectomy. Further studies specifically investigating the use of PNB vs local or perianal anesthesia are needed to identify the best approach to reduce postoperative pain in patients undergoing hemorrhoidectomy.

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