Randomized Trial

Effect of Two Doses of Hyaluronidase with Bupivacaine in Ultrasound-Guided Transversus Abdominis Plane Block for Post Cesarean Delivery Pain: A Randomized Trial

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Background: A transversus abdominis plane block provides reliable abdominal wall analgesia, but which adjuvants best sustain its effect remains debated. By facilitating diffusion of local anesthetics, hyaluronidase may improve block quality.

Objectives: This study evaluated the safety and efficacy of 2 hyaluronidase doses added to bupivacaine for bilateral transversus abdominis plane blocks in patients having a cesarean delivery.

Study Design: A prospective, randomized, double-blind, controlled clinical trial.

Setting: Benha University Hospital, Arab Republic of Egypt, from May 2023 through February 2024.

Methods: A double-blind, controlled randomized trial was performed with 114 patients having elective cesarean delivery. The patients were allocated equally into 3 arms: Group I (bupivacaine alone), Group II (bupivacaine plus 750 IU hyaluronidase), and Group III (bupivacaine plus 1500 IU hyaluronidase). The time to first rescue analgesia served as the primary outcome. Secondary outcomes encompassed 24-hour morphine requirements, Visual Analog Scale pain score at rest and on coughing, patient satisfaction, hemodynamics, and adverse events. Analyses employed the appropriate statistical tests (parametric or nonparametric), with subsequent post hoc comparisons for significant findings.

Results: Both hyaluronidase groups had significant prolonged analgesia (median 8.1 hours and 9.6 hours) compared to the control group (5.8 hours) ($P < 0.001$). Morphine requirements over the first postprocedure 24 hours diminished significantly ($P < 0.001$); Groups II and III had lower pain scores at rest and on coughing between postprocedure hours 2 and 12 (all $P < 0.05$). Patient satisfaction increased with hyaluronidase ($P = 0.0039$). No group differences were observed for adverse events, including postoperative nausea and vomiting or local anesthetic toxicity.

Limitations: This single-center trial with 24-hour follow-up may restrict generalizability and long-term safety assessment; also only 2 hyaluronidase doses were examined.

Conclusions: Adding hyaluronidase to bupivacaine for transversus abdominis plane block enhances analgesic duration and quality without compromising safety in patients having cesarean delivery. Both high and low doses appear equally effective, suggesting that even lower doses are sufficient for optimal effect.

Key words: Hyaluronidase, peripheral nerve block, postoperative pain, analgesia, bupivacaine, adjuvant, opioid-sparing, cesarean delivery, patient satisfaction, regional anesthesia, fascial plane block

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Effective pain management after cesarean delivery remains a cornerstone of enhanced recovery, yet achieving optimal analgesia while minimizing side effects continues to be a clinical challenge. Regional anesthesia strategies, notably the ultrasound-guided transversus abdominis plane (TAP) block, have become integral to multimodal analgesia for lower abdominal procedures, including cesarean delivery, due to their safety profile and ability to reduce opioid consumption (1,2).

The clinical efficacy of a TAP block largely depends on adequate diffusion of the local anesthetic solution within the fascial plane to cover multiple nerve branches (2).

To optimize this spread and prolong analgesic effect, several adjuvants, such as dexamethasone, dexmedetomidine, clonidine, and magnesium, have been widely studied (3,4). Hyaluronidase has emerged as a promising additive due to its enzymatic action in breaking down hyaluronic acid, thereby reducing tissue viscosity and facilitating better diffusion and absorption of local anesthetics. Hyaluronidase acts by hydrolyzing the glucosaminidic bonds between glucosamine and glucuronic acid in the extracellular matrix, resulting in improved tissue permeability (5).

However, despite its long history of clinical use in ophthalmology anesthesia, its potential role in fascial plane blocks has gained increasing attention, with early studies in orthopedic, gynecologic, and abdominal procedures suggesting enhanced local anesthetic spread and improved block efficacy (6-8). Yet, evidence remains limited, and the optimal dose in a TAP block, particularly after cesarean delivery, has not been clearly defined. {this paragraph could be combined with the preceding paragraph}

Our study evaluated post cesarean delivery analgesia by contrasting ultrasound-guided bilateral TAP blocks using bupivacaine only or bupivacaine combined with hyaluronidase at 2 doses, either 750 IU or 1500 IU. Our objective was to assess whether adding hyaluronidase enhances analgesic effectiveness, lowers opioid requirements, and improves patient satisfaction compared with bupivacaine alone, alongside monitoring for potential harms. We hypothesized that hyaluronidase would prolong analgesia and enhance block performance without excess complications, and that a 750 IU dose would be as effective as a 1500 IU dose.

Methods

The trial was prospectively conducted from May 2023 through February 2024 as a randomized, double-blind, controlled trial at XXX {provide name} university hospital. Ethics approval was granted by the XXX{provide} Faculty of Medicine committee (RC 4-8-2022), and the trial was prospectively registered on ClinicalTrials.gov (NCT05671172). Each patient signed a written informed consent. Procedures complied with Consolidated Standards of Reporting Trials (CONSORT) reporting standards and adhered to the Declaration of Helsinki.

Study Population

A cohort of 114 parturients aged 18–45 years, categorized as American Society of Anesthesiologists (ASA) Physical Status II, was recruited for this trial. All patients were scheduled for elective cesarean delivery with spinal anesthesia. Patients were excluded for emergency cesarean delivery; complicated pregnancy; coagulopathy or anticoagulant therapy; severe cardiovascular or respiratory disease; infection at the needle insertion area; known hypersensitivity to local anesthetic drugs or hyaluronidase; neurological disease affecting pain perception; psychiatric illness interfering with pain assessment; and obesity (body mass index [BMI, kg/m^2] $\geq$ 35).

Randomization and Blinding

A computer-generated randomization list with permuted blocks (size 6) allocated patients equally (1:1:1), developed by an independent statistician and secured until use. Allocation was concealed via sequentially numbered, opaque, sealed envelopes assembled at a pharmacy, and only opened immediately prior to preparing study solutions. All syringes were matched for volume and appearance and had anonymized codes to ensure masking. Group assignment was managed by an anesthesiologist not involved in any of the study patients' clinical care, and the study's assessments or analysis; the block-performing anesthesiologist, patients, outcome assessors, and statisticians remained blinded through database lock.

Intervention

Group I (Control): bilateral TAP block using 19 mL of bupivacaine 0.25% plus one mL saline 0.9% (per side). Group II (H750): bilateral TAP block using 19 mL of bupivacaine 0.25% plus 750 IU hyaluronidase in one mL saline (per side). Group III (H1500): bilateral TAP block using 19 mL of bupivacaine 0.25% plus 1500 IU hyaluronidase in one mL saline (per side).

All patients had a standard preoperative evaluation and were counseled about the study protocol. Intraoperatively, monitoring involved electrocardiogram, pulse oximetry, and noninvasive blood pressure monitoring. Patients received spinal anesthesia while seated position. A 25G Quincke spinal needle was used to intrathecally administer 2.5 mL of hyperbaric bupivacaine 0.5%.

TAP Block Technique

When the cesarean delivery was over, bilateral lateral TAP blocks were placed under ultrasound guidance. {it is only necessary to list specific equipment if the equipment is unique and there is no other equipment that can be used for the procedure.} A 22G short-bevel needle was directed in-plane to the interfascial space between the internal oblique and transversus abdominis muscles. Hydrodissection with 2 mL–5 mL of saline confirmed correct needle placement. Following negative aspiration, 20 mL of the study solution was deposited per side according to the patient's group allocation. To standardize technique, injections were made at the midaxillary line midway between the costal margin and iliac crest; a single anesthesiologist performed all blocks. Hemodynamic parameters were monitored throughout, and any resistance to injection or aberrant sonographic spread led to immediate needle adjustment prior to further injection.

Patients were monitored for symptoms of local anesthetic systemic toxicity (e.g., circumoral paresthesia, ear ringing, dizziness, and altered vision). In case of suspected local anesthetic systemic toxicity, immediate management included airway support, seizure control with benzodiazepines, and intravenous lipid emulsion therapy according to published guidelines (9). Other potential complications such as inadvertent intraperitoneal injection, vascular puncture, or hematoma formation were also monitored.

The postoperative analgesia regimen was multimodal. All patients received nonopioid analgesia consisting of intravenous acetaminophen (1,000 mg every 8 hours) and intravenous ketorolac (30 mg every 12 hours). Rescue analgesia was IV morphine sulfate (0.05 mg/kg), administered as a slow IV injection over 5 minutes if the Visual Analog Scale (VAS) pain score exceeded 4 mm.

Outcome Measures

The primary endpoint was the time to first rescue analgesia, defined as the period between the block completion and the initial request for supplemental pain medications. Secondary endpoints included VAS pain assessments at rest and with coughing at prespecified time points (in the postanesthesia care unit, one, 2, 4, 6, 8, 12, and 24 hours postprocedure); total morphine use over the first postprocedure 24 hours; early postoperative hemodynamic trends (hourly mean arterial pressure and heart rate for the first postprocedure 6 hours); patient-reported satisfaction at 24 hours postprocedure via a 5-point Likert scale, where one indicated very dissatisfied and 5 indicated very satisfied. Postprocedure adverse events monitored during hospitalization included nausea, vomiting, hypersensitivity, hematoma, signs of local anesthetic toxicity, and clinically apparent wound complications.

Statistical Analysis

Statistical analyses were carried out using IBM SPSS Statistics 26 (IBM Corporation). Continuous variables underwent normality assessment via Shapiro-Wilk test to determine appropriate parametric or nonparametric handling. Accordingly, results are reported as mean (SD) for normal data or median (interquartile range) for nonnormal data, while categorical variables are summarized as n (%). Intergroup comparisons for parametric outcomes used one-way analysis of variance succeeded by Bonferroni post hoc testing; nonparametric outcomes used the Kruskal-Wallis test with the Dunn multiple comparison procedure. Proportions were compared with the Pearson χ^2 test, resorting to the Fisher exact test when assumptions were violated. Two-tailed P values < 0.05 were deemed to have statistical significance.

Sample Size Calculation

The primary endpoint of the trial was the time to first rescue analgesia. Based on the findings of Petkar, et al (7), who reported prolonged TAP block analgesia when local anesthetic was supplemented with hyaluronidase, we assumed a minimum clinically important difference of 15 minutes with a common SD of 20 minutes. To observe this difference with 80% power and an α of 0.05, a sample size of 34 patients for each group was required. Allowing for a 10% dropout rate, 38 patients were recruited in each group, giving a total of 114 patients.

Results

Among 119 screened patients, 4 failed to meet the inclusion criteria and one refused participation, result-

ing in 114 patients. They were randomized in equal allocations to 3 arms (38 per group). No losses occurred, and all data were analyzed (Fig. 1).

The demographics of the 3 groups were well balanced at baseline, showing similar distributions of age, anthropometrics (weight, height, BMI). In addition, there were no significant between-group differences for TAP block performance time and procedure duration (Table 1).

The mean (SD) interval to first rescue analgesia was longer in the hyaluronidase groups relative to the control group (8.1 [3.4] hours and 9.6 [4.2] hours in Groups II and III vs 5.8 [3.5] hours in Group I; $P < 0.001$). Post hoc comparisons showed significance for Group II vs Group I ($P = 0.012$) and Group III vs Group I ($P < 0.001$), but not for Group II vs Group III ($P = 0.193$).

Mean total morphine consumption in the first postprocedure 24 hours decreased in Groups II and III relative to Group I (9.5 [4.1] mg and 8.1 [3.8] mg vs 11.8 [4.9] mg; $P < 0.001$). Post hoc analysis indicated lower use in Group II vs Group I ($P = 0.023$) and Group III vs Group I ($P < 0.001$), with no significant difference between Groups II and III ($P = 0.152$) (Table 2).

Postoperative VAS scores, both at rest and with coughing, were significantly lower in Groups II and III than in Group I at postprocedure hours 2, 4, 6, and 8 (all $P < 0.05$). Moreover, Group III had additional reductions compared with Group II at 6–8 hours postprocedure. At 12 hours postprocedure, only Group III maintained lower rest scores vs Group I, while no significant differences were noted in the postanesthesia care unit, at postprocedure hours one and 24 (Fig. 2).

Hemodynamic indices, heart rate, and mean arterial pressure, measured in the postanesthesia care unit and hourly up to 6 hours postprocedure were similar across the groups, with no statistically significant differences at any time point (Fig. 3).

Mean (SD) patient satisfaction scores favored Group III over the control group (4.0 [1.1] vs 3.4 [0.9]; $P < 0.001$). Group II similarly exceeded Group I (3.7 [1.1] vs 3.4 [0.9]; $P = 0.045$). However, there was no significant difference between Group II and Group III ($P = 0.089$).

The rates of postoperative nausea and vomiting and pruritus did not achieve statistical significance among the groups. Notably, no patient in any group had a hypersensitivity reaction, hematoma, wound-related complication, or local anesthetic toxicity (Table 3).

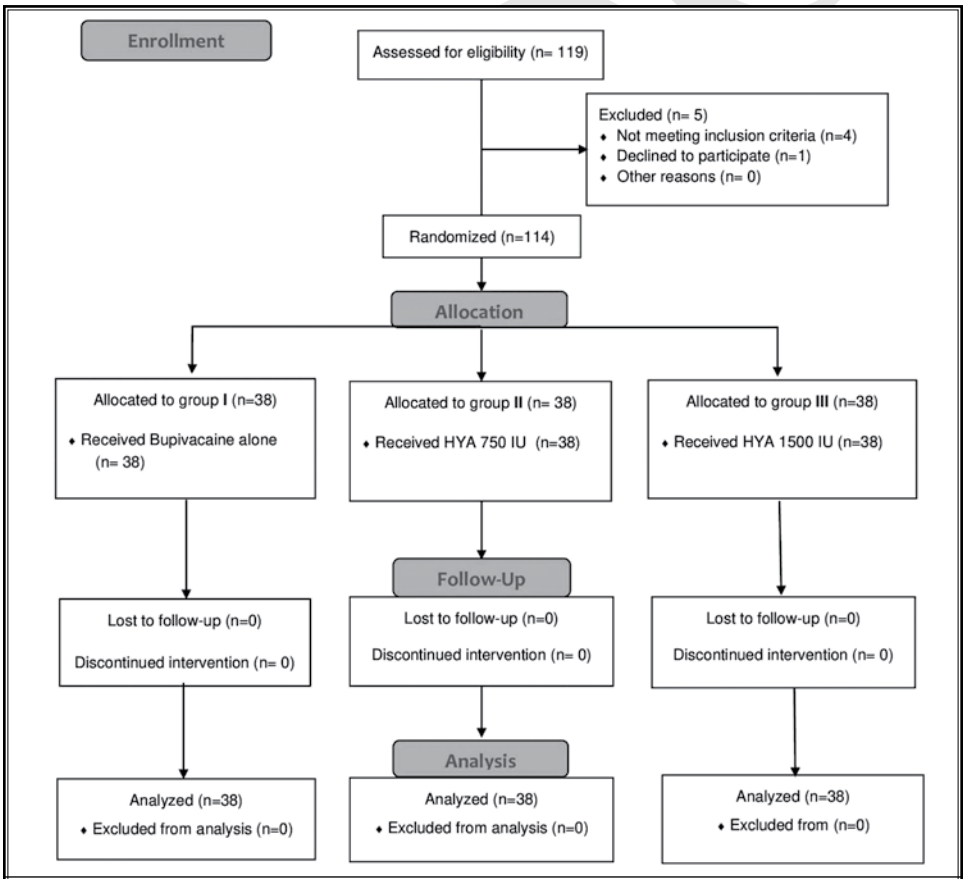

Fig. 1. *Consolidated Standards of Reporting Trials (CONSORT) flow diagram of patient enrollment, randomization, and follow-up.*

Discussion

In our randomized controlled trial, 2 hyaluronidase doses (750 IU and 1500 IU) were evaluated as adjuvants to bupivacaine for ultrasound-guided TAP block to provide post cesarean delivery analgesia. A total of 114 patients were al-

located equally to 3 arms, with baseline demographic and perioperative variables well balanced across groups. The primary outcome—the interval to first rescue analgesia—was significantly prolonged in both hyaluronidase groups compared with bupivacaine alone. Secondary outcomes findings were: a reduction in total 24-hour postprocedure morphine consumption and postprocedure VAS scores during the early procedure hours (2–8 hours), were significant in the hyaluronidase groups, with no statistically or clinically meaningful differences between Group III and Group II, despite minor numerical variations at select time points. Patient satisfaction scores were higher among patients who received hyaluronidase, reflecting a better overall analgesic experience. Importantly, hemodynamic parameters (heart rate and mean arterial pressure) remained stable across the groups, and the incidence of adverse events—including postoperative nausea and vomiting, pruritus, urinary retention, hematoma, or local anesthetic toxicity—did not achieve statistical difference among groups. Taken together, these results indicate that adding hyaluronidase to bupivacaine enhances TAP block analgesia without compromising safety, and that escalating the dose offers no extra advantage, thus supporting effective analgesia without unnecessary increases in enzyme dose or theoretical risk.

From a mechanistic perspective, our study's results align with prior evidence that hyaluronidase facilitates more uniform distribution of local anesthetic within fascial planes, thereby optimizing sensory block quality (10). Mechanistically, hyaluronidase acts by hydrolyzing hyaluronic acid, a major element of the extracellular matrix that contributes to tissue viscosity and acts as a diffusion barrier. By transiently reducing tissue resistance, the enzyme allows the injected local anesthetic to spread more freely and evenly across the TAP, increasing the likelihood of contacting multiple segmental nerves. This wider and more homogeneous distribution not only augments the density of the block but may also accelerate the onset of analgesia, since the drug reaches target nerve fibers more efficiently. Additionally, the facilitated dispersion reduces the chance of "patchy" or incomplete coverage, which is a recognized limitation of fascial plane blocks (11,12).

In this context, it is important to distinguish hyaluronidase from other commonly studied TAP block adjuvants. Adjuvants such as dexamethasone, dex-

Table 1. *Study patients baseline and perioperative demographics.*

	Group I (n = 38)	Group II (n = 38)	Group III (n = 38)	*P* Value
Age (yrs)	31.3 (6.1)	30.6 (7.8)	30.3 (7.9)	0.821
Weight (kg)	77.1 (10.3)	76.3 (10.9)	75.8 (11.6)	0.869
Height (m)	1.66 (0.07)	1.67 (0.07)	1.67 (0.07)	0.743
BMI (kg/m^2)	27.9 (3.8)	27.4 (3.7)	27.1 (3.9)	0.652
Block time (min)	8.8 (2.2)	9.2 (2.4)	9.0 (2.1)	0.672
Duration of surgery (min)	83.2 (21.1)	73.4 (20.8)	78.2 (21.6)	0.068

Values are presented as mean (SD). BMI; body mass index.

Table 2. *Primary outcome and analgesic consumption.*

	Group I (n = 38)	Group II (n = 38)	Group III (n = 38)	*P* Value	Post Hoc (P1, P2, P3)
Time to first rescue analgesia (h)	5.8 (3.5)	8.1 (3.4)	9.6 (4.2)	< 0.001*	P1: 0.012* P2: < 0.001* P3: 0.193
Total morphine consumption (mg/24h)	11.8 (4.9)	9.5 (4.1)	8.1 (3.8)	< 0.001*	P1: 0.023* P2: <0.001* P3: 0.152

Values are presented as mean (SD). * denotes {statistical or clinical?} significance. P1: *P* value between Group I and Group II. P2: *P* value between Group I and Group III. P3: *P* value between Group II and Group III.

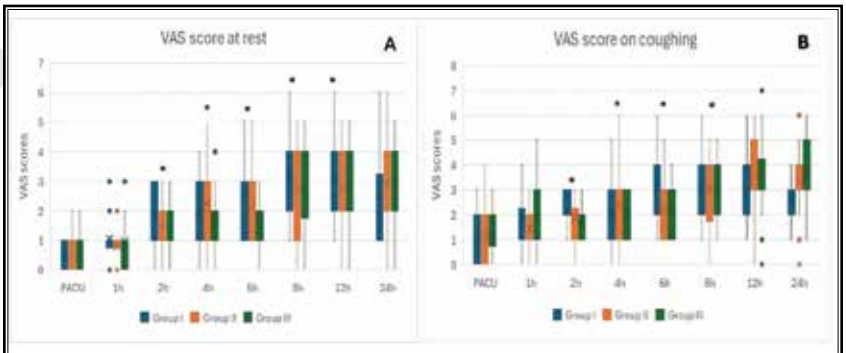

Fig. 2. *Postoperative pain scores. (A) Visual Analog Scale (VAS) scores at rest, in the postanesthesia care unit, and postprocedure hours one, 2, 4, 6, 8, 12, and 24. (B) VAS scores on coughing at the same time points. Values are presented as mean (SD). * denotes {statistical or clinical?} significance P < 0.05.*

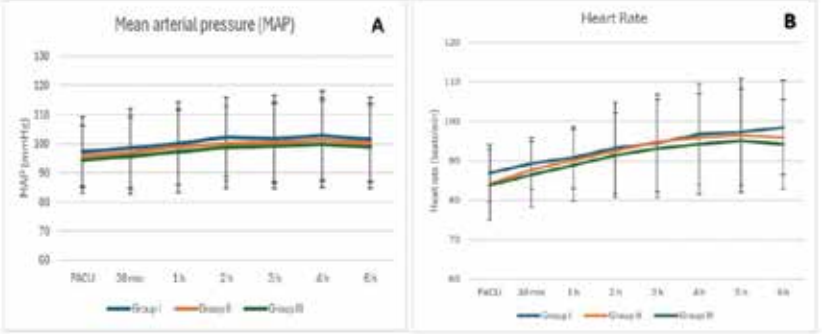

Fig. 3. *Postprocedure hemodynamic changes. (A) Mean arterial pressure (MAP) over the first 6 postprocedure hours. (B) Heart rate (HR) over the first 6 postprocedure hours. Values are presented as mean (SD).*

Table 3. *Patient satisfaction and adverse effects.*

	Group I (n = 38)	Group II (n = 38)	Group III (n = 38)	*P* Value
Patient Satisfaction Score	3.4 (0.9)	3.7 (1.1)	4.0 (1.1)	0.001*
PONV, n (%)	9 (30.0%)	5 (13.2%)	4 (10.5%)	0.134
Pruritus, n (%)	3 (7.9%)	3 (7.9%)	1 (2.6%)	0.402
Hypersensitivity reaction, n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	> 0.999
Hematoma, n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	> 0.999
LA Toxicity, n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	> 0.999

Values are presented as mean (SD). PONV: postoperative nausea and vomiting. LA: local anesthetic. *Post-hoc for satisfaction: P1 = 0.045*, P2 < 0.001*, P3 = 0.089.{additional explanation needed for post hoc *P* values}

medetomidine, clonidine, and magnesium have been explored to augment TAP block analgesia, mainly through receptor-mediated pathways that extend neural blockade without altering injectate spread (13). Hyaluronidase acts enzymatically to facilitate local anesthetic diffusion within the fascial plane, making it particularly suited to fascial plane techniques where distribution is critical to a successful outcome.

Consistent with our findings, several clinical studies across various abdominal procedures, including bariatric surgery (14), gynecologic operations (7), and laparoscopic cholecystectomy (15,16) have reported that adding hyaluronidase to the local anesthetic improves TAP block performance, most notably prolonging analgesia, lowering early postoperative pain scores, and reducing opioid use. These observations mirror our results regarding time to first analgesia request, VAS score improvement, and opioid sparing, supporting the reproducibility of hyaluronidase benefits across abdominal surgery types.

Mechanistically, these convergent clinical observations are supported by Santha (17), who reviewed hyaluronidase as an adjuvant and highlighted its capacity to depolymerize hyaluronic acid within connective tissue, transiently lowering interstitial viscosity and thereby facilitating wider, more homogeneous dispersion of the local anesthetic within the transversus abdominis fascial plane. This broader spread plausibly increases the likelihood of bathing multiple segmental nerves with a single injection, which explains our patients' lower early postprocedure VAS scores and delayed rescue requests without hemodynamic instability or added block-related complications.

Taken together, these studies span different surgical populations (bariatric, gynecologic, biliary) and TAP approaches (lateral and subcostal) yet consistently point in the same direction: hyaluronidase improves block quality and postoperative analgesic outcomes when added to long- or intermediate-acting local anesthetics (18). Importantly, none of these reports signal a safety concern at commonly used unit doses, which is concordant with our absence of hematoma or local anesthetic systemic toxicity and the comparable rates of minor adverse events across groups. At the same time, heterogeneity in dose (typically several hundred to approximately 1,500 IU); local anesthetic choice and concentration; timing relative to surgery; and outcome windows makes it difficult to define a single "optimal" dose. Our head-to-head comparison directly addresses this gap, demonstrating that 750 IU of hyaluronidase provides analgesic efficacy comparable to 1,500 IU without additional clinical benefit, an observation future dose-finding studies should formally test.

In contrast to earlier studies that mostly contrasted TAP blocks with vs without hyaluronidase in smaller samples or nonobstetric populations, our adequately powered randomized trial is the first to directly compare 2 dosing levels of hyaluronidase as an adjuvant to bupivacaine for cesarean delivery. It verifies the analgesic advantage of adding hyaluronidase and demonstrates that 750 IU performs on par with 1,500 IU. These results add clinically meaningful

evidence that optimal analgesia can be achieved with less drug exposure and simultaneously underscore the favorable safety profile of hyaluronidase in obstetric regional anesthesia.

Despite these benefits, safety concerns warrant attention. Although hyaluronidase enhances analgesia, its use as a regional anesthetic adjuvant raises theoretical safety concerns, including allergy, unintended extension of block, augmented systemic uptake of local anesthetic, and possible tissue effects. Hypersensitivity reactions have been described mainly in ophthalmic anesthesia, with reported incidences typically under 1%, especially for non–animal-derived formulations (19). In our trial, no hypersensitivity or allergic events occurred in either hyaluronidase group, aligning with previous TAP block studies that documented favorable safety profiles when hyaluronidase is added to local anesthetics (7,8,14,16).

A further theoretical concern is that hyaluronidase could promote systemic absorption of local anesthetic and predispose to local anesthetic systemic toxicity; experimental work showed no meaningful effect on the systemic disposition of amide agents (11,12). Consistently, we detected no features of local anesthetic systemic toxicity; existing guidance favors vigilant monitoring over avoiding such adjuvants (9). Likewise, concerns regarding impaired wound healing or hematoma formation appear unsubstantiated, as the enzyme's effect is brief and followed by rapid reconstitution of extracellular matrix components (11,18). The absence of wound complications and hematomas in our study further supports the safety of hyaluronidase-facilitated TAP blocks within standard dose limits.

Limitations

Our findings should be interpreted in light of certain constraints. First, conducting the trial in one center with a limited sample may reduce the extent to which results can be extrapolated to other institutions or diverse clinical contexts. Second, the 24-hour follow-up window did not allow assessment of sustained analgesic benefits, functional recovery, maternal-infant outcomes, or delayed adverse events. Third, although our study was powered to detect differences in analgesic duration and opioid consumption, it may not have been adequately powered for detecting rare complications. Finally, both low and high doses of hyaluronidase showed similar efficacy, but dose–response relationships beyond the studied range were not explored.

Conclusion

The adjunctive use of hyaluronidase with bupivacaine in bilateral TAP blocks for cesarean delivery extended analgesic duration, reduced postprocedure opioid consumption, and improved patient-reported satisfaction without increasing complications. Efficacy was similar between the 750 IU and 1,500 IU doses. Collectively, our results endorse hyaluronidase as a viable, safe enhancer of TAP block performance in obstetrics, while highlighting the necessity for multicenter studies with extended assessment to validate benefits and define dosing.

References

1. Sriramkes B, Sahoo N, Panigrahi S. Analgesic efficacy of ultrasound guided transverse abdominis plane block following cesarean section. *Int J Perioper Ultrasound Appl Technol* 2012; 1:5-8.
2. Fusco P, Cofini V, Petrucci E, et al. Transversus abdominis plane block in the management of acute postoperative pain syndrome after caesarean section: A randomized controlled clinical trial. *Pain Physician* 2016; 19:583-591.
3. Abdelrahman TN, Abu-Sinna RG. Comparing intravenous single low doses of magnesium sulphate versus dexamethasone as adjuvants to ultrasound guided transversus abdominis plane block for prolongation of postcesarean analgesia. *Open Anesth J* 2021; 15:23-29.
4. Gupta B, Gupta A, Verma RK, Shah P. Comparative study of dexmedetomidine and clonidine as an adjunct to levobupivacaine in transversus abdominis plane block in patients undergoing total abdominal hysterectomy: A randomized control study. *Int J Reprod Contracept Obstet Gynecol* 2019; 8:3992-3998.
5. Mohankumar A, Rajan M. Role of hyaluronidase as an adjuvant in local anesthesia for cataract surgery. *Indian J Ophthalmol* 2023; 71:2649-2655.
6. Hakim K, Ahmed M. Effect of addition of hyaluronidase as an adjuvant to local anesthetics in ultrasound-guided supraclavicular brachial plexus block. *Ain Shams J Anesthesiol* 2017; 10:12-17.
7. Petkar J, Naik SS, Devi S. A randomized controlled trial to study the effect of hyaluronidase as adjuvant in ultrasound-guided transversus abdominis plane block for postoperative analgesia in total abdominal hysterectomy. *J Musculoskelet Ultrasound Pain Med* 2020; 6:27-33.
8. Mohaned S, Badawi F, Ali HM, Refat G. Postoperative analgesic efficacy of bupivacaine with hyaluronidase in TAP block for lower abdominal surgeries. *Sohag Med J* 2017; 21:295-300.
9. Neal JM, Barrington MJ, Fettiplace MR, et al. The third American Society of Regional Anesthesia and Pain Medicine practice advisory on local anesthetic systemic toxicity: Executive summary 2017. *Reg Anesth Pain Med* 2018; 43:113-123.

10. de Moura BD, de Miranda DB, Govêia CS. Addition of hyaluronidase reduces failure of regional block in ophthalmic surgery: Meta-analysis of randomized clinical trials. *Biomed J Sci Tech Res* 2020; 29:22672-2268.
11. Schulze C, Bittorf T, Walzel H, Bader R, Mittelmeier W. Experimental evaluation of hyaluronidase activity in combination with specific drugs applied in clinical techniques of interventional pain management and local anaesthesia. *Pain Physician* 2008; 11:877-883.
12. Buhren BA, Schrumpf H, Hoff NP, Bolke E, Hilton S, Gerber PA. Hyaluronidase: From clinical applications to molecular and cellular mechanisms. *Eur J Med Res* 2016; 21:5.
13. Wang LZ, Huang JY, Chang XY, Xia F. Adjuvants in transversus abdominis plane blocks to prolong analgesia duration following cesarean delivery: A systematic review and network meta-analysis. *J Clin Anesth* 2026; 108:112067.
14. Marzouk MM, Said AM, Abdelaziz AA, Selima WZ, Yousef MW. Comparative study of ultrasound guided transversus abdominis plane block using bupivacaine with and without hyaluronidase in laparoscopic bariatric surgery. *Ain Shams Med J* 2020; 71:647-658.
15. Johnson MZ, O'Connor TC. Excellent postoperative analgesia with the addition of hyaluronidase to lignocaine for subcostal TAP block used in conjunction with systemic analgesia for laparoscopic cholecystectomy. *BMJ Case Rep* 2014; 7:bcr2013202911.
16. Sherif RA, Abd El-Nabi MF, Ali MA, El-Shaarawy AM. Ultrasound-guided transversus abdominis plane block using bupivacaine with or without hyaluronidase in laparoscopic cholecystectomy. *Egypt J Med Res* 2024; 5:211-218.
17. Santha N. A review on hyaluronidase as an ideal adjuvant to nerve blocks. *Ymer* 2022; 21:1078-1083.
18. Weber GC, Buhren BA, Schrumpf H, Wohlrab J, Gerber PA. Clinical applications of hyaluronidase. In: Labrou, N. (ed) *Therapeutic Enzymes: Function and Clinical Implications*. Springer, Singapore, 2019, pp 255-277.
19. Venkatakrishnan JV. Hypersensitivity reaction to injection hyaluronidase after multiple eye surgery: Presentation, management, and preventive strategies. *Indian J Ophthalmol* 2024; 72:1216-1218.