Obstetrical and Pediatric Anesthesia

Iliohypogastric-ilioinguinal peripheral nerve block for post-Cesarean delivery analgesia decreases morphine use but not opioid-related side effects

[L'analgésie post-césarienne par blocage nerveux ilio-hypogastrique et ilio-inguinal réduit les besoins de morphine mais non les effets secondaires reliés aux opioïdes]

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Purpose: To examine if ilioinguinal-iliohypogastric nerve block could reduce the need for post-Cesarean delivery morphine analgesia and thus reduce the incidence of opioid related adverse-effects.

Methods: A multi-level technique for performing the nerve block with bupivacaine was developed and then utilized in this two-part study. Part one was a retrospective assessment of Cesarean delivery patients with and without ilioinguinal-iliohypogastric blocks to determine if the technique reduced patient controlled analgesia morphine use and thus would warrant further study. The second phase was a randomized double-blind placebo-controlled trial to compare post-Cesarean morphine use and the appearance of opioid-related side effects between the anesthetic and placebo-injected groups.

Results: Both phases demonstrated that our method of ilioinguinal-iliohypogastric nerve block significantly reduced the amount of *iv* morphine used by patients during the 24 hr following Cesarean delivery. In the retrospective assessment, morphine use was 49 ± 30 mg in the block group *vs* 79 ± 25 mg in the no block group ($P = 0.0063$). For the prospective trial, patients who received nerve blocks with bupivacaine had a similar result, self-administering 48 ± 27 mg of morphine over 24 hr compared to 67 ± 28 mg administered by patients who received infiltrations of saline. However, despite the significant decrease in morphine use, there was no reduction in opioid-related adverse effects: the incidences of nausea were 41% and 46% ($P = 0.70$) and for itching were 79% and 63% ($P = 0.25$) in the placebo and nerve block groups, respectively.

Conclusion: A multi-level ilioinguinal-iliohypogastric nerve block technique can reduce the amount of systemic morphine required to control post-Cesarean delivery pain but this reduction was not associated with a reduction of opioid related adverse effects in our study group.

Objectif : *Vérifier si l'anesthésie par blocage nerveux ilio-inguinal et ilio-hypogastrique peut réduire les besoins post-césarienne de morphine et l'incidence des effets indésirables des opioïdes.*

Méthode : *Une technique de blocage nerveux multiniveau, avec de la bupivacaïne, a été mise au point et utilisée pour une étude en deux phases. La première consistait en une évaluation rétrospective des accouchements par césarienne avec et sans blocages ilio-inguinal et ilio-hypogastrique dans le but de déterminer si la technique réduit l'usage de morphine auto-administrée, ce qui pourrait justifier des études plus poussées. La seconde phase était un essai, randomisé et contrôlé en double aveugle contre placebo, réalisé pour comparer l'usage intergroupe de morphine post-césarienne et l'apparition d'effets secondaires reliés aux opioïdes.*

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Résultats : *Pour les deux phases de l'étude, l'anesthésie par blocage nerveux ilio-inguinal et ilio-hypogastrique a permis de réduire significativement la quantité de morphine iv utilisée pendant les 24 premières heures suivant la césarienne. Dans l'évaluation rétrospective, la morphine utilisée a été de 49 ± 30 mg chez les patientes qui ont reçu un bloc vs 79 ± 25 mg, sans bloc (P = 0,0063). Les résultats de l'essai prospectif sont comparables, l'auto-administration de morphine pendant 24 h étant de 48 ± 27 mg et de 67 ± 28 mg avec et sans bupivacaïne, respectivement. Cependant, il n'y a pas eu de réduction des effets indésirables reliés aux opioïdes : les incidences de nausée ont été de 41 % et de 46 % (P = 0,70) et de prurit, 79 % et 63 % (P = 0,25) chez les patientes avec placebo et bloc nerveux, respectivement.*

Conclusion : *Un blocage nerveux ilio-inguinal et ilio-hypogastrique a permis de réduire la quantité de morphine à action générale utilisée pour soulager la douleur post-césarienne, mais cette réduction n'a pas été associée à une baisse des effets secondaires reliés aux opioïdes.*

THE Pfannenstiel incision and subsequent manipulations associated with Cesarean section (CS) delivery are known to produce a significant degree of post-procedural pain. This pain can be effectively relieved with neuraxial or systemic opioid administration.[1] However, as with any postoperative opioid use, a high incidence of pruritus, nausea, vomiting, sedation, and occasionally respiratory depression may occur. Debilitating in themselves, these opioid-related adverse effects can produce additional problems for new mothers such as delayed initiation of breastfeeding and impairment of mother/infant bonding.

The postoperative pain that follows a CS with the Pfannenstiel incision has both a somatic component and a visceral component. The somatic pain generated at the incision site is conducted by the iliohypogastric and ilioinguinal nerves (IHII), which innervate the L1–2 dermatome distribution.[2] Generalized wound infiltration with local anesthetics can produce some reduction in post-CS delivery pain[3] but this route can be an ineffectual means of drug administration. We believed that, because of the IHII involvement, there was the potential for multiple anesthetic injection along this nerve track to produce a significant degree of post-CS pain relief.

In contrast to the somatic component of postoperative pain, the visceral pain component is diffuse with no peripheral nerve association.[4] We hypothesized that an enhanced IHII nerve block technique, in combination with early administration of oral medication, would decrease postoperative patient controlled analgesia (PCA) morphine use by effectively addressing the somatic and visceral pain pathways. By extension, we expected such a reduction in morphine use to be accompanied by reductions in the incidences of the most common opioid-related adverse effects, itching and nausea. Recognizing both the potential of IHII blocks and the limitations of previously published block techniques (e.g., single site injection), we developed a multi-level IHII block methodology for use following CS. This block procedure was incorporated into our postoperative analgesia regimen. Once members of the Division of Women's Anesthesia were comfortable administering the IHII blocks, we evaluated (retrospectively and prospectively) the effectiveness of this procedure in reducing PCA-morphine use following CS.

Materials and methods

This investigation was conducted at Duke University Medical Center. The various components of the study were each reviewed and approved by the Institutional Review Board and informed signed consent (when applicable) was obtained from all participants. The study population included both primiparous and multiparous women undergoing non-emergent CS (i.e., no fetal or maternal indications for immediate delivery). Parturients were excluded from both the retrospective and prospective analyses if they exhibited one of the following pathologies: preeclampsia; eclampsia; history of substance abuse; allergy to either local anesthetics or non-steroidal anti-inflammatory drugs; peptic ulcer disease; renal disease; progressive neurologic disease; or infection at the site of the IHII nerve block.

Anesthetic/analgesic techniques for Cesarean delivery

Anesthesia for CS was achieved using a standardized spinal (dose, 12 mg of 0.75% bupivacaine in dextrose) or epidural (dose, 400 mg of 2% lidocaine with 5 $\mu g \cdot mL^{-1}$ epinephrine) method at the discretion of the attending anesthesiologist.

PCA-morphine parameters

Postoperative PCA orders were written in a standardized fashion and were activated in the recovery room. There was a loading morphine dose of 0.04 $mg \cdot kg^{-1}$ and an intermittent dose of 0.02 $mg \cdot kg^{-1}$. The lockout interval was set at ten minutes; there was no continuous infusion. Up to three loading doses could be administered on pump initiation and nurses could increase the intermittent dose by 25% if pain remained greater than 50 on a 100 mm scale after one hour. No patients attained the maximum PCA-morphine dose allowed by these parameters.

IHII nerve block technique

A standardized method for performing the IHII nerve block was developed. The anterior superior iliac spine

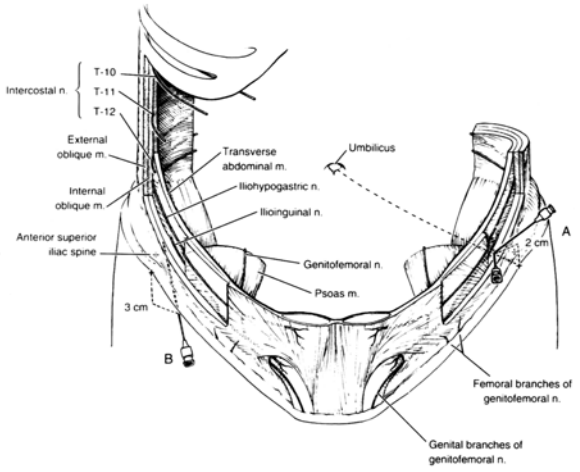

FIGURE 1 Anatomical schema depicting the locations of the iliohypogastric and iliolinguinal nerves along with two of the injection sites. Modified from Brown DL. Atlas of Regional Anesthesia and Analgesia (1992). WB Saunders, with permission.

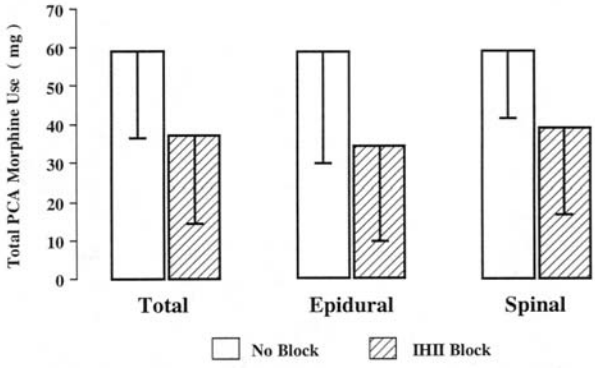

FIGURE 2 Mean (± SD) post-procedural morphine use of patients in the retrospective study. Dichotomizing the totals demonstrates that the reduction in morphine consumption associated with our iliohypogastric-ilioinguinal nerve block technique was not dependent upon the method of regional anesthesia used during the Cesarean section.

(ASIS) was identified (see Figure 1) and an introducer needle (a 22 gauge Whitacre needle; Becton Dickinson, Franklin Lakes, NJ, USA) was inserted at a point 2 cm medial and 2 cm superior to the ASIS. The blunt tip of the Whitacre needle allows for identification of the muscle fascia and serves to push away the untethered peripheral nerves present in the loose connective tissue between the muscle layers. The needle was advanced until a loss of resistance was noted upon piercing the fascia of the external oblique muscle. After a negative aspiration test, 2 mL of 0.5% bupivacaine with 5 $\mu g \cdot mL^{-1}$ of epinephrine were injected between the external and internal oblique muscle layers. Using the same loss of resistance technique, another 2 mL of anesthetic solution were injected between the internal oblique and transversus abdominus muscles. The needle was then returned to the dermis and directed medially and then laterally at angles of 15° in the same horizontal plane. The same six-injection procedure was repeated on the contralateral side. In total, 24 mL of local anesthetic solution were deposited. The IHII injections were performed in this standardized fashion following wound closure with staples, but prior to application of the dressing. The entire procedure took less than five minutes to perform. When appropriate (i.e., during the non-blinded studies), presence and adequacy of the IHII block was assessed by pinprick in the recovery room following regression of the neuraxial block used for CS anesthesia.

Retrospective IHII block study

We collected the charts of all parturients who had undergone CS under spinal or epidural anesthesia from July 1st 1996 through September 30th 1996. The IHII block methodology had been introduced in February 1996, so that all attending obstetrical anesthesiologists were proficient with the technique before study initiation. IHII blocks were administered routinely, but not exclusively, during the three-month interval. Neuraxial narcotics were not administered to any CS patients during this period. The records were culled based upon the pre-stated exclusion criteria. The remaining charts were reviewed to obtain PCA morphine use data (the primary end-point) as well as maternal demographic information.

Randomized controlled trial (RCT): IHII blocks and iv PCA-morphine use

The primary end-point for the double-blind RCT was 24 hr *iv* PCA morphine use by patients who received IHII block injections. Eligible parturients undergoing scheduled CS with Pfannenstiel incision under spinal or epidural anesthesia were recruited. Once written informed consent was obtained, patients were randomized by the investigational drug service at our institution (via computer-generated block randomization) to receive IHII injections of either 0.5% bupivacaine-epinephrine solution or placebo (saline). Blocks were performed following wound closure by anesthesiologists unaware of the treatment assignment.

Postoperative *iv* PCA-morphine orders and orders for naproxen sodium 500 mg *po* every 12 hr were written for all patients. Along with cumulative dose of *iv* PCA-morphine, the level of pain was measured using a visual analogue scale (VAS). The scale was a 100-mm unhatched horizontal line with the phrases "no pain" and "worst pain imaginable" at the left and right ends of the line, respectively. Pain scores were obtained at six, 12, 18, and 24 hr after arrival in the recovery room. Patients were not allowed to view their previous responses. Morphine usage was recorded from the PCA device and totalled after 24 hr. In addition, each patient's perceptions of her nausea and her itching were recorded as yes/no answers at each time point.

Statistical analysis

All statistics were calculated using a package obtained from the SAS Institute (Cary, NC, USA).

For the retrospective study, self-administered morphine use in $mg \cdot kg^{-1}$ was analyzed using an analysis of co-variance controlling for hours of access to PCA, oral medication use, and whether the patient's PCA morphine use was affected by the type of CS anesthetic (spinal or epidural) that they received.

The primary result of the retrospective study (difference in morphine consumption) was used to design the prospective portion of this investigation. With alpha = 0.05, the study required 45 patients in both the bupivacaine and placebo injection groups to provide 90% statistical power to detect a difference in morphine consumption of 20 mg over 24 hr. At completion of the RCT, morphine consumption was compared using Student's t test for unequal variances after logarithmic transformation; residuals were normally distributed. The other end-points were mean VAS pain scores over 24 hr, the percentage of patients with itching, and the percentage of patients with nausea. VAS scores were compared between groups using Student's t test for unequal variances while the percentage values were compared using Fisher's exact test.

Results

Retrospective IHII block study

Between July and September of 1996, 120 patients underwent a scheduled CS at our institution. Initial review of the records resulted in the removal of 19 patients because of the presence of one or more exclusion criteria. Of the remaining 101 patients, 51 received an IHII block. Assessment of the procedure showed a > 95% success in achieving diminished sensation to pinprick in the L1–2 distribution after resolution of the neuraxial block. Demographic data, CS duration, and type of procedural anesthetic used are presented in the first two columns of Table I. The make-up of the two groups was similar.

TABLE I Patient demographic and procedural data

Parameter	*Retrospective study*		*RCT*	
	No block	*IHII block*	*Placebo block*	*IHII block*
Sample size	50	51	28	31
Age	26 ± 7	27 ± 7	31 ± 6	30 ± 6
Height (cm)	164 ± 8	161 ± 8	163 ± 7	163 ± 7
Weight (kg)	86 ± 19	86 ± 21	90 ± 23	88 ± 19
BMI ($kg \cdot m^2$)	29 ± 6	30 ± 9	34 ± 9	33 ± 8
GA (weeks)	37 ± 2	37 ± 2	38 ± 2	38 ± 2
CD duration (min)	88 ± 39	81 ± 20	86 ± 16	88 ± 14
Type of procedural anesthetic				
Epidural (%)	24 (66)	19 (37)	7 (25)	6 (19)
Spinal (%)	17 (34)	32 (63)	21 (75)	25 (81)

Maternal data (mean ± SD where applicable) for patients enrolled in the two studies. RCT = randomized controlled trial; IHII = ilioinguinal-iliohypogastric; BMI = body mass index; GA = gestational age (estimated); CD = Cesarean delivery.

TABLE II Post-procedural morphine use, pain control and side effects

Variable	*Retrospective study*		*RCT*	
	No block	*IHII block*	*Placebo block*	*IHII block*
Sample size	50	51	28	31
Morphine use (mg/24 hr)	79 ± 25	49 ± 30*	67 ± 28	48 ± 27*
Mean VAS score (mm)	-	-	22 ± 14	17 ± 10
% Itching	-	-	79	65
% Nausea	-	-	43	45

Within each study, *denotes a significant difference in *iv* morphine use between the two treatment groups; actual *P* values are reported in the text. Data were not compared between studies. Visual analogue scale (VAS) scores and the incidence of side effects were not recorded in the retrospective study. RCT = randomized controlled trial; IHII = ilioinguinal-iliohypogastric.

The PCA characteristics for the two groups are presented in Table II. For the primary end-point, morphine use, patients who received an IHII block self-administered significantly less morphine than those who did not receive 12 injections of the bupivacaine-epinephrine mixture ($P = 0.0063$). The reduction in morphine use associated with the IHII block was not dependent upon the type of anesthesia (spinal or epidural) used for the procedure (Figure 2).

RCT: IHII blocks and iv PCA morphine use

Based on a power analysis of the retrospective data, a total of 90 patients were required for this portion of the

study. At completion, 45 patients had received the IHII bupivacaine-epinephrine injections and 45 had been injected with saline. Due to the double-blind nature of this trial, block success was not tested after resolution of neuraxial anesthetic; because we had a low-turnover of clinicians during this period, we assumed that the previous block success rate of > 95% continued. During the study, there was attrition from both groups (actual group assignments were determined at completion when the treatment code was broken by the investigational drug service). In the saline group, two patients were excluded because of incomplete data forms, three were excluded because they were given analgesics other than the specified study drugs during the postoperative period, and one was excluded because of a subsequently-determined history of substance abuse. In the bupivacaine-epinephrine group exclusions were as follows: one for incomplete data form, one at patient request due to itching, one did not receive a Pfannenstiel incision, and one did not receive naproxen sodium as ordered. In addition, one patient experienced a generalized seizure, lasting about two minutes, shortly after the IHII block was administered. Afterward, the attending anesthesiologist was informed that she had a prior history of eclampsia in 1993 and closed head injury in 1990. The etiology of this seizure was never determined, meaning that intra-vascular injection could not be ruled out.

Of the 90 patients enrolled, 79 completed the study. The charts were assembled and the study code was broken. Upon closer scrutiny, it was determined that several patients (20 total, ten in each group) had their PCA morphine access discontinued prior to the 24 hr time point. This resulted from visiting obstetricians' and non-anesthesia care givers' unfamiliarity with the study protocol. Since the primary end-point of the study was 24 hr PCA-morphine use and because dosing of PCA morphine can occur at different rates over time, we made the conservative decision not to include these patients in the post-hoc analysis. With these exclusions, there remained 31 patients in the bupivacaine group and 28 in the saline injection group. Their demographic data, which are similar to that of the retrospective study groups, are presented in columns three and four of Table I.

Mean PCA-morphine use, efficacy (i.e., VAS pain scores) and the incidence of side effects for parturients who received bupivacaine-epinephrine or placebo (saline) IHII injections are presented in Table II. Morphine use by the women who were given the saline injections was similar to that observed for the no block patients in the retrospective analysis. As predicted by the retrospective study, IHII block significantly reduced the amount of self-administered morphine following CS delivery. Patients in both groups received adequate pain relief as evidenced by the similar VAS scores (P = 0.12). Despite the difference in opioid use, the incidence of adverse effects was the same between the two groups (Table II; itching, P = 0.25; nausea, P = 0.79). However, the 95% confidence intervals for the absolute differences in the proportions with both variables were large (itching, difference of -14%, range -37% to +10%; nausea, difference of +2.3%, range -23% to +28%).

Discussion

The purpose of this study was to evaluate the benefits and limitations of a multi-level IHII block technique for post-CS pain control. The primary end-point was *iv* PCA morphine use as we hypothesized that an effective IHII block would decrease the need for opioid analgesia.

IHII blocks have been reported to produce excellent postoperative pain control in adults and children following such treatments as hernia repair and groin surgery.[5] The nerve blocks have also been assessed for reducing pain following CS, albeit with less efficacy than with the other procedures.[6–9] Part of this reduced effectiveness is no doubt due to the diffuse nature of post-CS pain. However, there are two variables amongst these previous IHII/CS studies that preclude a full assessment of the technique: 1) block methodology; and 2) post-procedural patient monitoring.

Before initiating our study, we evaluated the prior investigations. We concluded that the various injection techniques were not ideal for producing an effectual IHII block. For instance, both Bunting and McConachie[6] and Ganta *et al.*[8] used a single injection on each side to administer relatively large volumes (10 mL) of local anesthetic (0.5% bupivacaine). The ability of this methodology to reproducibly generate an effective IHII block is unclear because neither group reported their block success rate. In a later IHII-CS study, Huffnagle *et al.*[9] also injected 20 mL of 0.5% bupivacaine, 10 mL in each side. These investigators recorded a 50% incidence of post-procedural block failure amongst women who received the injections prior to elective CS. For all these reports, we felt that the injection techniques did not produce conditions that allowed for optimal (and reproducible) exposure of the IH and II nerves to the anesthetic agent. Multiple injections along the nerve pathways appeared to be the logical alternative. And indeed, our method, which took approximately five minutes to complete, produced an IHII block success rate of > 95%.

Coupled with the injection patterns, variations in patient treatment and assessment methodologies have

also made it difficult to fully assess the potential of IHII nerve block to control post-CS pain. Bunting[6] and Ganta[8] both compared the VAS scores over time, which is less than ideal[10] while Kuppuvelumani[7] measured pain (on a four-point scale) only once. Nonetheless, these studies did note a reduction in analgesic requirement. However, this result must be viewed in context: they were all based on decreases in patient-requested active intervention by health care workers, specifically, a reduction in the amount of nurse-injected pethedine or papaveretum. With this consideration, one cannot eliminate "differences in accessibility" as an artifactual contributor to the final result. Certainly the use of PCA to control post-CS pain (now recognized to provide superior pain relief in this and other postoperative situations)[11] could have altered one or both treatment groups' response.

Huffnagle *et al.*'s study on IHII nerve blocks[9] did use PCA morphine use as an end-point but they found that the amount of morphine self-administered by the no block control group was similar to the amount administered by those who received IHII blocks, either before or after CS. They concluded that IHII blocks were of no benefit to the patient. In contrast, we have demonstrated (both retrospectively and prospectively) that a multiple injection IHII block technique can reduce post-CS morphine requirement and provide effective pain control. We attribute this result to the superiority of multiple anesthetic injections along the nerve tracks for producing effective IHII block when compared to a single injection on each side. It is worth noting that our control patients (i.e., those who received saline or no injection) and all of Huffnagle *et al.*'s patients self-administered similar amounts of morphine during the 24 hr post-CS period.[9] This indicates that patients at both institutions had similar post-procedural pain control requirements, further supporting the primacy of the multilevel methodology.

One observation limited our satisfaction with this IHII block technique: the failure to reduce the appearance of opioid-related adverse effects. Such a result is consistent with other post-CS morphine studies,[12] but the mechanism behind this observation is unclear. While our study, which involved a yes/no response at four time points, was not designed to correlate morphine administration patterns with the appearance of adverse effects, more intensive monitoring coupled with attempts to grade the severity of itching and nausea would be informative. Along these lines, it should be noted that the size of the confidence intervals for the absolute differences in proportions suggest that studying a larger population receiving the IHII blocks might also show a statistically significant reduction in either or both itching and nausea. Nonetheless, a conservative interpretation of our data would still lead one to expect a considerable number of women who received IHII blocks to itch or be nauseous if morphine is used for additional analgesia during the post-delivery period. Currently, we view this limitation as a constraint against advocating the incorporation of the IHII block procedure into the routine care of post-CS patients. As such, we have concluded that this methodology may only be useful in situations where other, more standard, methods of post-CS analgesia are contraindicated.

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En route for the CAS Annual Meeting