A comparison of post-incisional subcutaneous, intramuscular, and subcutaneous plus intramuscular infiltrations of lidocaine in post-caesarean section pain control

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Background. How best to relieve pain after caesarean section (CS) is still debated by many obstetricians. Pre- and post-incisional infiltrations with local anaesthetics have been widely tested and compared. However, the effect of the site of post-incisional infiltration with a local anaesthetic on the quality of pain reduction is not well documented.

Objectives. To compare the effects of post-incisional infiltration of lidocaine into the subcutaneous tissue, rectus abdominis, or both subcutaneous tissue and rectus abdominis on pain after CS.

Methods. Two hundred candidates for elective CS were randomly allocated to four matched groups of equal size. They received post-incisional infiltration of either 1% lidocaine (in the rectus abdominis, the subcutaneous tissue, or both) or saline. The pain intensity and analgesic demand after CS, as well as the time to ambulation and breastfeeding, were documented and compared between the groups.

Results. Post-CS pain intensity and analgesic demand were significantly lower, and the time to ambulation was significantly less, in the lidocaine groups than in the placebo group. The time to breastfeeding, however, was comparable between the two groups. Among the patients who received lidocaine, the site of infiltration was associated with no significant differences in terms of post-CS pain intensity and need for analgesics, or time to ambulation and breastfeeding.

Conclusion. The site of post-incisional local wound infiltration with lidocaine is not a clinically important factor in pain relief after CS.

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Pain after caesarean section (CS) is still a common and important source of patient dissatisfaction in many obstetric centres. Although it is always essential to relieve patient discomfort, the management of post-CS pain differs from that in the general surgical population because mothers need to recover quickly in order to take care of their babies and breastfeed successfully.[1]

There are various ways to manage pain after CS, ranging from the traditional administration of opioid/non-opioid medications to novel technologies such as continuous epidural analgesia and patient-controlled methods.[2,3] Like many other therapeutic approaches, however, these pain management techniques have significant drawbacks such as potential adverse effects or complications, limited efficacy, inaccessibility and high cost.[4]

Infiltration of the incision wound with local anaesthetic has been claimed to be safe and effective in reducing post-operative pain.[5] Although the exact mechanism is unknown, it is generally believed that post-incisional local anaesthetic infiltrations act through peripheral neural blockade and an anti-inflammatory effect.[6]

We hypothesised that the site of analgesic infiltration may have an effect on the quality of post-CS pain relief. For the first time, to the best of our knowledge, this study compares the efficacy of pain relief with post-incisional subcutaneous, intramuscular, and subcutaneous plus intramuscular infiltration of lidocaine after elective CS.

Materials and methods

In this prospective, double-blind, placebo-controlled, randomised clinical trial, 200 candidates for elective CS (American Society of Anesthesiologists I - II) with uncomplicated singleton pregnancies (≥37 weeks' gestation) were recruited from Alzahra Teaching Centre, Tabriz, Iran, from June 2010 through June 2011. Exclusion criteria were a history of maternal medical or obstetric illnesses, evidence of fetal compromise, previous surgery in the operative site, and any known allergy to medications. The study was approved by the ethics committee of Tabriz University of Medical Sciences in accordance with the Helsinki Declaration, and written informed consent was obtained from all the participants.

Randomisation was performed with computer random number generation. On the day of the operation, the surgeon was provided with a sealed envelope in which was a syringe containing a 20 ml solution of 1% lidocaine with 1:100 000 adrenaline or 20 ml 0.9% sodium chloride, accompanied by an instruction. All the 200 syringes were prepared by a pharmacist who was not involved

in the study. Each envelope was marked with a randomisation number that was disclosed to the investigators only after completion of data analysis. Each participant was allocated to one of the following four groups:

- **Intramuscular (IM).** Before the wound was closed, 20 ml of local anaesthetic mixture including 1% lidocaine and 1:100 000 adrenaline was injected into the rectus abdominis wound edges.
- **Subcutaneous (SC).** Before the wound was closed, the same mixture was injected into the subcutaneous tissue around the incision wound.
- **Subcutaneous and intramuscular (SCIM).** A combination of the intramuscular and subcutaneous injections described above was used, each with a half volume of the anaesthetic mixture (total volume 20 ml).
- **Placebo (P).** Before the wound was closed, 20 ml 0.9% sodium chloride (saline) was injected into the subcutaneous tissue and rectus abdominis around the incision wound.

The injection sites around the incision wound were at 12, 1.30, 3, 4.30, 6, 7.30, 9 and 10.30 o' clock (2.5 ml in each site).

The patients did not receive any systemic analgesic premedication. Intra-operative sedation was achieved by administrating 1 - 2 mg intravenous midazolam if needed. Based on a standard protocol, all patients received spinal anaesthesia after hydration with 500 ml Ringer's lactate solution. Standard monitoring included electrocardiography, arterial blood pressure and pulse oximetry. After thorough examination of the spinal column and appropriate preparation and draping, a standard non-cutting pencil-point needle (24-gauge or less) was inserted at L3/L4 (or at lower interspaces if for an anatomical reason insertion was not possible at L3/4), with the patient in the lateral position. All patients received 60 - 70 mg 5% lidocaine (1.2 - 1.5 ml) and were then placed in the supine position. All skin incisions were Pfannenstiel, and Kerr incisions were used for the uterus. During the operation the blood pressure was checked every 3 minutes and patients with decreases in blood pressure ≥20% from baseline were given intravenous ephedrine. Sensory levels were determined based on a dermatome chart (Astra, Zürich, Switzerland) using a pinprick test. Patients were

discharged from the recovery area when their vital signs were stable, if no surgery-related complications had been detected, and when the spinal block was regressing (i.e. at least 2 dermatomes below the nipple line). After the operation and during their stay in the recovery room, analgesia with intravenous morphine 5 mg was provided at the patients' request.

All the patients received standard departmental post-CS pain relief, i.e. diclofenac sodium 100 mg (50 mg rectal suppository, Novartis Pharmaceuticals, NSW, Australia), starting immediately after the operation and then every 8 hours for 24 hours.[7] They were allowed a rescue morphine dose (5 mg intramuscularly) for breakthrough pain before 8 hours had elapsed.[8]

The variables studied were recorded by a doctor who was blind to the study groups. Duration of the spinal anaesthetic block was measured as the time interval from intrathecal injection to when a two-segment regression in the level of block (T4) was detected and documented.

Post-operative pain was assessed by a self-rating 10 cm visual analogue scale (VAS) numbered 0 - 10 (0 = no pain, 10 = the worst pain imaginable).[9] This scale has been used previously in post-CS patients who have received spinal anaesthesia.[10,11] Pain was assessed at predetermined intervals of 2, 3, 4, 6, 8, 12 and 24 hours after surgery, at rest and with movement, which was standardised as elevation from the horizontal to the sitting position.

Duration of analgesia was defined as the time that elapsed between discharge from the recovery room and the first post-operative demand for rescue analgesia. Number of demands was also documented. Patients were encouraged to move around and to breastfeed their baby as soon as possible, and the times of first post-operative ambulation and first breastfeeding (in the women who wanted to breastfeed) were recorded.

Healing of the incision wound was assessed one week after discharge when the patient returned for removal of the stitches. If there was any redness, hotness, oedema, discharge or dehiscence, healing was considered inadequate.
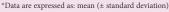
Table 1. Demographic and general data of the patients in the four groups studied*

Variable	SC (*n*=50)	IM (*n*=50)	SCIM (*n*=50)	P (*n*=50)	*p*-value[†]
Age (years)	29.14 (±2.88), 23 - 34	28.72 (±3.34), 25 - 36	29.98 (±3.24), 23 - 36	29.76 (±3.45), 23 - 36	0.22
Level of education (years)	10.06 (±1.74), 5 - 15	10.68 (±2.22), 5 - 13	10.34 (±1.98), 6 - 14	10.58 (±2.28), 4 - 16	0.41
Weight (kg)	71.20 (±5.75), 58 - 85	72.80 (±4.76), 63 - 81	70.10 (±8.01), 56 - 84	71.48 (±6.84), 55 - 90	0.23
Gravidity	2.28 (±0.57), 2 - 4	2.24 (±0.59), 2 - 4	2.18 (±0.48), 2 - 4	2.38 (±0.60), 2 - 4	0.35
Operative time (minutes)	61.92 (±9.48), 30 - 94	59.66 (±6.69), 50 - 72	57.54 (±11.47), 30 - 72	59.38 (1±1.90), 30 - 77	0.19
Duration of spinal block (minutes)	73.72 (±4.83), 66 - 87	72.82 (±4.70), 63 - 79	74.22 (±5.26), 66 - 91	73.86 (±6.04), 60 - 91	0.59

SC = subcutaneous; IM = intramuscular; SCIM = subcutaneous and intramuscular; P = placebo.
*Data are expressed as: mean (± standard deviation), range.
[†]*p*≤0.05 was considered to be statistically significant.

Table 2. Post-operative pain scores in the four groups studied at different intervals*

Time (hours)	SC (*n*=50)	IM (*n*=50)	SCIM (*n*=50)	P (*n*=50)
Pain scores at rest (VAS)				
2	2.87 (±1.23)	2.58 (±1.01)	2.36 (±1.23)	3.98 (±1.80)
3	3.33 (±1.65)	3.11 (±1.87)	2.91 (±1.34)	4.23 (±1.90)
4	3.63 (±1.54)	3.51 (±1.43)	3.26 (±1.07)	4.51 (±1.23)
6	3.78 (±1.76)	3.68 (±1.14)	3.32 (±1.56)	4.53 (±1.59)
8	3.43 (±1.50)	3.32 (±1.32)	3.12 (±1.89)	4.31 (±1.23)
12	3.19 (±1.32)	3.00 (±1.12)	2.91 (±1.46)	3.89 (±1.49)
24	2.21 (±1.40)	2.08 (±1.08)	1.95 (±1.27)	3.21 (±1.55)
Pain scores on movement (VAS)				
2	3.96 (±1.64)	3.76 (±1.40)	3.68 (±1.41)	4.76 (±1.55)
3	4.48 (±1.84)	4.41 (±1.59)	4.22 (±1.79)	5.52 (±1.46)
4	4.52 (±1.17)	4.46 (±1.63)	4.28 (±1.51)	5.86 (±1.88)
6	4.70 (±1.28)	4.58 (±1.29)	4.42 (±1.39)	5.98 (±1.38)
8	4.42 (±1.43)	4.31 (±1.38)	4.12 (±1.04)	5.71 (±1.45)
12	4.30 (±1.28)	4.16 (±1.01)	3.88 (±1.37)	5.12 (±1.75)
24	3.08 (±0.40)	2.97 (±0.66)	2.74 (±0.80)	4.30 (±1.20)

SC = subcutaneous; IM = intramuscular; SCIM = subcutaneous and intramuscular; P = placebo; VAS = visual analogue scale.
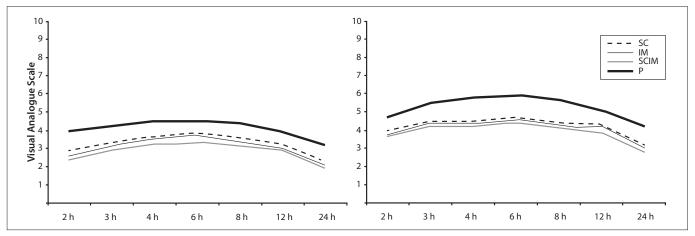*Data are expressed as: mean (± standard deviation).

Fig. 1. Changes in mean post-operative pain scores at various time intervals in the four groups studied at rest (left) and on movement (right) (SC = subcutaneous; IM = intramuscular; SCIM = subcutaneous and intramuscular; P = placebo).

With assumption of an alpha level = 0.05 and a beta error = 0.8, 47 patients were needed in each group to detect a 1-point difference on a VAS of 0 - 10.[8] To account for possible loss, 50 patients in each group (*N*=200) were enrolled. Data were analysed with SPSS for Windows version 18.0 (SPSS Inc., Il., USA). Statistical methods included the one-way analysis of variance (ANOVA) test, chi-square test, Fisher's exact test and repeated measures analysis (RMA) plus the Tukey *post hoc* test, where appropriate; *p*-values <0.05 were considered to be significant.

Results

The four groups were comparable with regard to patient age, level of education, weight, height and gravidity, operative time, and the duration of spinal anaesthetic block (Table 1).

Post-operative pain scores at rest and on ambulation are summarised in Table 2. At all time intervals the RMA revealed significant differences between the groups in terms of post-operative pain scores at rest and on ambulation (*p*<0.001 for all). On *post hoc* analysis, however, the differences were significant only between the P group and the other three groups as a whole (*p*<0.001 for all). Based on the RMA there was no significant difference in terms of post-CS pain scores, at rest or with movement, between the SC and IM groups (*p*=0.88 and 0.62, respectively), the SC and SCIM groups (*p*=0.32 and 0.54, respectively), or the IM and SCIM groups (*p*=0.76 and 0.49, respectively).

The changes in mean post-operative pain scores in the study groups at various intervals are depicted in Fig. 1. The mean duration of analgesia was significantly shorter in the P group than in the other three groups (one-way ANOVA, *p*<0.001). There was no significant difference between the SC, IM and SCIM groups with regard to mean duration of analgesia (Fig. 2). Patients in the placebo group demanded significantly more rescue analgesia after the operation
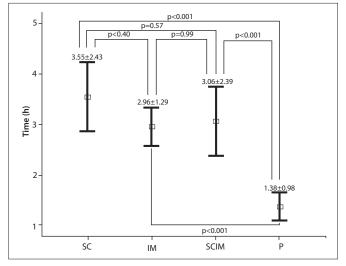
Fig. 2. Duration of analgesia in the four groups studied. The mean duration of analgesia was significantly lower in the placebo group than in the three others. Error bars show 95% confidence interval of mean. The data over the bars are presented as means ± standard deviations (SC = subcutaneous; IM = intramuscular; SCIM = subcutaneous and intramuscular; P = placebo).
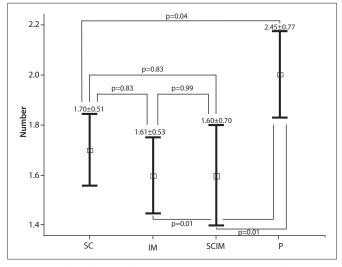

Fig. 3. Number of doses of rescue analgesic required in the four groups studied. The mean number of demands was significantly higher in the placebo group than in the three others. Error bars show 95% confidence intervals of means. The data over the bars are presented as means ± standard deviations (SC = subcutaneous; IM = intramuscular; SCIM = subcutaneous and intramuscular; P = placebo).

than women in the other three groups (one-way ANOVA, $p=0.002$). The mean number of doses of rescue analgesia was comparable between the SC, IM and SCIM groups (Fig. 3).

The mean time to first post-operative ambulation was significantly longer in the P group than in the other three groups (one-way ANOVA, $p<0.001$). The SC, IM and SCIM groups were comparable in this regard (Fig. 4).

Forty-one mothers (82.0%) in the SC group, 42 (84.0%) in the IM group, 39 (78.0%) in the SCIM group, and 45 (90.0%) in the P group decided to breastfeed their babies. Breastfeeding started a mean of 3.72 hours (standard deviation (SD) ±1.53, range 1 - 9) after
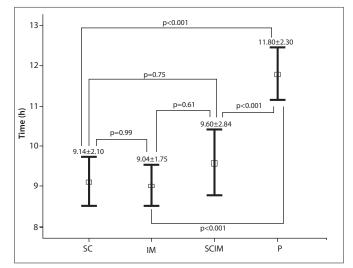

Fig. 4. The times to the first post-operative ambulation in the four groups studied. The mean time to the first post-operative ambulation was significantly higher in the placebo group than in the three others. Error bars show 95% confidence intervals of means. The data over the bars are presented as means ± standard deviations (SC = subcutaneous; IM = intramuscular; SCIM = subcutaneous and intramuscular; P = placebo).

the operation in the IM group, 3.24 hours (SD ±1.51, range 1 - 8) after in the SC group, 3.95 hours (SD ±1.94, range 1 - 8) after in the SCIM group, and 3.73 hours (SD ±1.87, range 1 - 8) after in the P group, with no significant difference between the groups (one-way ANOVA, $p=0.21$).

No clinically significant side-effects associated with lidocaine use were recorded.

Discussion

This study investigated the influence of infiltration site on post-CS pain scores and analgesic requirement in women receiving post-incisional local lidocaine. The findings showed that all three sites of infiltration, i.e. subcutaneous, intramuscular, and subcutaneous plus intramuscular, were significantly and equally effective in reducing pain and demand for rescue analgesia in comparison with patients who received placebo.

Although studies investigating the effect of local anaesthetic infiltration on post-operative pain management have been reported in the literature, the results are widely heterogeneous and the debates have largely been focused on the appropriate time of injection.[12,13] To the best of our knowledge, the present study is the first to focus on the site rather than the timing of wound infiltration.

It is hypothesised that pre-emptive analgesia cannot completely block all the pain signals from an incision wound, because the mechanisms that generate such pain are diverse and complex.[14] The post-operative pain relief obtained after infiltration of a short-acting anaesthetic such as lidocaine (1 - 2 hours) cannot be due to peripheral neural blockade alone,[15] because its analgesic effect is superior to placebo as much as 24 hours after infiltration. Likewise, it is proposed that amide local anaesthetics have potent and long-lasting anti-inflammatory qualities.[6] We therefore hypothesised that the site of infiltration could have a role in pain relief using local anaesthetics.

Although the best results in terms of post-operative pain scores were achieved after combined subcutaneous and intramuscular infiltration (Fig. 1), differences between the three intervention groups did not reach significance. However, average post-operative pain intensities at rest and on movement were lower than 3.5 and 4.5, respectively, in the intervention groups and lower than 4.5 and 6, respectively, in the placebo group. These figures are clinically important, because only scores lower than 4.5 indicate mild pain.[16]

There was no significant difference between the groups that received lidocaine with regard to the time at which a rescue analgesic was demanded, or the frequency of demand, or time to the first post-operative ambulation.

Little evidence exists on the relationship between administration of analgesia/anaesthesia and the initiation or continuation of breastfeeding. Those providing analgesia need to be confident that agents used to control the pain after CS do not have a negative impact on the mother's ability to breastfeed successfully.[17]

Although concern has been expressed that local wound infiltration with lidocaine may interfere with the process of wound healing,[18] we did not encounter any such problems among our patients who received lidocaine. There were also no clinically significant side-effects associated with its use, such as allergies or cardiovascular and central nervous system effects.

It should be noted that our main objective was to investigate the effect of infiltration site on pain relief after elective CS. Other important and still controversial issues in this regard, such as the cost-effectiveness of wound infiltration and the possibility of an association between wound infiltration and the development of chronic pelvic pain,[19] were not included. However, we emphasise that these important topics merit thorough investigation in future studies.

Another source of concern in the present study may be the possibility of a cross-reaction in terms of analgesia between the lidocaine used for local infiltration and the lidocaine used as an anaesthetic agent. However, the similarity between the study groups in terms of the method of anaesthesia could preclude this worry.

Conclusion

This study showed that although post-incisional wound infiltration with 1% lidocaine is superior to placebo in reducing pain after CS and the number of doses of post-operative rescue analgesic, there is no significant difference between the subcutaneous, intramuscular, and subcutaneous plus intramuscular routes of infiltration.

Conflicts of interests. None to declare.

Source of support. None to declare.

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