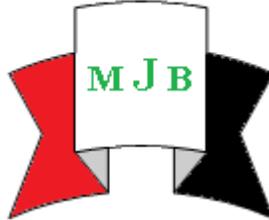


Preemptive Analgesia For Cesarean Section in Al- Najaf City

Basima Sh. Al-Ghazali Majed Dayem Al-Hassani Amal Muner Mubark
Hind Abd-Al Rassol mugeir Al-Shukri
College of Medicine , Kufa University



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Abstract

Background: Delivery by caesarean section (CS) is becoming more frequent. Childbirth is an emotion-filled event, and the mother needs to bond with her baby as early as possible. Any intervention that leads to improvement in pain relief is worthy of investigation. Local anaesthetics have been employed as an adjunct to other methods of postoperative pain relief.

Objective: To insure the efficacy of infiltration of lidocaine 1% in the surgical site of Cesarean Section, just before incision ,in decreasing postoperative pain , in comparison to other forms of preemptive analgesia that includes central nerve block (spinal anesthesia) , and multi modal parental analgesia.

Patients and Methods: This is a prospective, randomized, controlled trial study in which patients undergoing CS were randomly divided into four groups:-

Group A Patients (control plain GA), Group B Patients with multi modal analgesia
Group C Patients with local tissue infiltration, Group D Patients with spinal anesthesia .

The protocol for induction and maintenance of general anaesthesia was similar for A , B&C groups.

Group A control patients (plain GA) without supplementary analgesia.

Group B parental multi modal analgesia (Acetamenophen & Diphene) given IM. just pre operatively , and a Fentanyl 50Mg IV. just after delivery of the baby.

Group C patients received 20 ml of 1% Lidocaine infiltration 1-2 minutes before skin incision.

Group D have Spinal Anesthesia under Bupivacaine hyperbaric 0.5% 10mg intrathecally. Post-operative pain was evaluated in patients, at 30 min, 2, 4, 6 and 24 hr after surgery by visual analogue score (VAS), while lying still, and with movement. Time of first request for analgesia , and total amount of Pethidine consumed in 24 hr were recorded.

Results: The study enrolled a total number of 100 patients, 25 in each group. No side effects were recorded in all groups.

The total consumption of opioid (pethidine) after 24 hours was significantly different among the four groups 144.00mg in group A, 134.00mg in group B, 96.00mg in group C and 76.00mg in group D ($P \leq 0.05$), SD= 54.619 , 47.258, 37.697, 35.707 for Group A,B,C and D respectively.

Higher dose of analgesia was used by Group A&B, whereas lower dose used by Group C&D, so there are significant differences ($p \leq 0.01$) between the last two methods than the former two methods. However the lowest dose was recorded in the spinal anaesthesia.

The first request for opioid was statistically different among the four groups .

الخلاصة :

الولادة عن طريق العملية القيصرية (CS) اصبح أكثر تواترا. الولادة هي حدث ملئ بالعاطفة، وتحتاج الأم لتوثيق العلاقة مع طفلها في أقرب وقت ممكن. أي تدخل يؤدي إلى تخفيف الألم يستحق التحقيق. وقد استخدمت الدراسة التخدير الموضعي كعامل مساعد لأساليب أخرى لتخفيف الألم بعد الجراحة.

الهدف: لضمان فعالية تسلسل ليدوكائين ١٪ في موقع العملية القيصرية قبل شق البطن في خفض الألم بعد الجراحة، بالمقارنة إلى المسكنات الوقائية الأخرى التي تشمل وسط كتلة العصب (التخدير الشوكي)، والمسكنات الوريدية المتعددة.

المرضى والطرق: هذه دراسة مسيطر عليها متوقعة عشوائية للمرضى الذين يمرضون بعمليات قيصرية وقد قسموا بشكل عشوائي الى اربع مجاميع. المجموعة أ التخدير العام فقط المجموعة (ب) المرضى الذين يخضعون للتخدير العام مع فقدان الشعور بالألم الشكلي متعدد الوسائط. المجموعة الثالثة (س) المرضى الذين يخضعون للتخدير العام مع تسلسل الأنسجة المحلية، المجموعة الرابعة (د) المرضى الذين يخضعون للتخدير الشوكي.

النتائج: التحق الدراسة ما مجموعه ١٠٠ مريضا، ٢٥ في كل مجموعة. لم تسجل أية آثار جانبية في جميع الفئات. وكان إجمالي استهلاك المواد الأفيونية (البينثيدين) بعد ٢٤ ساعة اختلافا كبيرا من بين المجموعات الأربع في المجموعة (أ) $mg\ 144.00$ ، $mg\ 134.00$ في المجموعة ب، $mg\ 96.00$ في مجموعة س و $mg\ 76.00$ في مجموعة د $SD = 54.619$ ($P \leq 0.05$) ، 37.697 ، 47.258 ، 35.707 المجموعة أ، ب، س، د على التوالي. تم استخدام أعلى جرعة من التسكين من قبل المجموعة (أ) و (ب)، بينما أقل جرعة المستخدمة من قبل المجموعة (س) و (د)، لذلك هناك فروق ذات دلالة إحصائية ($P \leq 0.01$) بين الطريقتان الاخيرتان و الاثنتان السابقتان على العموم تم تسجيل أقل جرعة في التخدير الشوكي. وكان أول طلب للأفيونية مختلفة إحصائيا بين المجموعات الأربع.

Introduction

The idea of pain prevention was first introduced into clinical practice by Crile in 1913 and further developed by Walland Woolf.⁽¹⁾ There has been considerable intervention using preemptive analgesia since Wall raised the possibility that pain after surgery might be reduced by preventing intraoperative nociceptive impulses from reaching the spinal cord.⁽²⁾ in any post-cesarean section patient, poor pain control may interfere with ambulation, breastfeeding, and early maternal bonding with the infant⁽³⁾ Furthermore Women with severe acute postpartum pain had a 2.5-fold increased risk of persistent pain and a 3.0-fold increased risk of postpartum depression compared to those with mild postpartum pain.⁽⁴⁾ The advent of various multimodal analgesia techniques has greatly facilitated the management of postoperative pain.⁽⁵⁾ Opioids like pethidine and morphine, are the most widely used and cost-effective agents. Augmentation of intravenous analgesia has been achieved with regional

nerve blockade, particularly for patients undergoing caesarean delivery^(6,7)

The local anesthesia is used to protect the central nervous system from the deleterious effects of noxious stimuli. According to some neural pain pathway theories, the stimulation of superficial pain receptors may further sensitize the nervous system to painful sensation elimination of some of the superficial components of the pain after caesarean delivery could modulate the perception of deeper visceral pain. The data from previous studies suggest that the infiltration of local anaesthesia into the wound during caesarean delivery appears to be effective in reducing postoperative narcotic requirements.⁽⁸⁾

Preemptive analgesia involves the administration of an analgesic before a painful stimulus in order to prevent the altered processing of afferent input which amplifies postoperative pain; effective preemptive analgesia should prevent the establishment of central sensitization caused by incisional and inflammatory injuries⁽⁹⁾. **Preventive analgesia** is based on

the assumption that the only way to prevent central sensitization is to completely block any pain and afferent signals from the surgical wound from the time of incision until final wound healing. This concept focuses on the intensity and duration of the analgesic intervention rather than on timing⁽⁸⁾ It is believed that by applying an analgesic medicine or technique, pain will either subside or be prevented prior to the painful stimulus, thus preventing central sensitization and consequently decreasing the need for postoperative analgesia⁽¹⁰⁾. Owing to this 'protective' effect on the nociceptive system, pre-emptive analgesia has the potential to be more effective than a similar analgesic treatment initiated after surgery. Theoretically, immediate postoperative pain may be reduced and the development of chronic pain may be prevented. Although some clinical studies have demonstrated significant effects on acute postoperative pain, no major clinical benefits of pre-emptive analgesia have been documented. Other pharmacological interventions, including anti hyperalgesic drugs such as NMDA-receptor antagonists and gabapentin, may interfere with the induction and maintenance of sensitization. Future studies will investigate the analgesic effect of prolonged multimodal combinations of different classes of 'traditional' analgesics and 'antihyperalgesics' on postoperative pain.^(11,12)

Although several trials showed that various antinociceptive techniques applied preoperatively were more effective in reducing postoperative central sensitization phenomena than postoperative administration, reviews of clinical findings have been mostly negative. However, there is still a widespread belief among clinicians in the efficacy of preemptive analgesia⁽¹⁰⁾ The aim of this study, therefore, was. To compare the efficacy of

local tissue infiltration with lidocaine 1% before CS. At the surgical site, for pain relief after surgery with other forms of preemptive analgesia : including central nerve block(spinal anesthesia) and multi modal parental analgesia. And to confirm the relationship between the level of pain and serum cortizol level of the patient (as an index of level of stress)

Patients and Methods

A randomized clinical trail was conducted at the department of Obstetrics &Gynaecology,in AL Zaahra teaching hospital. AL Najaf city , Iraq. from 15 January 2011 to 15 July 2011.

A total number of 100 female patients aged 20-40 years, scheduled for elective caesarean section, 75 female under general anesthesia, And 25 female patients under spinal anaesthesia were studied.

For all patients the following parameters were measured:-

1-age ,parity,gestational age,sex of baby.

2-type of anesthesia.

3-pre operative measures:Bp,PR,RR, WBC,Hb%,RBS GUE.

4-Serum Cortizol level was measured 2hrs after operation.

In all cases, written informed consent was obtained before inclusion in to the study.

The study was performed as prospective, randomized controlled trial, The use of standard 10 mm visual analog scale (VAS) for scoring pain was explained to the patient pre-operatively. The general anaesthesia and spinal anaesthesia techniques were standardized and remained the same in all the cases.

At the end of the procedure the patients were divided randomly in four groups:-

1-Group A patients received General Anaesthesia.

The patient lie in supine position or left uterine displacement,pre oxygenation 100% for3 min. with standard monitoring

of PR, SpO₂, BP, RR, & ECG. then start:A-Induction:-

IV line, induction with Ketamine 2mg/kg IV or, with Propofol 100-200mg(3-5mg/kg) or Pentothal 4-7mg/kg followed by short acting Muscle Relaxant Succinylecholine 1-2mg/kg IV.,then Endotracheal Intubations. (RSI)

B- Maintenance:- Inhalational Halothane 1% in 100% Oxygen or Isoflurane 1%-2%(volatile anesthetic agent),Intavenous Propofol infusion, incremental small doses of Ketamine 25mg, Fentanyl 50 Mg, and long acting muscle relaxant usually Panchronium 0.08 ml/kg or Atracurium 0.5mg/kg and Syntocin usually given with delivery of the baby (5.u) direct (15.u)infusion. Sometimes ergote given no more than 0.5mg, fluid give 500-1000ml crystalloid solution.

C-Recovery(Emergence):-

Usualy begin early in maintenance by withdrawing the Volatile Anesthetic Agent, Propofol infusion, ketamine increaments, and Muscle Relaxant increament. Then after insuring that the patient is recovering from neuro-muscular block, a Reversal Agent administered : (Neostigmine 0,04mg/kg preceded by anticholinergic agent like Atropine 0.02mg/kg). Then after the patient regain the muscle power to sustain adequet airways & ventilation, extubation may be performed while cleaning airways, then respiratory care should be continued till complete recovery.

2-Group B patients received G.A with multi modal analgesia. Patients given Paracetamol 300 mg IM and diclofenac 75mg IM 15min before operation, then 50Mg fentanyl IV just after delivery of the baby.

3-Group C patients received G.A with lidocaine infiltrations:- pre incision 1% of 20ml of lidocaine at the site of the incision (1-2 min before incision).

4-Group D patients received spinal anaesthesia:-

Patient lie in sitting position. Two IV lines-G18 cannulae done and crystalloid solution (ringer lactate or normal saline)., Intrathecal xylocaine 70-80mg (heavy, hyperbaric 5%) or Bupivacaine 10mg (0,5% heavy type hyperbaric)., given by spinal needle (stander 12ml G22- black one) at the level of L3 -L4, then oxygen administered by face mask and sometime the patient got sedated by either meclozidam 2-3mg i.v, or propofol drip 10mg/min. While keeping high standard of monitoring : PR, SpO₂, BP, RR, & ECG).

The patients were treated by the same anaesthetics, and all patients had Pfannenstiel incision.

Two hours after operation 2ml of blood withdraw and serum cortisol measured for all patient by ELISA :-

sample collected and allowed to clot for serum sample, centrifuge the specimen to separate the plasma or serum from the cells.

Sample may be store at temperature of -2C for up to 30 days. then 0.025ml of the appropriate serum reference, control or specimen to room temperature (20-27C). Then add 0.050 ml of the working Cortizol Enzyme Reagent to all wells. swirl the micro pipe gently for 20-30 second to mix. cover and incubate for 60 minutes at room temperature, discard the content of the micro plate by decantation or aspiration. Add 300ml of wash buffer repeat two additional time for a total of three washes (automatic or manual plate washer can be used). Then add 0.100ml of working substrate solution to all wells (always add reagents in same time to minimize reaction time differences between wells). then incubate at room temperature for 15 minute. then add 50ml of stop solutions and mix for 15-20 second. then read

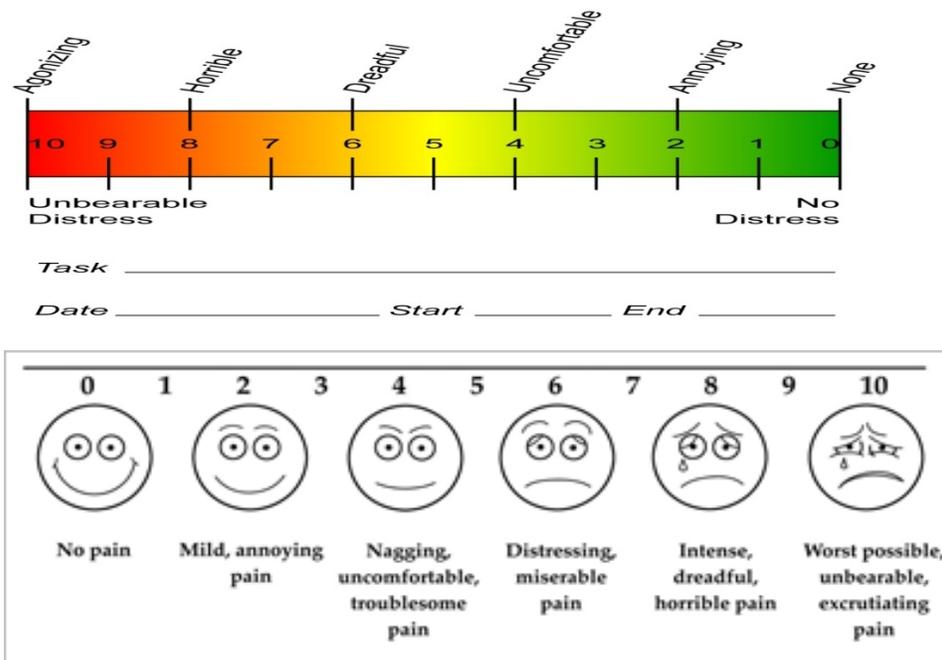
absorbent within 30minute of adding the stope solutions.

The patients received opioids (pethidine) as a postoperative analgesia, on demand and when visual analogue score was equal or more than four.

Observations concerning opioid consumption and the time for the first

analgesic request were documented. The total dose of analgesic drug was calculated for each patient. Post-operative pain was evaluated at 30 minutes, and 2, 4, 6 and 24 hours after operation using 10 mm visual analogue scale.

Visual analogue scale



numerical pain score (0 -10)

٠	٢	٤	٦	٨	١٠
مرتاح	ألم بسيط	ألم متوسط الشدة	ألم شديد	ألم شديد جدا	أسوأ ألم يمكن تخيله

Statistical analyses

All analyses were performed using commercially available software ,Statistical Package for Social Sciences (SPSS version18).

Significant differences of continuous variables were assessed by ONE WAY ANOVA Analysis. (F-tests $P \leq 0.01$).A P-value ≤ 0.05 and ≤ 0.01 was considered as

statistically significant and highly significant at 5% and1% respectively.

Result :

Table (1) Clinical characteristics of different groups

Method	Age(Yrs)	GA(wks)	Parity
1- G.A	30.88(6.22)	38.48(1.29)	1.12(1.09)
2- G.A with multimodal analgesia	33.04(5.67)	38.52(1.23)	1.60(1.11)
3- G.A. with lidocaine infiltration	29.72(5.47)	38.60(1.00)	1.40(1.04)
4- Spinal method	30.48(6.28)	38.48(1.00)	1.80(1.32)
P value	0.235NS	0.980NS	0.195NS

No significant differences were observed in the age, gestational age and parity, of four studied groups.

Table (2):No. of the patients who required different doses of Pethidine

	Dose of pethidine	No. of patients in group A	No. of patients in group B	No. of patients in group C	No. of patients in group D
1-	50mg	3	3	10	15
2-	100mg	7	7	9	7
3-	150mg	5	10	4	3
4-	200mg	10	5	2	Nil

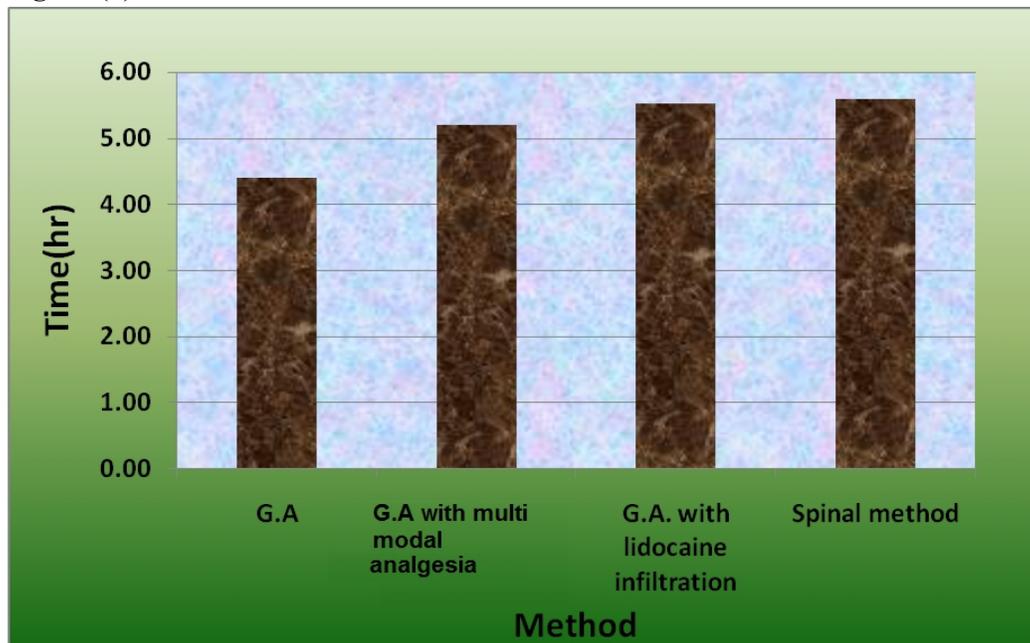
Table (3) Mean total Dose of Analgesic used by the patients

Method	Mean	±SD	P value
1- G.A(group A)	144.00	54.619	0.000
2- G.A with multimodal analgesia(group B)	134.00	47.258	
3-G.A.with lidocaine infiltration(group C)	96.00 ^{(a,b)*}	47.697	
4- Spinal method(group D)	76.00 ^{(a,b)*}	35.707	

The total consumption of opioid (pethidine) after 24 hours was significantly different between the four groups 144.00mg in group A and 134.00mg in group B and 96.00mg in group C and 76.00mg in group D ($P \leq 0.05$), SD= 54.619 , 47.258, 37.697, 35.707 for Group A,B,C and D respectively.

Higher dose of analgesia was used by Group A&B, whereas lower dose used by Group C&D where there is significant differences ($p \leq 0.01$) between last two methods than the former two methods, however the lowest dose was recorded in the spinal anaesthesia. as show in table (2,3)

Figure (1)



The more time interval until first request of patient for analgesia was recorded by Group D(spinal anaesthesia) &Group C(G.A with lidocaine infiltration),they were both of them significantly differ($p \leq 0.01$)from Group A(Patients with

G.A alone) .Group B, also need more time interval until first request of patient for analgesia, while he is still in comparison with Group A, but significantly differ. at ($p \leq 0.05$).

Table (4) Mean total serum cortisol level in patients used different method.

Method	Mean	±SD	P value
1- G.A	27.37	16.491	0.107
2- G.A with multimodal analgesia	23.39	12.020	
3- G.A. with lidocaine infiltration	22.91	18.082	
4- Spinal method	16.82 ^{(a,)*}	12.869	

^{a,*}significant differences at $p \leq 0.05$ with group 1

In general there is no significant differences in serum cortisol level were recorded between different methods except between spinal anesthesia and plain G.A, where the lowest results in serum cortisol level was recorded in spinal anesthesia as show in table (4)

Discussion

Post-cesarean delivery pain relief is important. Good pain relief will improve mobility and can reduce the risk of thromboembolic disease, which is increased during pregnancy. Pain may also impair the mother's ability to optimally care for her infant in the immediate postpartum period and may adversely affect early interactions between mother and infant. Pain and anxiety may also reduce the ability of a mother to breast-feed effectively.⁽¹³⁾

Many studies have confirmed the positive effects of preemptive analgesia and investigated various methods of application such as the presurgical administration of NSAIDs, or the presurgical administration of ketamine as an NMDA antagonist and peritoneal infusion of long-acting local anesthetics through abdominal incisions⁽¹⁴⁻¹⁷⁾

In this study, the effect of local anaesthetic infiltration of the wound before opening of the skin on postoperative pain was investigated. So found that surgical incision infiltration with 2% 10ml of lidocaine significantly prolonged the time interval until the first request for analgesic, and found significant reduction in opioid consumption and Pain scores post operatively in compared with(G.A alone) and multi modal analgesia ,while spinal anaesthesia showed more significant prolongation in time interval for the first dose of analgesia and more significant reduction in opioid consumption and pain scores post operatively in compared with local anaestheticinfiltration,(G.A alone) and multi modal analgesia. Also showed that

the more time interval until the first request for analgesia(which is more significant) in patient treated with spinal anaesthesia&G.A with lidocaine infiltration(while the patient still) when compared with G.A alone & with multi modal analgesia and more significant prolongation in time interval until first request of patient for analgesia(while the patient is moving)in spinal anaesthesia&G.A with lidocaine infiltration when compared with (G.A alone)and with patients who were given multi modal analgesia. G.A with multi modal analgesia have appeared significant results in comparison with G.A alone in time interval until first request of patient for analgesia.

There are many studies that their result approximately smaller to result of this study like Tan CH et al andBamigboye . A. studies have evaluate the use of local anaesthesia after abdominal hysterectomy or caesarean delivery^(18,6) andLowenstein L et al which show that Preemptive analgesia with lidocaine 1% is a simple, cheap and efficient mode to reduce pain in the first hours after hysterectomy.⁽¹⁹⁾

Other studies have shown conflicting results,likeHeidFetal which find that subfascial wound instillation of 40 ml ropivacaine 0.75% (contact time 10 min.) demonstrated almost no analgesic effect after abdominal hysterectomy under remifentanyl–isoflurane based general anaesthesia.⁽²⁰⁾and Moiniche S et al concluded an overall lack of evidence for any important effect (rather than evidence for a lack of effect) of incisional local anaesthesia in most abdominal procedures despite the numerous studies available.⁽²¹⁾ the conflicting evidence maybe due to the short duration of action of the local anaesthetics like lidocaine as preemptive analgesic to block postoperative pain.

others studies have demonstrated that local anaesthetic infiltration was effective after

parietal surgery such as hernia repair.^(22,23) In the study carried out by Sinclair et al⁽²⁴⁾ the pain scores were reduced in the first 24hours .In the study byTverskoy et al.⁽²⁵⁾ pain score were reduced.& the time interval from infiltration to the first request for analgesia was evaluated ,the duration of analgesia was significantly prolonged at 2-7 hours .also there was significant reduction (approximately 50%) in supplementary analgesic consumption . The infiltration of the wound with local anaesthesia significantly decreased postoperative pain and narcotic use (pethidine) in the postoperative period.⁽²⁶⁾ The inflammatory, metabolic, and endocrine changes in response to surgical injury is termed the surgical stress response. local cytokines are produced at the site of injury, dependent on both nociceptive stimulation and other factors such as anxiety, fear, and the degree of tissue damage. These changes result in an increase in serum cortisol, insulin, glucagon, and acute-phase reactants (principally cytokines).⁽²⁷⁾

In our study serum cortisol level was measured for all four groups and have been showed no significant differences among the results except between spinal anesthesia and plain G.A . the lowest results in serum cortisol was recorded in the group of patients with the spinal anesthesia who had significant decrease in the postoperative pain and this explain the significant effect of the pain on the serum cortisol level of the patient.⁽²⁸⁾ This supported by Sharain et al⁽²⁹⁾ which shows that Higher cortisol levels in the local anaesthesia group were consistent with the greater experience of pain. Other studies, for example Zimmer et al.⁽³⁰⁾ have also shown significant correlations between pain and cortisol levels. Also Okur et al⁽³¹⁾ suggest that wound infiltration with bupivacaine decreases the stress response to surgery and postoperative pain.

Conclusion

Local analgesia infiltration as adjunct to general anaesthesia is of benefit in caesarean section by :-

1-Reducing opioid consumption and postoperative pain.

2- Prolongation of the time for the first request dose of analgesia when compared with GA alone & with multi modal analgesia.

But Spinal anesthesia was more superior than local anaesthetic infiltration. There is significant relationship between serum cortisol level and pain threshold of the patient.

We recommend use of preemptive analgesia as a routine in obstetric, especially with the current status of under-developed acute pain services in this country.

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