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Case for local infiltration analgesia: Is all the evidence in black and white?

Post-operative pain has the potential for significant adverse effects on the physiology and can also drown the patient into psychological suffering. The source and degree of nociceptive stimulation differ among individuals and surgeries and hence multimodal analgesic approaches have been encouraged for pain relief. With local infiltration or infiltration in the pain sensitive planes, afferent impulses from the site of incision and injury are reduced. This reduces the sensitisation and consequent hyperalgesia. The risks associated with parenteral administration of analgesics, risks associated with central neuraxial block and the injury and injection to surrounding structures in nerve and plexus blocks are avoided. As part of multimodal technique, there can be a reduction in requirements of opioids. Simplicity and safety are the hallmarks of the technique.

The usefulness of wound infiltration for small incisions performed under monitored anaesthesia care is well-known. Infiltration for surface injuries, ring blocks for digits and circumcision are some examples. This is true especially in emergency situations when effective management of lacerations is achieved in a short time.^[1]

Longer acting and non-cumulating local anaesthetic (LA) agents are preferred for post-operative analgesia. Some LAs such as ropivacaine, in modern practice, have an intrinsic vasoconstricting property. Epinephrine containing solutions can reduce bleeding from the incision site when used before incision and prolong analgesia. Other additives have been used with LAs, such as steroids, ketorolac, tramadol, clonidine, morphine, ketamine, magnesium and capsaicin.^[2-8] Tramadol infiltration into the wound alone has been

effective as an analgesic, without affecting wound healing in a study on rats.^[8] Capsaicin can be an effective adjunct during the first few days after inguinal hernia repair.^[7] Ultra-long-acting liposomal bupivacaine preparations provide longer duration of analgesia as compared to traditional preparation and can potentially replace infusions of LAs and are undergoing trials.^[9,10]

Single dose infiltration can be achieved with either needle or by instillation through a catheter placed at the end of the procedure. Continuous infusion through the catheters has also been effective in reducing post-operative pain.

The advantage of post-operative analgesia for procedures with small incisions such as herniotomy and herniorrhaphy is well-known. For longer incisions; larger volumes of the drug need to be deposited subcutaneously, aided by injection in additional planes for success. Infiltration techniques have been used in disparate procedures such as hysterectomy, caesarean sections, abdominal surgeries, open colonic surgeries, hip and knee replacement procedures, breast surgeries, laparoscopic procedures, cardiothoracic surgeries, bariatric surgeries, etc.^[11-20]

Post-operative pain after joint replacement surgeries can be severe with prolonged inpatient stay, increased risk of infection and deep vein thrombosis. Seminal work of Kerr and Kohan, two orthopaedic specialists, consisted of peri-articular injections in all the planes affected in surgical trauma, with the aim to avoid sedation.^[21] A combination of ropivacaine, ketorolac and epinephrine is popular, with total volumes reaching between 150 and 200 ml.^[20-22] The technique

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is associated with superior pain relief and reduced morphine consumption as compared with epidural analgesic technique^[22] and produce results comparable to femoral nerve blocks.^[23] The plasma concentrations of ropivacaine remains within the safe limits.^[19]

A recent systemic review of the analgesic efficacy of LA infiltration after breast surgeries in 10 trials involving 699 patients suggested moderate reduction in pain and opioid consumption post-operatively.^[24]

The LA agents can be administered before incision, intraoperatively and at the end of surgery. Post-traumatic hyperalgesia and hyperexcitability of central nervous system can be reduced by post- or pre-administration of LAs. Preincisional infiltration with lignocaine when compared with post-incisional administration was found to provide better relief (although insignificantly) from early post-operative pain in elective inguinal hernia procedures.^[25] The authors in this study propose that inhibition of peripheral sensitisation may have a major role in impeding development of acute pain and thus prevention could be more useful in attenuating post-operative pain.

Continuous subcutaneous infusion of bupivacaine 0.25% was found to provide superior post-operative analgesia and reduction of morphine requirements after caesarean section, as compared to placebo (normal saline) infusion.^[15] In a Cochrane review of 20 randomised controlled trials (RCTs) of caesarean section under regional anaesthesia and one study involving general anaesthesia, with wound infiltration/irrigation or abdominal nerve blocks, there was reduction in opioid consumption; additional benefit was provided by non-steroidal analgesic agents (NSAIDs).^[26]

One undesirable effect of opioids is the transfer through breast milk to the neonates with risk of neonatal sedation. The locally administered LAs are absorbed systemically and secreted in breast milk but no significant side-effects on babies have been documented.^[27]

Caudal epidural analgesia is the mainstay of paediatric analgesia; properly performed infiltration with LAs can be as effective as caudal block, qualitatively and in duration.^[28]

A recent study comparing ultrasound guided rectus sheath block (0.25% bupivacaine, 0.5 mg/kg) with

wound infiltration (0.25% bupivacaine, 1 mg/kg) in children found more effective analgesia and safe plasma concentrations of bupivacaine in the former group.^[29]

Published in this issue of Indian Journal of Anaesthesia is the study of instillation of bupivacaine in the surgical drains after modified radical mastectomy.^[30] 20 ml each of bupivacaine (0.25%) was instilled into the chest wall and the axillary drain and clamped for 10 min; the duration of analgesia was prolonged in the group where bupivacaine was used. Surprisingly, in the group where normal saline was used, there was appreciable prolongation of analgesic duration, attributable to the pressure on nerve endings by the volume and the dilution and wash-off of the inflammatory mediators involved in pain.

The gray areas of the infiltration block: The evidences mentioned above are largely in favour of widespread use of LA agents for infiltration of surgical wounds. It is difficult however to declare that the wound infiltration with LA agents alone could be beneficial in major laparotomies and orthopaedic procedures as the studies also include addition of NSAIDs and vasoconstrictors to LAs along with other multimodal interventions.^[31]

The LAs deposited in different volumes may interfere with local inflammatory mechanisms. In an RCT of 38 healthy women undergoing caesarean section, subcutaneous wound infusion of bupivacaine, 0.5% was compared with normal saline and wound exudate was sampled through a drain at different time intervals for 24 h.^[32] Significant reductions in levels of interleukin 10 and increases of substance P was observed in wounds in the bupivacaine group when compared to the saline group. Other markers of inflammation did not differ significantly between the groups.

In a study on rats about the effects of infiltration with bupivacaine and ropivacaine on wound healing, it was found that the levels of histological markers of inflammation were higher on the 3rd day in the bupivacaine group and there was no difference later, at 14th day; there was no evidence of impairment of wound healing overall.^[33] LAs may affect first two stages of healing, the inflammatory and granulation/proliferation stages. Differences in terms of concentration and pH among the different LAs used may affect the findings. An exhaustive

review by Brower and Johnson of both *in vivo* and *in vitro* studies regarding the adverse effects of LA infiltration on wound healing suggests that the risk is more with continuous infusions and the same can be attenuated with lower concentrations of LAs.^[34] It is important to note that the analgesia is most needed in the first two stages of inflammation. There are no clinching and statistically convincing evidences against the use of LAs when their analgesic benefits are taken into account. The final impact of these changes needs to be studied further to ascertain the macro parameters such as wound healing, pain, infection, scarring, etc.

The non-analgesic beneficial effects of LAs: The LA wound infiltration can have other benefits in addition to the anti-nociceptive effects; LAs administered subcutaneously exhibit bacteriostatic and bactericidal actions.^[35] In a laboratory study, human breast cancer cells and mammary epithelial cell lines were exposed to lignocaine and bupivacaine.^[36] There was inhibition of cell viability, with apoptosis of the breast tumour cells. The findings of this study suggest the potential benefit for use of LAs for skin infiltration during oncological surgeries of the breast.

The verdict overall is in favour of judicious use of local infiltration analgesia, as part of balanced anaesthesia, notwithstanding some doubts regarding the effects on wound healing and inflammation, as evidences against its routine use are still weak and inadequate.

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Announcement

Conference Calender - 2015

Name of the conference: 63rd Annual National Conference of the Indian Society of Anaesthesiologists, ISACON 2015

Date: 25th to 29th December 2015

Venue: B. M. Birla Auditorium & Convention Centre, Jaipur, India

Organising Secretary: Dr. Suresh Bhargava

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Website: www.isacon2015jaipur.com

Name of the conference: TRISZAC 2015, 31st Annual Conference of Indian Society of Anaesthesiologists, South Zone and 39th Annual Conference of Kerala State Chapter

Date: 6th to 9th August 2015

Venue: Hotel KTDC Samudra & Uday Samudra Beach Hotel, Kovalam,

Trivandrum

Organising Secretary: Dr. Gopakumar D

Contact: +91 98476 39616

E-mail: triszac2015@yahoo.in

Website: www.triszac2015.com

Name of the conference: KISACON2015, 31st Annual Conference of Indian Society of Anaesthesiologists, Karnataka State Chapter

Date: 9th to 11th October 2015

Venue: S N Medical College, Bagalkot

Organising Secretary: Dr. Ramesh Koppal

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E-mail: rameshkoppaldr@gmail.com

Website: www.kisacson2015.com