

Systematic Review of Clinical Evidence for Local Anesthetic Wound Infiltration in Reduction of Post-Surgical Pain

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Abstract

Local anesthetic infiltration prior to surgical incision closure is a frequently used technique in the operating room. Debate continues, with clinicians, as to the effectiveness of this technique in pain reduction. A literature review using PubMed with the criteria of "local anesthetic infiltration and pain reduction" was conducted for the use of local anesthetic infiltration prior to surgical closure. The search provided 137 results that were then categorized and reviewed, the studies that reviewed the effectiveness (pain reduction) of single dose infiltration of local anesthetics into the surgical wound was small, only numbering 23 studies. The use of local anesthetics before surgical incision or a continuous infusion of the local anesthetics into the surgical wound in the immediate post-operative period is more widely studied, but the effectiveness of this practice varies greatly between studies. The efficacy of using a single pre-closure local anesthetic infiltration ranged from producing a modest reduction in post-surgical pain to no change in post-surgical pain. This systematic review revealed that few studies have examined the effectiveness of local anesthetic infiltration into surgical incisions on post-operative pain outcomes and these results vary greatly as to the effectiveness of this surgical practice.

Keywords: Pre-incisional; Post-incisional; VAS; Opioid; Surgery; Pain management

Introduction

Post-operative acute pain management is a major health issue and is costly to the health care system [1]. Complications of peripheral nerve blocks (paralysis and neurological deficits), both single injection and continuous infusions, are rare but do exist which can result in permanent and chronic issues [1].

Currently, the standard treatment for acute post-operative pain is the use of systemic opioids, but these are not without complications. Drowsiness, nausea, vomiting, ileus, urinary retention and pruritus, are all side effects of opioids and can lead to longer lengths of stays but more importantly poor patient outcomes [2,3]. Alternatively, there is growing use of i.v. acetaminophen post-operatively [4,5].

This practice limits the post-operative use of opioids and decreases opioid-induced adverse events [6]. However, the use of acetaminophen is to be used with caution in certain patient populations like those with hypervolemia related to dehydration or blood loss, those suffering from chronic alcoholism, chronic malnutrition and severe kidney impairment. Furthermore, i.v. acetaminophen is contraindicated in individuals with severe hepatic impairment [4,5].

Another approach to control post-operative pain and limit post-operative opioid usage is local anesthetic wound infiltration prior to wound closure. In theory this approach should lessen peripheral and central hyperalgesia and minimize wound inflammation producing less post-operative pain without impairing wound healing [3,7].

The technique of injecting local anesthetics into the various layers of the surgical incision (wound) is a commonly used practice in general

anesthesia surgical cases [7]. Surgical wound infiltration with local anesthetics has continued to increase in popularity since the mid 1990's [8]. It is relatively inexpensive, technically not difficult, and may potentially reduce the post-operative discomfort [9].

There are two main approaches to local anesthetic wound infiltration. The first is a preemptive model which applies the anesthetic prior to surgical incision. The second model applies the anesthetic immediately prior to surgical closure at the end of the surgical case. Several studies have applied both models and administered local anesthetic both prior to and at closure.

Injecting local anesthetics prior to surgical incision into the surgical wound has been more extensively studied [10-16]. The results in this area are mixed with several studies showing significant pain reduction [11,12,14] while other studies did not find a reduction in pain or had mixed results [10,13,16-18].

The technique of injecting local anesthetics after the surgical incision has been made (prior to ending the surgical procedure) and its reduction in post-operative pain remains in debate as to the effectiveness in both animal and human studies [19].

The focus of this systematic review was to determine the available literature addressing the use of one time local anesthetic infiltration after the surgical incision (wound) has been made and prior to wound closure.

The outcomes examined were the reduction in post-operative pain using either a Visual Analog Scale or reduction in opioid usage. A review of the literature finds inconclusive evidence on the effectiveness of local infiltration prior to surgical closure in reducing post-operative pain [19-21].

Methods

Search strategy

Using the search engine PubMed and the search parameters of “local anesthetic infiltration and pain reduction” as well as “local anesthetic infiltration and wound healing” resulted in 137 documents. Both criteria were used to ensure that the search captured any aspects of local anesthetic infiltration and a broad area of local anesthetics and surgical incisional usage. The PubMed search, done November 2013 identified 117 papers.

This was based on the criteria of “local”, “anesthetic”, “infiltration”, and “pain reduction”. Another search was run on the same date using the criteria of “local”, “anesthetic”, “infiltration”, and “wound healing” resulting in 47 papers.

Some of the papers in the two searches repeated thus an overall total of 137 results were obtained. As this search did include several review articles, the specific articles that were reviewed were pulled and if additional to what was found in the original PubMed searches they were then included in the overall total of 150.

Inclusion of articles

The majority of the articles (n=122) were excluded (Figure 1) if they stated perioperative without differentiating pre versus post incisional injection of the local anesthetic, used combinations of another medication like opioids, magnesium sulfate or topical anesthetics, continuous local anesthetic infusions, tumescent instillations (high volume), local anesthetic versus topical anesthetics, peripheral nerve blocks, local anesthetic versus general anesthesia or were not available in English, as these are not the focus of this review.

The remaining 28 publications were sorted into two categories: pre-incisional administration, prior to surgical incision, and post-incisional, administration at the time of wound closure.

One of the post-incisional administration articles was a review article [22] and the original studies from the review were included in this analysis but the review article was excluded.

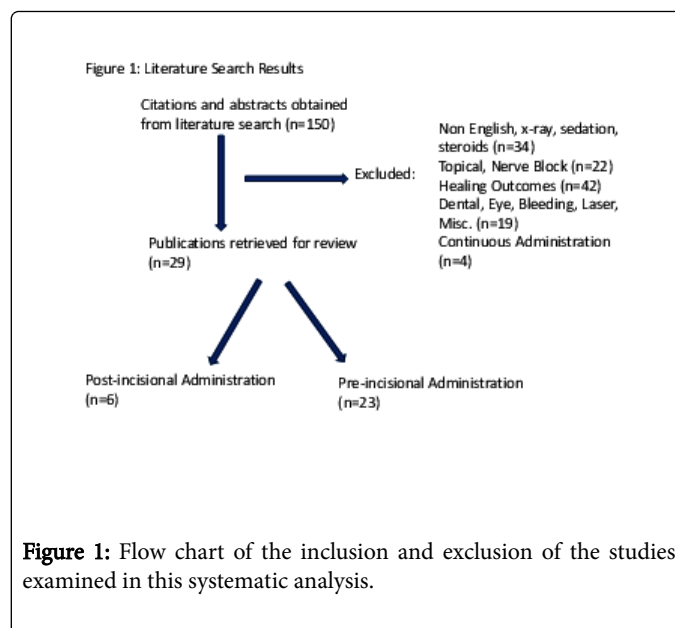


Figure 1: Flow chart of the inclusion and exclusion of the studies examined in this systematic analysis.

The inclusion criteria included all surgical sites, retrospective and prospective studies, as well as any meta-analysis/systematic reviews. Any studies that used a single infiltration of local anesthetic, both pre and post-incision with pain reduction measurements, were included as the number of studies found for post incision only was very limited.

Assessment of article quality

Articles were assessed for quality (Table 1) by assessing study design (approach, inclusion/exclusion criteria, randomization, methods), subjects (inclusion criteria, demographics, control matching), outcomes, and implementation (blinding, follow-up). Article quality was assessed independently by the two authors and any discrepancy in scoring was discussed and a consensus was reached between the two authors.

Score	Study Design	Subjects	Outcome	Implementation
Good – 2	Clear description of design Design appropriate for study question Clear inclusion/exclusion criteria Procedures for randomization clearly described (if applicable) Experimental methods (doses/treatment schedule) clearly defined	Subjects meet inclusion criteria Demographics for all subject groups are included Controls adequately match study subjects	Clearly defined including methods of measurement Outcome measures answer the study question	Groups comparable at baseline Blinding in maintained across study All patients accounted for at end of study Valid methods Appropriate and well described statistics Are summary statistics needed for a meta-analysis included in the paper
Fair – 1	Missing 1 of the criteria listed above	Missing 1 of the criteria listed above	Missing 1 of the criteria listed above	Missing 1 of the criteria listed above
Poor - 0	Missing greater than 1 of the criteria listed above	Missing greater than 1 of the criteria listed above	Missing greater than 1 of the criteria listed above	Missing greater than 1 of the criteria listed above

Table 1: Criterion for determining the quality of papers included in the systematic analysis.

Normalization of VAS scores for comparison across studies

To compare the effectiveness of the local anesthetics in reducing pain in the post-operative period, a normalized change in VAS was calculated for all studies that presented VAS scores with SEM or SD. The choice was made, by both authors, to use standard deviations. If the study listed a standard error of the mean, this was converted using a standard statistical formula ($SD=SEM \times \text{square root of } n$). Several studies did not present either group averages or SEM or SD and could not be included in this comparison. Several different visual analog scales were used (as some used a 0-100 or 0-5 scale) across studies. A standard 0-10 scale was chosen to normalize data to. All studies examined were converted into this 0-10 VAS scoring standard.

Results

The objective of this study was to determine the evidence base for the use of local anesthetic infiltration at the end of surgery prior to wound closure and its effectiveness in pain reduction using a VAS score and a reduction in post-operative opioid consumption. The included articles ranging in quality from poor to good and examined local anesthetic infiltration with a variety of local anesthetics (n=10 bupivacaine, n=4 ropivacaine, n=3 lidocaine articles), various surgical sites (n=9 tonsillectomy, n=4 iliac crest harvesting procedures, and n=1 saphenous vein stripping studies), a number of different pain outcomes

(n=14 VAS, n=5 additional analgesic consumption), and large variations in clinical sample sizes (18-100 patients in a study). The lack of consistency between studies prevents a meta-analysis of the findings and so we present the results as a systematic review and grouped by surgical site (Table 2). The largest groups of studies were examining the effectiveness of local anesthetic infiltration on post-tonsillectomy pain. Nine studies were found that included a total of 623 patients and focused on the efficacy of local anesthetics infusion on post-tonsillectomy pain [21]. All of these studies were prospective randomized designs, with ages ranging from 2 to 65 years of age. Five of the studies look at children (2 to 17 years of age), 3 studies addressed a mix of children and adults (ages 8-65) and one study only had adults (no ages listed) [21]. Studies examined used bupivacaine compared to saline (placebo), bupivacaine compared to ropivacaine or a three group comparison of bupivacaine, ropivacaine and saline. The doses of bupivacaine ranged from 3-6 ml of 0.25% to 0.5%, the doses of ropivacaine ranged from 0.2% to 2% and lidocaine of 1.5-5 ml of 1%-2%. All studies but one used the pre-incisional injection of the tonsillar bed, with six of the studies (out of nine total) finding a reduction in post-operative pain via a pain scale similar to the visual analog scale. [23-27]. Two studies did find that post-operative pain was not reduced [22,28], one stating that after consideration of the usage of other analgesics that they saw no reduction in the amount of the other analgesics required for patient comfort [29].

Study Design	# of Patients	Surgery Type	Intervention	Outcome	Quality Score of paper	Reference
Randomized Control	46	Tonsillectomy	Ropivacaine versus Bupivacaine	Post-operative pain reduced, no difference in comparison groups	7	Akoglu [26]
Prospective Randomized DBL BL	52	Tonsillectomy	Lidocaine	Effective in pain reduction	5	Sorensen [24]
Prospective Randomized DBL BL	70	Tonsillectomy	Bupivacaine	Pre-incisional injection not effective	7	Vanan
Prospective Randomized DBL BL	20	Tonsillectomy	Bupivacaine	Pre-incisional injection effective	5	Arikan [27]
Prospective Randomized DBL BL	60	Tonsillectomy	Bupivacaine versus ropivacaine	Pre-incisional injection neither effective in pain control	8	Unal [28]
Randomized Control	20	Tonsillectomy	Lidocaine 1% and 0.125% bupivacaine vs. control	Pre-incisional injection but no reduction in pain	1	Arcioni
Prospective randomized DBL BL	41	Tonsillectomy	Ropivacaine 1% vs. saline	Pre-incisional soaked swabs (topical)	6	Oghan
Randomized Prospective DBL BL	19	Tonsillectomy	Lidocaine 2% vs. saline	Pre-incisional injection had more rapid return to normal function	8	Naja [25]
Prospective, DBL BL	68	Tonsillectomy	Bupivacaine	Pre and post effective	8	Molliex [30]
Prospective, DBL BL	19	Tonsillectomy	Bupivacaine vs. Saline	Pre-incisional injection no difference in first 24 hrs		Johansen [29]
Prospective, DBL BL	14	Tonsillectomy	Bupivacaine vs. Saline	Pre-incisional injection effective		Jebeles '91
Prospective, DBL BL	22	Tonsillectomy	Bupivacaine vs. Saline	Pre-incisional injection effective		Jebeles [23]

Prospective Randomized blinded	92	Tonsillectomy	Bupivacaine vs. saline	Pre-incisional effective	injection, Not		El-Hakim
Prospective, DBL BL	42	Tonsillectomy	Bupivacaine vs. saline	Pre-incisional effective	injection, Not		Stuart
Prospective, randomized	50	Tonsillectomy	Bupivacaine vs. saline	Pre-incisional effective	injection, Not		Schoem peds
Prospective, randomized	51	Tonsillectomy	Bupivacaine vs. saline	Pre-incisional effective	injection, Not		Schoem Adult
Prospective, DBL BL	18	Vein Stripping	Bupivacaine	Not effective			Kuan [20]
Prospective, DBL BL	100	Iliac Crest	Ropivacaine	Effective			Schaan [34]
Prospective, Single BL	24	Iliac Crest	Bupivacaine	Effective			Chern [33]
Prospective	34	Iliac Crest	Bupivacaine	Effective			Hoard [32]
Random, Prospective	29	Iliac Crest	Bupivacaine	Effective for first 4 hours		2	Todd [31]

Table 2: Summary of the study design, number of patients, surgical site, outcomes and quality of the study for each of the trials included in this systematic analysis

One of the highest quality tonsillectomy studies examined pre-incisional versus post-incisional injection of bupivacaine (0.25% with 6 ml used in children and 9 ml used in adults), using saline injection as a control. This was a randomized, double blinded, placebo-controlled study, of 68 patients ranging from 8 to 65 years of age. Pain was assessed by the visual analog scale at varying time intervals from 1 to 21 hours. It was noted that there was not a significant difference between the bupivacaine pre- and post-incisional groups in pain reduction, but there was a significant difference in these groups compared to the saline groups. This study did address the use of other analgesics (acetaminophen) when assessing the VAS score, but the researchers did not note doses or frequency of those analgesics, as they were looking at the pre versus post-incisional infiltration and if differences in post-operative pain was more effective in the pre- versus the post-incisional groups [30]. This study suggests that in tonsillectomy either pre- or post-incisional infiltration of bupivacaine may produce a reduction in post-surgical pain when compared to the saline (control) group.

The next largest group of studies included four studies that examined Ropivacaine (7.5% 10 mls) or Bupivacaine (0.5% from 4-20 mls) versus a control site of saline or no injection in Iliac Crest bone harvesting surgery. In all studies the local anesthetic was injected post-procedure and looked at visual analog scale. None of the studies noted whether other analgesics were used by the patients. The total number of patients from the four studies was 187, and all studies concluded that pain was reduced at the local anesthetic site compared to the control site [31-34].

One additional study examined the use of Bupivacaine 2 mg/kg in saphenous vein stripping. The study examined 18 female patients undergoing bilateral saphenous vein stripping, injecting either the right or left surgical site and using the other side as a control. Ten of the 18 were injected prior to closure and the remaining 8 were injected prior to surgical incision, but in all cases the subjects were unaware which the bupivacaine injected site was and which was the control (not injected site). Neither pre- nor post-incisional administration of bupivacaine showed a reduction in pain, as assessed by a visual analog scale [20].

To compare the efficacy of local anesthetic infiltration in the reduction of post-surgical pain, the pain scores were extracted from the studies included in this review and normalized to a 10 point VAS scale (Figure 2). A majority of the studies used local anesthetic (pre- or post-incision) in tonsillectomies and demonstrated highly variable reductions in postoperative pain. Several studies stated a significant reduction ($p < 0.05$) in postoperative pain but in many cases the overall change in the VAS from the control to the local anesthetic groups was small or the error bars were large.

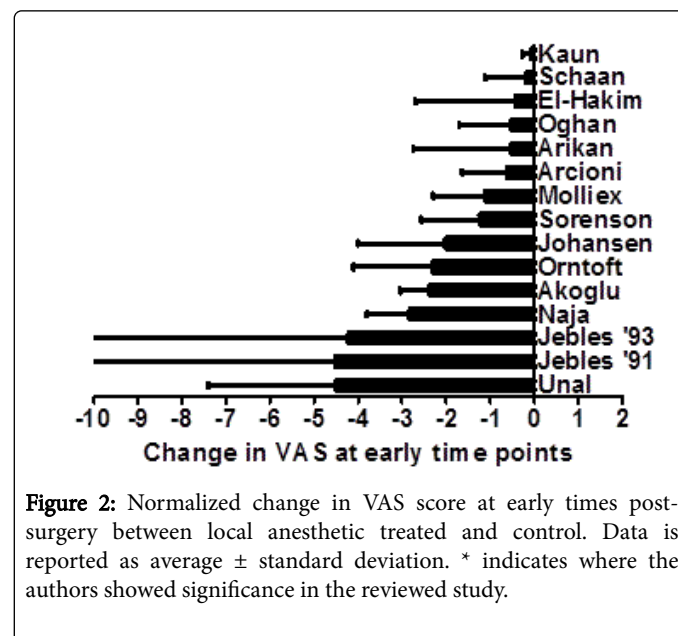


Figure 2: Normalized change in VAS score at early times post-surgery between local anesthetic treated and control. Data is reported as average \pm standard deviation. * indicates where the authors showed significance in the reviewed study.

Discussion

The use of a multimodal approach to pain relief is not new and the use of local anesthetics in surgical wound, both prior to and post incision is a common practice in the surgical suite [8]. Surgeons want to reduce post-operative pain in their patients, while reducing the

potential side effects associated with opioids and other analgesics. In spite of the widespread use of this practice, the evidence base for local anesthetic infiltration prior to surgical closure has not been assessed in the literature. This review demonstrates that despite the widespread use of this practice across a variety of surgical sites there is a paucity of high quality evidence to support this practice. In addition, the variability in study designs and patient populations make it difficult to draw global conclusions about the effectiveness of this approach in reducing post-operative pain and opioid consumption. The limited numbers of studies which show a positive effect of this preemptive approach to control post-surgical pain highlight the need for further well designed randomized controlled trials across a variety of surgical sites.

The varied type of local anesthetics used from study to study, further complicates the issue of whether using local anesthetics reduces pain post-operatively as efficacy might be dependent upon the duration of action of the different local anesthetics employed. With studies looking at different local anesthetics and often if one type is more effective than another continues to muddy the true effectiveness in reducing post-operative pain. An ideal local anesthetic would have a short onset of action, minimal side effects, would not affect wound healing and would last 12-24 hours thus reducing the need for other analgesics in the post-operative period while still reducing post-operative pain. As to the question of whether injecting the local anesthetic prior to or post incision is also in debate, and when you consider that studies on the same site (i.e. tonsillectomies) do not agree as to the effectiveness of pre-incisional injection, the effectiveness of the less studied topic of post-incisional injection begs for further research.

A clear limitation in any clinical study looking at post-operative pain and pain control is the use of the VAS scale as a sole outcome. The VAS scale is a proven standard of measure for patient pain but is based on patient subjectiveness. There is not a current guideline as to how large a change in VAS should be to be considered not just statistically significant but also physiologically and clinically significant. In the current review, several studies claimed a change in VAS of 20% was significant while others did not. With this in mind the need for further good quality retrospective and prospective studies remains paramount, as the technique of injecting local anesthetics to reduce surgical pain is a commonly used practice. Alternatively, future study designs could be strengthened by including other "non subjective" measures of pain control such as overall analgesic consumption, discharge time, and perhaps patient satisfaction. The majority of studies found, in this literature search, did not address the amount or frequency of opioid or other analgesics. Further studies need to be conducted addressing not only the reduction in VAS but the overall dosing and frequency of other pain reducing medications.

Although the use of local anesthetic infiltrated into the surgical wound prior to incision has been studied more extensively, the results are still not conclusive as to the effectiveness in reducing post-operative pain. Only a few studies address the use of additional analgesics to help control pain in the post-operative period. Studies that examine the technique of post-incisional injection of local anesthetics, and their effectiveness are lacking. One study looked at Levobupivacaine injected prior to trocar insertion on 101 patients undergoing a laparoscopic cholecystectomy did not find a significant reduction in post-operative pain as measured by a VAS [16]. As noted above, six of the nine studies found the use of local anesthetic infiltrated pre-incision while examining post-operative pain in tonsillectomies, did find a pain reduction post-operatively but only one

addressed the use of other analgesics to reduce pain. In that study it was determined that pain was not significantly further reduced when local anesthetic as injected [29]. The use of continuous infusion of local anesthetics, that is to say a continuous infusion into the surgical site, has been shown to be effective, in the studies examined [35,36] but often requires inpatient hospitalization and special infusion devices and thus is more costly. The other methods previously discussed, pre and post-incisional one time tissue infiltration, are often done for both inpatient and outpatient procedures thus not significantly altering procedural costs. In today's health care atmosphere this must and is an important consideration.

In conclusion further investigation needs to be done on the use of local anesthetics, as an augment to general anesthesia, in reducing post-operative pain while potentially reducing other analgesic usage thus reducing the potential adverse side effects of medications like opioids. The use of post-incisional infiltration of the surgical incision with local anesthetics was not found to be significantly studied, and the studies that do exist they do not agree of the effectiveness.

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