Effect of steroid in local infiltrative analgesia in one-stage bilateral total knee arthroplasty. A paired-randomized controlled study

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Total Knee Arthroplasty

- Most successful for advanced OA knees
- Severe post-operative pain unresolved
- Multimodal, opioid sparing
- Options:
  - Peripheral nerve blocks
  - Epidural infusion
  - Patient-controlled analgesia

Local infiltrative analgesia (LIA)

Andersen. *Anaesthesia* 2009
Banerjee. *Orthopedic* 2013
LIA

- Intra-op peri-articular injection of:
  - Local anesthetic, adrenaline and NSAID
- Minimal side effects
- Proven effectiveness in multiple RCTs and meta-analysis

- Limitations
  - Short duration
  - Unclear role of individual components

Andersen and Kehlet. *Br J of Anaes* 2014
Xu. *The Knee* 2014
Ng. *JOA* 2012
Study Aim and Hypothesis

• **Aim**
  – Evaluate the role of steroid in LIA

• **Hypothesis**
  – Potent and long acting anti-inflammatory enhances LIA
LIA without steroid
(n=26)

Deep
75mg Ropivacaine
7.5mg Ketorolac
0.5mg Adrenaline

Subcutaneous
75mg Ropivacaine
7.5mg Ketorolac

LIA with steroid
(n=26)

Deep
75mg Ropivacaine
7.5mg Ketorolac
0.5mg Adrenaline
40mg Triamcinolone

Subcutaneous
75mg Ropivacaine
7.5mg Ketorolac

Follow-up at 6 weeks and 3 months

Avoid steroid in subcutaneous tissue and tendon

Randomization
RESULTS
## Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>LIA without steroid (n = 26)</th>
<th>LIA with steroid (n = 26)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>VAS at rest</td>
<td>1.4 ± 2.1</td>
<td>1.7 ± 2.3</td>
<td>0.30</td>
</tr>
<tr>
<td>VAS during activity</td>
<td>6.5 ± 2.0</td>
<td>6.4 ± 2.3</td>
<td>0.80</td>
</tr>
<tr>
<td>Passive ROM</td>
<td>94 ± 18</td>
<td>94 ± 19</td>
<td>0.80</td>
</tr>
<tr>
<td>Active ROM</td>
<td>93 ± 17</td>
<td>92 ± 18</td>
<td>0.43</td>
</tr>
<tr>
<td>Pre-op MTFA</td>
<td>13.6 ± 6.2</td>
<td>13.1 ± 5.8</td>
<td>0.79</td>
</tr>
<tr>
<td>Post-op MTFA</td>
<td>3.4 ± 3.7</td>
<td>3 ±  3.5</td>
<td>0.69</td>
</tr>
<tr>
<td>OT time (min)</td>
<td>73.2 ± 26</td>
<td>77 ± 30</td>
<td>0.24</td>
</tr>
<tr>
<td>Knee Society Score</td>
<td>41 ± 14</td>
<td>41 ± 13</td>
<td>0.62</td>
</tr>
</tbody>
</table>

**Clinical, Radiological and Functional parameters are comparable**
VAS score at rest and during activity

** denote p-value <0.05
Active and passive ROM

Degrees

** denote p-value < 0.05
### Post-operative parameters

<table>
<thead>
<tr>
<th></th>
<th>LIA without steroid (n = 26)</th>
<th>LIA with steroid (n = 26)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to achieve SLR</td>
<td>1.9 ± 1.7</td>
<td>1.2 ± 0.7</td>
<td><strong>0.0067</strong></td>
</tr>
<tr>
<td>Knee Society Score</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At 6 weeks</td>
<td>83.1 ± 10</td>
<td>82.6 ± 11</td>
<td>0.53</td>
</tr>
<tr>
<td>At 3 months</td>
<td>89.8 ± 5.6</td>
<td>89.1 ± 5.6</td>
<td>0.80</td>
</tr>
<tr>
<td>Wound complications</td>
<td>0</td>
<td>0</td>
<td>1.0</td>
</tr>
<tr>
<td>Infections</td>
<td>0</td>
<td>0</td>
<td>1.0</td>
</tr>
</tbody>
</table>
DISCUSSION
Limitation of current evidence

- 7 RCTs on LIA with steroid
- **Methodological limitations**
  - Pre-op analgesics not controlled
  - Short outcome measurements
  - Variable controls (*NSAID/ adrenaline*).
  - Mental health, social status not mentioned.

### Predictors of outcomes of total knee replacement surgery

**Demographic and psychosocial predictors of acute perioperative pain for total knee arthroplasty**

Maya L Roth MA¹, Dean A Tripp PhD², Mark H Harrison MD¹-³, Michael Sullivan PhD³, Patricia Carson BSc⁴

**Does Preoperative Psychologic Distress Influence Pain, Function, and Quality of Life After TKA?**

Alfonso Utrillas-Compaiired MD, PhD, Basilio J. De la Torre-Escuerdo MD, PhD, Ana J. Tebar-Martínez MD, MPH, Ángel Asúnsolo-Del Barco MD, PhD
• **First within subject study to investigate role of components in LIA**

• **Pain most subjective**

• Control confounders:
  – Pain perception
  – Peri-op analgesia
  – Psychological state
  – Social-economic backgrounds

• Increase statistical power
  – Paired t-test, Wilcoxon test
  – Reduce variance
  – Increase power (with same no. of subjects)
Conclusion

• LIA with steroid provides better pain relief and early rehabilitation outcomes after TKR
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THANK YOU
Statistics

- **Power analysis** (alpha 0.5, power 0.8)
  - 25 patients to detect difference in 2 VAS (minimal clinical important difference)
- Paired t-test for parametric variables
- Wilcoxon test for non-parametric variables
- Fisher’s exact test for categorical variables
- GraphPad software, San Diego, CA, USA

Katz. *J or Ortho Surg and Res* 2015
Tubach. *Ann Rheum Dis* 2005
Farrar. *Pain* 2001
How does LIA with steroid work?

Surgical trauma and local inflammation

Corticosteroid

Phospholipase / Arachidonic acid/ COX-2

Inflammatory mediators (ie. Prostaglandins)

Local anesthetic

Peripheral nociceptors

PNS/CNS Sensitization

Robbin and Cotran’s. *Path Basis of Disease* 8th Ed. 2010
Clinical implication

• **Readiness to discharge criteria**
  – Stable medical and wound condition
  – Good pain control (VAS rest <3; activity < 5)
  – Physical (active flexion ≥90deg)
  – Functional (self-care, independent walking)

• **Within subject comparison on POD 3**

<table>
<thead>
<tr>
<th>Both knees pass</th>
<th>Both knees fail</th>
<th>No steroid knee passed only</th>
<th>Steroid knee passed only</th>
</tr>
</thead>
<tbody>
<tr>
<td>9 (29%)</td>
<td>8 (26%)</td>
<td>0 (0%)</td>
<td>14 (45%)</td>
</tr>
</tbody>
</table>

With just HKD 26!!!

Kehlet. *Acta Orthopaedica* 2011
Ng. *JOA* 2012
Chan. *Arthritis Care and Res* 2014
Egmond. *Acta Orthopaedica* 2015
Sensitization reduction

• Less rest pain *at 6 weeks*
  – Beyond action of triamcinolone (~14 days)
• Acute pain can leads to chronic pain via *sensitization*
• Steroid blocks origin of inflammation and pain
• Reduces sensitization ➔ prolong effect?

<table>
<thead>
<tr>
<th>Steroid</th>
<th>Common concentration (mg per mL)</th>
<th>Common equivalent dose (mg)</th>
<th>Approximate duration of action (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methylprednisolone acetate (Depo-Medrol)</td>
<td>40 or 80</td>
<td>40</td>
<td>8</td>
</tr>
<tr>
<td>Triamcinolone acetonide (Kenalog)</td>
<td>10 or 40</td>
<td>40</td>
<td>14</td>
</tr>
<tr>
<td>Triamcinolone hexacetonide (Aristospan)</td>
<td>20</td>
<td>40</td>
<td>21</td>
</tr>
<tr>
<td>Dexamethasone acetate (Decadron-LA†)</td>
<td>8</td>
<td>8</td>
<td>8</td>
</tr>
</tbody>
</table>

Carr. Lancet 1999
Yue. Chin Med Jounral 2013
Clinical importance of changes in chronic pain intensity measured on an 11-point numerical pain rating scale

John T. Farrar\textsuperscript{a,*}, James P. Young Jr.\textsuperscript{b}, Linda LaMoreaux\textsuperscript{b}, John L. Werth\textsuperscript{b}, R. Michael Poole\textsuperscript{b}

Determining the clinical importance of treatment benefits for interventions for painful orthopedic conditions

Nathaniel P. Katz\textsuperscript{1,2}, Florence C Paillard\textsuperscript{1} and Evan Ekman\textsuperscript{2,3}

- **Minimal clinical important difference (MCID)**
  - Smallest change in measured outcome perceived as beneficial (or detrimental) by the patient
- **2pt** changes in VAS (0 -10) is clinically important in OA knees

Katz. *J or Ortho Surg and Res* 2015
Tubach. *Ann Rheum Dis* 2005
Farrar. *Pain* 2001
Efficacy of steroid addition to multimodal cocktail periarticular injection in total knee arthroplasty: a meta-analysis

Xinyu Zhao, Jun Qin, Yang Tan, Rahul Mohanan, Dongcai Huan

The impact of including corticosteroid in a periarticular injection for pain control after total knee arthroplasty

A DOUBLE-BLIND RANDOMISED CONTROLLED TRIAL

- 7 RCT (345 LIA with steroid TKR)
- No differences in infection and wound complications
- No patella tendon rupture
- Still underpowered
- 3500 TKRs to detect 50% differences in infection rate

Zhao. J or Ortho Surg and Res 2015
Hoshino. BJJ 2015