

DOUBLE-BLINDED PROSPECTIVE TRIAL OF PREGABALIN IN MANAGEMENT OF POSTOPERATIVE TOTAL KNEE REPLACEMENT PAIN

LH Ong (MBBS), AM Merican (MS ORTH), CK Chan (MS ORTH), AA Abbas (MS ORTH)

National Orthopaedic Centre of Excellence in Research & Learning, Dept of Orthopaedic Surgery, Faculty of Medicine, University of Malaya, Malaysia

INTRODUCTION

Total knee replacement is one of the most common elective operations being done nationwide in Orthopaedics department with average cases of 10 – 15 a month in every tertiary hospital in Malaysia. The International Association for the Study of Pain (IASP) defines pain as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage”

We hypothesized that adding oral pregabalin 150mg one hour prior to surgery and 75mg 12 hourly for subsequent two days will improve the Visual Analogue Score (VAS) and better range of movement of knees with no increase in side-effects in patients post total knee replacement

METHODOLOGY

We performed a randomized, double-blind trial of pregabalin (150mg one hour prior to surgery and 75mg 12 hourly for subsequent two days) vs control on 16 patients who underwent unilateral or bilateral total knee replacements. Patients were screened for inclusion and exclusion criteria. The main outcomes measured were visual analogue score for pain of knees, range of movement of knees and incidence of possible side-effects.

Both groups received standard postoperative pain relief regime comprising: 1. peri-articular cocktail injection of Vancomycin 500mg, Marcain/Adrenaline 0.2ml, and triamcinolone 40mg and made up to 50ml with normal saline (0.9% sodium chloride solution). 2. Postoperative analgesia were intravenous parecoxib 40mg od then celecoxib 200mg 12 hourly with tramadol 100mg 8 hourly and paracetamol 1g 6 hourly.

Mode of Pain Control	Drugs
Spinal anaesthesia	• Intrathecal morphine
Femoral nerve block	• 10ml levobupivacaine (5mg/ml)
Periarticular injection	• Marcaine-adrenaline 0.2ml • Triamcinolone 40mg • Sodium chloride (0.9%) • Vancomycin 500mg
Analgesics	• IV parecoxib 40mg x 2 doses • Celecoxib 200mg bd • Tramadol 100mg tds • Paracetamol 1gm qid

RESULTS

Of the 16 patients, 10 had both knees replaced, whilst 6 underwent unilateral total knee replacement. After randomisation, 10 patients were assigned to the pregabalin group (bilateral =7, unilateral=3) and 6 were in the control group (bilateral=3, unilateral=3)

	Pregabalin	Control	p value
Mean VAS (6h)	4.67	6.80	0.005
Mean VAS (24h)	3.89	6.80	0.003
Mean VAS (48h)	3.00	7.00	0.003

Table 1. Postoperative Visual Analogue Scale (VAS)

	Pregabalin	Control	p value
Mean flexion (6h)	30.00	25.00	0.309
Mean flexion (24h)	47.50	40.00	0.305
Mean flexion (48h)	58.75	47.50	0.242

Table 2. Postoperative range of flexion (degrees)

All patients did not report any side effects related to pregabalin.

DISCUSSION

Pregabalin is marketed mainly for use in neuropathic pain associated with diabetic peripheral neuropathy, refractory partial seizure and fibromyalgia. However, literature reviews have revealed pregabalin is beneficial in acute pain relief in molar tooth extraction¹, endoscopic thyroidectomy², laparoscopic cholecystectomy³ and gynaecological surgery⁴ In post total knee replacement, Buvanendran et. al showed that perioperative pregabalin is beneficial for post total knee arthroplasty neuropathic pain at 3 and 6 months post-op⁵. Pradeep Jain et. al in a recent trial showed mean morphine consumption was significantly reduced by pregabalin first 48 hours post total knee replacement⁶.

This study revealed statistically significant reduction in Visual Analogue Scale (VAS) scoring of patients that underwent total knee replacement at first 48 hours post-op. However, the knee range of movement in patients with pregabalin, although better, was not significantly more so than the control group. This may be due to the short follow-up duration of this study. To determine the true affect of postoperative pregabalin on range of motion after total knee replacement a longer term follow-up of the study subjects is warranted.

CONCLUSION

Preliminary data showed that perioperative and post-operative administration of pregabalin in addition to multimodal analgesia improved visual analogue score for pain and range of movement of knee the knee with no increase in side-effects in patients who underwent unilateral and bilateral total knee replacements.

REFERENCES

- Hill CM, Balkenohl M, Thomas DW, Walker R, Mathé H, Murray G Pregabalin in patients with postoperative dental pain. *Eur J Pain.* 2001;5(2):119-24
- Kim SY, Jeong JJ, Chung WY, Kim HJ, Nam KH, Shim YH. Perioperative administration of pregabalin for pain after robot-assisted endoscopic thyroidectomy: a randomized clinical trial. *Surg Endosc.* 2010 Nov;24(11):2776-81. Epub 2010 Apr 8
- Agarwal A, Gautam S, Gupta D, Agarwal S, Singh PK, Singh U Evaluation of a single preoperative dose of pregabalin for attenuation of postoperative pain after laparoscopic cholecystectomy *Br J Anaesth.* 2008 Nov;101(5):700-4. doi: 10.1093/bja/aen244. Epub 2008 Aug 20
- Jokela R, Ahonen J, Tallgren M, Haanpää M, Korttila K. Premedication with pregabalin 75 or 150 mg with ibuprofen to control pain after day-case gynaecological laparoscopic surgery. *Br J Anaesth* 2008;100:834-40
- Buvanendran A, Kroin JS, Della Valle CJ, Kari M, Moric M, Tuman KJ Perioperative oral pregabalin reduces chronic pain after total knee arthroplasty: a prospective, randomized, controlled trial *Anesth Analg.* 2010 Jan 1;110(1):199-207. doi: 10.1213/ANE.0b013e3181c4273a. Epub 2009 Nov 12
- Pradeep Jain, Annu Jolly, Vaibhav Bholla, Sweta Adatia, and Jayashree Sood Evaluation of efficacy of oral pregabalin in reducing postoperative pain in patients undergoing total knee arthroplasty *Indian J Orthop.* 2012 Nov-Dec; 46(6): 646-652