

Safety Of Single Intra-Articular Local Anesthetic Infusion In Knee Arthroscopy: An In Vivo Histological Study On Rat Cartilage

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Disclosures

I have no financial interests or relationships to disclose.

Introduction

- Local anesthetics & arthroscopy
 - Procedures under local anesthesia¹
 - Post- op pain management²
- Major clinical evidence of toxicity
 - Pain pumps / post op constant effusion of local anesthetics
 - Mostly glenohumeral joint³
 - Knee joint also affected⁴

Toxicity of non continuous effusion

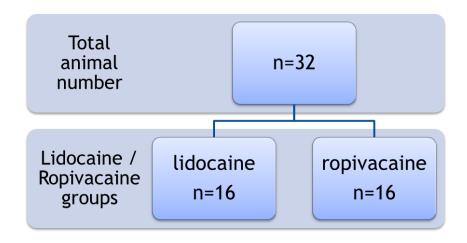
- Studies supporting toxic effects
 - Inflammation⁵
 - reduced number of living cells⁶
- Studies showing no toxicity
 - No significant difference from placebo⁷
 - Same potential from cells received for autologus chondrocyte cultivation under local or spinal/general anesthesia⁸
- Lack of consensus in vivo

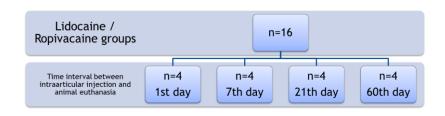
Objectives

- Intra-articular injection of
 - -Lidocaine 2% OR
 - -Ropivacaine 0.75%
- In vivo
- Detect possible toxic effects at different time intervals after injection
- Null hypothesis "there is no histological difference on the cartilage after injection of either local anesthetic or normal saline (placebo)"
- Compare the less toxic ropivacaine with lidocaine

MATERIALS AND METHODS

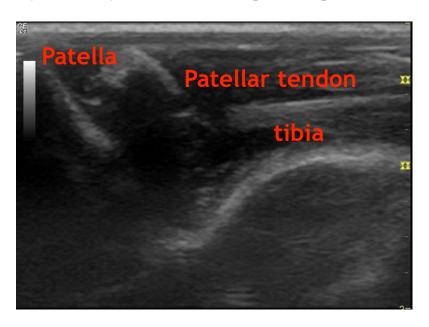
- 32 Sprague-Dawley rats weighting 250 g
- Two groups of 16 (lidocaine group / ropivacaine group)
- Intra-articular injection at the left knee of
 - 0.2 ml of lidocaine 20mg /ml (16mg/kg) OR
 - 0.2ml of ropivacaine 7.5mg/ml (6mg/kg)
- Equal amount of N/S (0.2ml) at the right knee
 - Placebo
- Animals of both group humanely sacrificed at days at days 1, 7, 21, 60

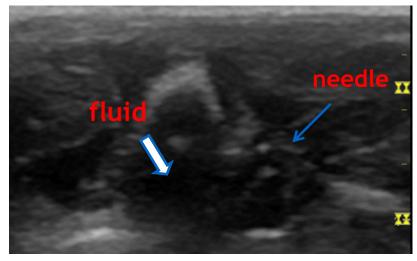




MATERIALS AND METHODS

- Animals anesthetized by IM ketamine (8mg/Kg)
- Povidine /alcoholic solution for skin preparation
- 29 G needle parapatellar aproach
- US guidance (GE Healthcare LOGIQ)





MATERIALS AND METHODS

- Animals euthanasized 1,7, 21 & 60 days after IA injection (ketamine 30 mg/kg)
- Knees resected soft tissue removed
- Specimens were placed in 10% buffered formalin
- Decalcification / Insertion in paraffin
- Sliced in microtome
- Stain (Haematoxyline Eosine, proteoglucan stainin Safranin 'O')
- Examination at light microscope

MANKIN Histology Histopathology Grading System

Structure	Score	Proteoglycan Staining	Score
Normal	0	Normal	0
Surface Irregularities	1	Slight Reduction	1
Pannus	2	Moderate Reduction	2
Cleft to Transitional Zone	3	Severe Reduction	3
Cleft to Radial Zone	4	No Dye Noted	4
Cleft to Calcified Zone	5	Cellularity	
Complete disorganization	6	Normal	0
l 			
Tidemark Integrity		Diffuse Hypercellularity	1
Intact	0	Cloning	2
Crossed by Blood Vessels	1	Hypocellularity	3

HHGS: Sum of structure, cell, Safranin O stain and Tidemark integrity

lidocaine 20mg /ml (16mg/kg) ropivacaine 7.5mg/ml Right Knee

Left Knee

Safranin O Stain for cartilage proteoglycan evaluation (20X): no significant differences between the animal groups

Statistics

- Non parametric Mann Witney U test
- Comparison of
 - Left knee (tested) vs Right Knee (placebo)
 - 2. Left Knee of Lidocaine group ns Left knee of ropivacaine goup
- Significance level: .05

Results

 No Significant difference between HHGS of lidocaine and placebo (N/S) IA injection at 1,7,21 & 60 days after infusion

 No Significant difference between HHGS of ropivacaine and placebo (N/S) IA injection at 1,7,21 & 60 days after infusion

 No Significant difference between HHGS of ropivacaine and lidocaine IA injection at 1,7,21 & 60 days after infusion

Discussion -limitations

- From pain pumps IA effusions => dose related
- Most evidence of toxicity from in vitro studies (cell cultures)
 - In vivo => dilution from joint fluid
 - Integrity of articular surface⁹
- More sensitive methods for cartilage damage
 - Cell count
 - PCR for agrecan II / collagen expresion
 - Mankin score: subjective semiquantitive method of evaluation

REFERENCES

- 1. Marret, Emmanuel, Marc Gentili, Marie Pierre Bonnet, and Francis Bonnet. 2005. "Intra-Articular Ropivacaine 0.75% and Bupivacaine 0.50% for Analgesia after Arthroscopic Knee Surgery: A Randomized Prospective Study." *Arthroscopy Journal of Arthroscopic and Related Surgery* 21 (3): 313-16
- 2. Rokhtabnak, F, M R Ale Bouyeh, A Seyed Siamdust, M Masoomshahi, and M Aghajani. 2015. "Comparison of the Effects of Intra-Articular Sole Ropivacaine and Combined Ketorolac and Ropivacaine for Pain Control after Knee Arthroscopy Surgery." British Journal of Pain 9: 149-56
- 3. Gulihar, Abhinav, Shibby Robati, Haider Twaij, Alan Salih, and Grahame J.S. Taylor. 2015. "Articular Cartilage and Local Anaesthetic: A Systematic Review of the Current Literature." *Journal of Orthopaedics* 12. Prof. PK Surendran Memorial Education Foundation: \$200-210
- 4. Buchko, Jordan Z., Tanner Gurney-Dunlop, and Jason J. Shin. 2015. "Knee Chondrolysis by Infusion of Bupivacaine with Epinephrine through an Intra-Articular Pain Pump Catheter after Arthroscopic ACL Reconstruction." *The American Journal of Sports Medicine* 43 (2): 337-44
- 5. Dogan, N, Af Erdem, Z Erman, and M Kizilkaya. 2004. "The Effects of Bupivacaine and Neostigmine on Articular Cartilage and Synovium in the Rabbit Knee Joint." The Journal of International Medical Research 32: 513-19
- 6. Yazdi, Hamidreza, Bahahreh Tabatabaeian Nimavard, Mohammadali Shokrgozar, Mohammadmehdi Dehghan, Reza Jamei Moayedi, Mohammad Majidi, and Tahmineh Mokhtari. 2014. "An Evaluation of the Delayed Effect of Intra-Articular Injections of Lidocaine (2 %) on Articular Cartilage: An Experimental Study in Rabbits." European Journal of Orthopaedic Surgery & Traumatology 24 (8): 1557-61.
- 7. Iwasaki, Koji, Hideki Sudo, Yasuhiko Kasahara, Katsuhisa Yamada, Takashi Ohnishi, Takeru Tsujimoto, and Norimasa Iwasaki. 2016. "Effects of Multiple Intra-Articular Injections of 0.5% Bupivacaine on Normal and Osteoarthritic Joints in Rats." Arthroscopy - Journal of Arthroscopic and Related Surgery 32 (10). Arthroscopy Association of North America: 2026–36
- 8. Ravnihar, K., Barlič, A., & Drobnič, M. (2014). Effect of intra-articular local anesthesia on articular cartilage in the knee. *Arthroscopy: The Journal of Arthroscopic & Related Surgery*, *30*(5), 607-612.
- 9. Chu, Constance R., et al. "In vitro exposure to 0.5% bupivacaine is cytotoxic to bovine articular chondrocytes." *Arthroscopy: The Journal of Arthroscopic & Related Surgery* 22.7 (2006): 693-699.