

# INTRA-ARTICULAR ANAGLESIA

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# INTRA-ARTICULAR ANALGESIA

## INTRODUCTION

The field of hip and knee arthroplasty have seen huge advances in the past 20 years. Sophisticated implants have been developed, surgical techniques refined and postoperative rehabilitation streamlined in order to enhance postoperative recovery and overall quality of life. <sup>[1]</sup> The largest limiting factor for these procedures is the significant pain experienced postoperatively by many of these patients. <sup>[2]</sup>

Various acute pain management protocols have been devised with the goals of controlling postoperative pain and accelerated rehabilitation and return to function.

Current analgesic guidelines from local and international authorities purport a multimodal approach to perioperative pain control. <sup>[3, 4]</sup> Yet the side effects of these multimodal analgesics defeat the secondary goal of accelerated rehabilitation: regional anaesthesia impacts on motor function, opioids may lead to drowsiness or debilitating nausea and long term NSAIDs may impair wound healing. <sup>[5]</sup>

Thus the advent of intra-articular analgesia saw the exciting potential for ensuring good analgesia with limited side effects that would impair a quick return to normal function. Its popularity has waned since a zenith in the early 1990's and literature continues to indicate large discrepancies in evidence and opinion. <sup>[6- 9]</sup>

This morning's discussion aims to examine the controversy regarding intra-articular analgesia by

- examining the various agents,
- methods of delivery,
- dosing strategies and
- procedure- based uses proposed.

The potential benefits and adverse effects of intra-articular analgesia in the management of acute perioperative pain will also be considered.

Finally the efficacy of the intra-articular route will be compared with more conventional analgesic routes.

## HISTORY OF INTRA-ARTICULAR ANALGESIA

Intra-articular analgesia is by no means a novel concept. The first documented use of intra-articular corticosteroids in the management of joint pain occurred in the early 1950's. <sup>[10]</sup> Since then this route of analgesia has established itself as a corner stone in the management of chronic, inflammatory arthritides. Intra-articular corticosteroids provide acute pain relief with minimal side effects compared to systemic dosing and moderate an anti-inflammatory effect which may retard disease progression and improve joint function. <sup>[10]</sup> The use of peri-articular corticosteroids in the management of chronic mechanical joint pain is also well recognised. <sup>[11]</sup>

This discussion however, focuses on the use of intra-articular analgesia in the perioperative setting for the management of acute pain. Subsequently alternative forms of intra-analgesia should be considered; namely local anaesthetics, opioids and other adjuncts.

Local anaesthetic infiltrations of the joint have been in use since the 1980's and indeed earlier than this in veterinary practise. <sup>[12, 13]</sup> The use of local anaesthetic in the joint coincides with the

introduction of out-patient arthroscopies in a move to identify opioid sparing techniques whilst providing effective analgesia. [12] Intra-articular instillation of local anaesthetic agents was not a huge deviation on the previous practise of peri-articular infiltration at and around the incision site and was generally readily accepted despite the fact that limited evidence existed at the time to confirm its efficacy.[12]

Intra-articular opioids and the concept of peripheral opioid receptor engagement was by comparison a rather revolutionary idea when it was first introduced in the early 1990's. Despite the fact that the first described use of intra-thecal opioids was as early as 1901, it was only after the 1979 publication of the use of epidural opioids by Behavtr that peripheral routes of opioid administration were entertained by the anaesthetic community. [14] Its use in acute pain management following arthroscopy and arthroplasty has been hotly debated over the past 20 years. Little consensus still exists on its use in the perioperative period. [7]

Numerous other adjuncts have also been described: intra-articular tramadol, clonidine, magnesium sulphate, ketamine and neostigmine have all been evaluated in the management of acute joint pain. [15-18] These agents have been the focus of much of the more recent research in this field and perhaps an indication that despite its initial promise the clinical utility of intra-articular analgesia in acute pain control is limited.

## JOINT ANATOMY AND PAIN PHYSIOLOGY

In order to appreciate the intra-articular route for pain management, a quick review of its functional anatomy is called for. A joint is an articulation interface between two bones. The manner in which these two bones articulate may differ. Joints may be classified according to their structure, function or anatomical position (Tables 1 and 2). [19] When considering intra-articular analgesia in the acute pain setting, it is the synovial diarthroses of the hip and knee joints that have seen most of this field's focus.

**Table 1. Classification of Joint according to Structure** [19]

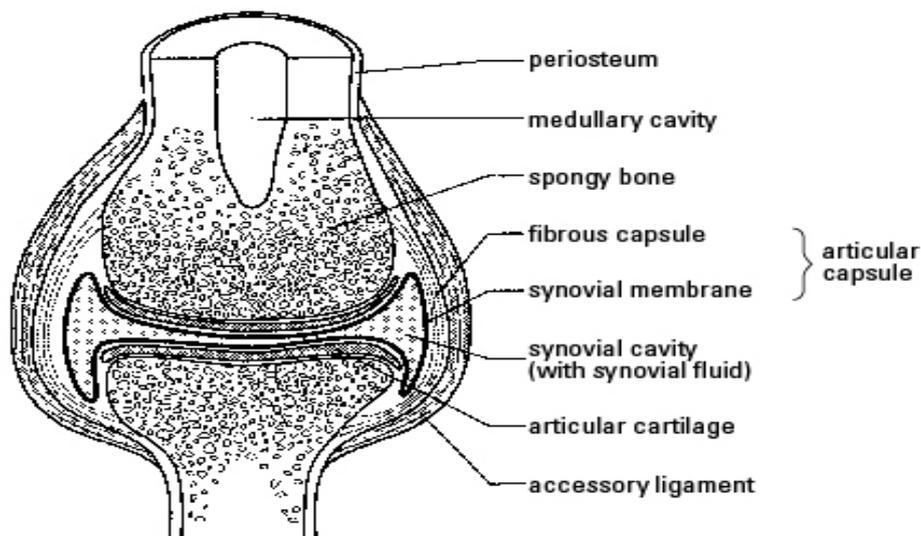
Type of Joint	Description	Range of Motion	Example
<b>Fibrous</b>	Bones joined by dense connective tissue	Minimal	Skull sutures
<b>Fibrocartilagenous</b>	Joined by cartilage	Limited	Symphysis Pubis
<b>Synovial</b>	Not directly joined. Bones united by dense connective tissue that forms an articular capsule around a synovial cavity	Large	Hip Knee

**Table 2. Classification of Joint according to Function** [19]

Type	Description	Range of Motion	Example
<b>Synarthrosis</b>	Most are fibrous joints	Minimal	Skull sutures
<b>Amphiarthrosis</b>	Most are fibrocartilagenous joints	Limited	Intervertebral discs
<b>Diarthrosis</b>	All are synovial Joints	Large	Hip Knee

In a synovial joint the ends of the communicating bone are covered in a layer of articular cartilage that functions as an impact absorber. Intra-articular discs may also be present in some joints for further shock-absorption. The bones are connected by an articular capsule of thick, fibrous structure which is supplied with blood vessels, lymphatics and nerves and encloses the joint cavity. Discrete thickenings of this capsule are known as ligaments and provide further stability to the joint. The inner surface of the articular capsule is lined by a synovial membrane. This membrane consists of Type A synoviocytes with macrophage-like phagocytic properties that remove debris from the joint cavity; and Type B synoviocytes that secrete synovial fluid. Synovial fluid is a viscous fluid that bathes and lubricates the joint. [19]

**Figure 1. Anatomy of a Synovial Joint – the Knee** [21]



The physiology involved in the perception of pain from the joint should also be considered briefly. Nociception occurs at the level of the joint with peripheral receptor exposure to a variety of stimuli: mechanical damage at surgery, chronic inflammation or chemical irritants. Free, encapsulated and complex nerve endings are present in the synovial membrane, periosteum, ligaments and tendons. [20]

Stimuli are relayed via afferent fibres to second order neurons in the spinal cord. Synovial joints are all innervated by a combination of afferent fibres: thick and thinly myelinated A fibres and unmyelinated C fibres. Yet it is the unmyelinated C-fibres that predominate, with only 20% of all nerves myelinated. [20] Chemical mediators found within the joint may sensitize these afferent fibres or stimulate them directly. These include substances such as prostaglandins, histamine, hydrogen ions and bradykinin produced in inflammation; substance P and endogenous opioids. [3, 20]

The ascending spinothalamic and spinomesencephalic tracts within the spinal cord relay this pain stimulus to the thalamus, somatosensory cortex and reticular formation centres. These areas integrate the input and generate information regarding the site and type of pain and mediate the autonomic and behavioural response to the stimulus. [3]

This basic reflex arc is influenced by a variety of other factors in the acute setting: descending inhibitory pathways, sympathetic nervous system stimulation, bio-psycho-social factors and prior central sensitization. All will interact to produce the complex sensory and emotional experience that is acute pain. [3]

## USES OF INTRA-ARTICULAR ANALGESIA

The intra-articular route of analgesic administration lends itself to surgery involving synovial diarthroses. Much is written about its place in orthopaedic surgery with a focus on:

- knee arthroplasty,
- hip arthroplasty and
- knee arthroscopy and related procedures.<sup>[22- 24]</sup>

This form of analgesia with its emphasis on optimising recovery and minimising side effects – particularly those of systemic opioids - is particularly useful in these operative procedures. Arthroscopies are frequently conducted as day case procedures but may produce significant postoperative pain especially in the presence of ligamentous repair. The post-operative goals in this group include early discharge home with effective analgesia, return to normal function and minimising nausea and vomiting.

Arthroplasties of weight bearing joints may produce even more severe pain, which may in turn limit post-operative rehabilitation. Post-operative goals in this group include effective analgesia, early mobilisation and rehabilitation with normal motor and sensory function of the limb minimal sedation and nausea or vomiting. It is thus appreciable that the intra-articular route for analgesia is advantageous in these settings.

Its use in other orthopaedic procedures including shoulder arthroscopy and arthroplasty has been described.<sup>[25]</sup> Other uses within the field of orthopaedics include use during relocation of joint dislocations – both in the emergency room and in theatre in the paediatric population. It has also been employed in surgery on the temporomandibular joint by the maxillofacial surgeons.<sup>[26]</sup>

## PROPOSED BENEFITS

Intra-articular analgesia in the form of opioids, local anaesthetics and adjuncts has various theoretical benefits over conventional systemic analgesia in joint surgery. As alluded to previously it is the combination of effective analgesia with minimal side effects that allows for more rapid recovery of function post-operatively.

Effective analgesia is pivotal following arthroplasty:

- It improves patient satisfaction and
- enhances mobility and cooperation with physiotherapy regimes allowing for
- more effective rehabilitation and recovery of normal function after surgery.<sup>[1]</sup>
- It may also reduce the incidence of immobility associated post-operative complications including orthostatic pneumonias and deep vein thrombosis.<sup>[1]</sup>
- Good analgesia in the acute phase following surgery is necessary to reduce the incidence of future chronic pain associated with the joint.<sup>[1]</sup>

The intra-articular route aims to provide this efficient analgesia locally at the site of nociception. Subsequently reduced doses of opioids may be administered to provide similar degrees of analgesia with fewer systemic side effects than intravenous or intramuscular routes:

- Reduced sedation that may limit mobility and rehabilitation or discharge home.
- Reduced post-operative nausea and vomiting which may also reduce mobility and limit day case surgery.
- Reduced respiratory depression and overall safety.
- Reduced subsequent opioid and other analgesic requirements over the first 3 days following surgery.<sup>[1, 27]</sup>

Local anaesthetics may be administered alone or in combination with the opioids via the intra-articular route. Dosing regimens with regards to local anaesthetics are not reduced at all and thus the potential for toxicity from these agents still exists. [28] The chief advantages of administering intra-articular bupivacaine as opposed to performing a regional technique is again due to the potential for rapid recovery post procedure. [1] Further factors include reduced theatre time for placement and reduced possibility of neurological damage.

Regional anaesthesia – including neuraxial techniques and peripheral nerve blocks – provides excellent analgesia but also produces some degree of motor impairment of the affected limb. [1] This in turn may render postoperative mobilization and rehabilitation more difficult. Mobilisation post arthroscopy is expected immediately following the procedure whereas arthroplasty patients are generally initiated on a rehabilitation programme 24 hours post-surgery. Thus single shot regional techniques may have less of an impact than indwelling catheter techniques. [1]

## ADVERSE EFFECTS

Intra-articular analgesia was originally thought to have very few, if any adverse effects. An attitude that this route was innocuous and should be made use of is reflected in the literature during the early 1990's.

More recent evidence shows that this approach was somewhat misplaced. [29, 30] Both local and systemic side effects may occur from the provision of intra-articular analgesia. [30] Systemic effects differ according to which agent is employed locally and mirror those experienced when the agent is employed via intravenous or intra-muscular routes, likely due to the agent's systemic uptake and actions.

Local effects reflect significant cytotoxicity for the chondrocytes within the joint. Current literature has highlighted the potential for early apoptosis and significant necrosis within the existing chondrocytes in the presence of ketamine and bupivacaine administered intra-articularly. [30] S-ketamine at all concentrations ranging from 10 – 500mcmol/L generates varying degrees of damage; whereas bupivacaine reflects a dose-dependent toxicity. [30] Intra-articular morphine and corticosteroids at varying doses do not seem to generate cytotoxicity. [30]

Whether these new findings are clinically significant remains to be demonstrated. Their relevance in arthroplasty surgery where all cartilage is effectively removed from the joint is probably moot, however future studies with long term follow up is necessary in arthroscopy patients whom receive intra-articular bupivacaine.

**Table 3. Local and Systemic Adverse Effects of Intra-articular Analgesic Agents** [1, 27, 30]

Analgesic Agent	Systemic S/E	Local S/E
<b>Morphine</b>	Limited: sedation, nausea & vomiting, respiratory depression, pruritus	Nil
<b>Bupivacaine</b>	CNS and CVS toxicity Anaphylaxis with allergy	Chondrocyte toxicity
<b>Ketamine</b>	Limited: CVS excitation, sialorrhoea, psychomimetic effects	Chondrocyte toxicity
<b>Clonidine</b>	Limited: hypotension, bradycardia, sedation	Not studied
<b>Tramadol</b>	Limited: nausea & vomiting, constipation	Not studied
<b>Neostigmine</b>	Limited: bradycardia, weakness, nausea & vomiting	Not studied
<b>Corticosteroids</b>	Limited: hyperglycaemia, immunosuppression, delayed wound healing	Nil

## ANALGESIC AGENTS EMPLOYED

A multitude of different agents are currently administered via the intra-articular route in the peri-operative period. It should be noted that currently little standardization exists within the international literature with regards to acceptable agent combinations or dosing ranges. [3, 4]

Local anaesthetics have been administered via this route both as single shot techniques at the time of surgery and as continuous infusions via catheters during the post-operative period. [5, 23] Lignocaine, bupivacaine, mepivacaine, prilocaine and ropivacaine have all been employed successfully. [8, 24, 26] Bupivacaine appears to be the most studied with the most citations in the current literature. Dosing ranges for bupivacaine vary significantly with ranges between 60 and 400mg (1- 6.6mg/kg in an average 60kg adult patient). [1, 30]

Concentrations of the local anaesthetic solution administered also vary with some centres using 0.5% and others preferring 0.25%. Adrenaline is generally added to the local anaesthetic in an attempt to prolong duration of action locally via reducing systemic uptake. Bupivacaine is used alone or in combination with morphine, tramadol, ketamine and other adjuncts including clonidine, corticosteroids, neostigmine and magnesium sulphate. [15 – 18, 31]

Opioids are administered intra-articularly as a single dose during surgery. Morphine is the most popular opioid employed, though Pethidine and tramadol have also been studied. [16, 32] Again, dosing ranges vary greatly with 1- 10mg cited (0.02 – 0.2mg/kg in a 60 kg adult). [1, 7] There is however an emphasis on using smaller doses via this route. Morphine has been used alone, but is frequently administered with a cocktail of local anaesthetic, adrenaline and corticosteroids. [1] The synergism that exists between the opioid and local anaesthetic is well appreciated.

Other agents used in intra-articular analgesia in the acute setting exist primarily as adjuncts that are combined with local and or opioids within the joint to improve the quality of analgesia. Corticosteroids – particularly methylprednisolone – have been described in combinations to counter local inflammation from surgery and augment analgesia.[1] However concern regarding immunosuppression, impairment of wound healing and neurotoxicity has limited its use in more recent years. Ketamine has also been postulated as a useful additive yet its cytotoxicity may also curb future use. [29, 30] Neostigmine, magnesium sulphate and clonidine have also been proposed as adjuncts but limited evidence in the current literature supports their use or establishes their safety. [16 – 18, 31]

It should be recognised that most proponents of intra-articular analgesia accept that it should form part of a standard multimodal analgesia plan. They acknowledge that other forms of analgesia – simple analgesics such as Paracetamol and NSAIDs and indeed limited opioids – will be necessary during the peri-operative period. [1, 33]

**Table 4. Analgesic Agents Employed in Intra-Articular Analgesia**

Agent	Dose	Volume	Method	Combination
<b>Bupivacaine</b>	60 – 400mg (1- 6.6mg/kg)	Vary according to concentration 12 – 40ml	Single shot Continuous infusion	Alone, opioids, corticosteroids, clonidine, ketamine, MgSO <sub>4</sub> , Neostigmine
<b>Lignocaine</b>	250 – 600mg (4 – 10mg/kg)	20ml	SS, CI	Alone
<b>Ropivacaine</b>	500 – 750mg (8 – 12.5mg/kg)	10ml	SS, CI	Alone and opioids
<b>Mepivacaine</b>	2mg/kg	10ml	SS	Alone and opioids
<b>Prilocaine</b>	200mg	20ml	SS	Alone
<b>Morphine</b>	1 – 10mg	0.1 – 1ml	SS	Alone and LA
<b>Pethidine</b>	37.5 – 200mg (0.5 – 3mg/kg)	1 - 5ml	SS	Alone and LA
<b>Tramadol</b>	50 - 100mg	-	SS	Alone and LA
<b>Ketamine</b>	0.5mg/kg	-	SS	LA and opioids
<b>Clonidine</b>	150mcg	20ml	SS	LA
<b>Corticosteroids</b>	Vary 40mg	Vary 2- 5ml	SS	LA and opioids
<b>Magnesium Sulphate</b>	150mg	20ml	SS	LA
<b>Neostigmine</b>	500mcg	-	SS	LA

LA – local anaesthetics, CI – continuous infusion, SS – single shot

Preferred analgesic cocktails differ from site to site based on anaesthetist and orthopaedic surgeon's experience and preference as well as patient characteristics and procedure. Current practise at Inkosi Albert Luthuli Hospital for hip arthroplasty in selected patients sees a combination of:

- ✓ Morphine 10mg
- ✓ Bupivacaine with adrenaline 200mg (40ml 0.25% solution)
- ✓ Ketorolac 30mg

An alternative mixture published by Ranawat and Ranawat and employed in their practise at Lenox Hill Hospital in New York includes:

- ✓ Bupivacaine with adrenaline 0.5% 200-400mg
- ✓ Morphine 4-10mg
- ✓ Methylprednisolone acetate 40mg – Not for diabetic or immunocompromise
- ✓ Cefuroxime 750mg – Vancomycin if allergic to penicillin
- ✓ Normal saline 20ml. [1]

## **MECHANISM OF ACTION OF ANALGESICS**

An in depth review of the mechanism of action of each of the afore mentioned agents used in intra-articular analgesia is beyond the scope of this review. Attention should instead be focused on how these drugs act locally at the site of administration within the joint.

Local anaesthetics act as they would at any other site. Through the sodium channel blockade mitigated in afferent nerve fibres they inhibit transmission of the nociceptive stimulus from the articular surface to the central processing centres. Theoretically the afferent sensory fibres supplying the joint capsule, periosteum and ligaments should be bathed in local anaesthesia and thus experience greater impulse inhibition than efferent motor fibres supplying muscle

bodies around the joint. Subsequently reduced motor fall out should be experienced than with neuraxial or peripheral nerve block techniques which impair conduction in both motor and sensory fibres. [33, 34]

Intra-articular morphine acts through a combination of systemic and locally mediated effects. Systemic uptake of the drug does occur, however plasma opioid concentrations in patients receiving IA morphine are probably too low to explain the degree of analgesia rendered. [35] Peripheral opioid analgesia is a fairly novel idea. The recognition of kappa, gamma and mu opioid receptor's production within the dorsal root ganglion of the sensory afferent fibres and observation that these receptors may be transported peripherally within these afferents led to the idea of using these peripheral receptors directly and exclusively. [3, 31]

Direct activation of these peripheral opioid receptors is induced with intra-articular opioid administration. Activation of these receptors modulates sensory impulse propagation through inhibition of high-voltage gated calcium channels within the fibres. [31] Opioid receptor expression within these peripheral fibres is up regulated during periods of trauma and inflammation by the presence of catecholamines, cytokines and endotoxins; as is the presence of endogenously occurring opioids including enkephalins, endorphins and dynorphins. [31]

Peripheral opioid receptor stimulation generates analgesia at the source whilst limiting side effects. This is due to a reduced in required dose doses is needed with local administration and since most of the adverse effects encountered with opioids are due to central nervous system stimulation. [3, 4, 31]

Drugs used as adjuncts work similarly to their systemic actions with the exception of neostigmine. Its local effects are not fully understood. Proposed mechanisms of analgesia include modulation of hyperpolarisation of sensory neurons, reduction in release of pronociceptive substances and activation of peripheral antinoceptive pathways. [15]

## **METHODS OF ADMINISTRATION**

Method of administration of intra-articular analgesia is another factor within this field that lacks any uniformity. Numerous techniques have been described regarding timing of first dose of analgesic agent, site of administration within the joint and catheter placement techniques for post-operative infusions. [1, 5 - 8]

Most techniques include a single shot technique with one dose of analgesic agents administered by the surgeon intra-operatively under direct vision. [1, 8] Catheter placement within the intra-articular space for continuous post-operative local anaesthetic infusion is also described. Catheter site placement is not standardised and is generally limited to those patients not requiring intra-articular drains post-operatively. [1]

The agents are generally administered intra-operatively after joint replacement or arthroscopy prior to closure of the joint at the end of the procedure. [32] Pre-emptive techniques whereby agents are administered prior to the surgery have also been utilised, though concern regarding correct site of placement of the drugs limits this approach. [32]

Anatomic site of instillation of anaesthetic varies from operator to operator and according to procedure.

Sites for Hip Arthroplasty infiltration are as follows:

- ✓ Before initial reduction – anterior capsule
  - Iliopsoas tendon
- ✓ After final reduction – Synovium
  - Abductors
  - Posterior capsule
  - Gluteus maximus
  - Fascia lata. <sup>[1]</sup>

Knee arthroplasty sites include:

- ✓ Before insertion of liner and reduction – posterior capsule
  - Posteriolateral and medial structures
- ✓ After reduction – Synovium and capsule
  - Collateral ligaments
  - Illeotibial band
  - Periosteum. <sup>[1]</sup>

It is appreciable from these sites of administration that “intra-articular” analgesia is more correctly “peri-articular” analgesia. Indeed anatomical studies performed on cadaveric specimens following these intra-articular techniques at the knee have demonstrated spread of agents from the proximal thigh to the lower leg. <sup>[36]</sup> Concentration of agents was however, appreciably higher within the popliteal fossa. <sup>[36]</sup>

## **EFFICACY VERSUS ALTERNATIVES**

Despite the fact that much work has gone into reviewing the clinical utility of intra-articular analgesia over the past 20 years, little consensus exists. In order to make sense of this controversy, we must ask ourselves several questions regarding its use: Does intra-articular analgesia work? Does it work as efficiently as other analgesic options in terms of pain control? Does it really limit adverse effects and improve post-operative rehabilitation? Is any one agent more useful than another when employing the intra-articular route? Should intra-articular analgesia be employed in our current practise?

### **Does Intra-Articular Analgesia Work?**

There is much debate over this key point. The current literature is split into strong believers and tough critics of this route of administration. <sup>[7, 9, 23, 37]</sup> It is interesting to observe that the bulk of support comes from the orthopaedic literature whilst the anaesthetic publications are generally more sceptical.

Recent systematic reviews all seem to agree that few conclusions can be drawn on the current pool of existing evidence. <sup>[6, 7, 9]</sup> They do note that there is a trend to reduced post-operative pain scores with reduced opioid requirements in patients with mild-to-moderate pain. <sup>[8, 9, 39]</sup> However, both Kalso and Rosseland indicate that due to the poor quality of the existing evidence from methodologically flawed trials, it was difficult to draw any conclusions at all and indeed meta-analysis would prove meaningless. <sup>[7, 37]</sup> Both called for further high-quality trials within the field in order to aid future decision making. Wei’s subsequent review and meta-analysis focused on more recent work specifically in the field of day case arthroplasty and found a similar reduction in post-operative pain in procedures of short duration. <sup>[9]</sup>

Therefore, it is likely that intra-articular analgesia does work for the management of mild to moderate pain. Further study is needed to confirm and quantify this statement.

### **Does it work as efficiently as other Analgesic Options?**

It is difficult to compare intra-articular analgesia in terms of efficacy at controlling post-operative pain as most trials employ it as part of a multi-modal analgesic plan. [1, 33] Simple analgesics are still administered as are systemic opioids during the peri-operative period. All agents contribute to the analgesia and facilitate recovery.

Again, conflicting evidence exists. Some studies indicate the route's superiority over intravenous and intra-thecal routes for opioid administration in terms of degree of analgesia based on visual analogue scales, rehabilitation progress and overall opioid requirements. [28, 34, 37] Others suggest that the intra-articular route generates no analgesic effect at all and is thus significantly less effective than conventional systemic options. [7, 38, 39]

Due to scanty research in this regard and the conflicting evidence which exists, it is not possible to answer the question regarding intra-articular analgesia's efficacy when compared to more traditional options.

### **Does it really limit Adverse Effects and Improve Post-operative Recovery?**

Despite convincing theoretical arguments regarding the intra-articular route to limit systemic side effects and accelerate post-operative recovery, little clinical evidence exists to support these claims. [24, 34] The trend towards reduced pain scores within the first 24 hours following surgery does not necessarily translate into enhanced recovery and early rehabilitation. Few studies actively interrogate this point.

There is evidence that due to reduced and peripheral dosing, plasma opioid levels are reduced with less sedation and post-operative nausea and vomiting. [35] There is also a reduced incidence of peripheral nerve injury in those patients receiving intra-articular local anaesthetic rather than peripheral nerve blocks. [40]

Increasing amounts of new evidence regarding chondrocyte toxicity in the face of intra-articular analgesia is in itself a worrying adverse effect that needs to be considered. [29, 30] This evidence is limited to pre-clinical trials at this point, and future research will reveal the extent of this problem within the clinical sphere. However, at this point it seems prudent to avoid the intra-articular use of all agents with demonstrated chondrocyte toxicity, specifically in arthroscopies and joint reductions where original cartilage is retained within the joint.

Consequently, intra-articular analgesia may limit the systemic and local side effects when compared to other forms of analgesia; however chondrocyte toxicity may limit its use in the setting of arthroscopy.

### **Is any one Agent more Useful than Another when Employing this Route?**

As discussed previously, a myriad of drugs are available to be employed by the intra-articular route. Much of the more recent literature focuses on the use of morphine and/ or bupivacaine. Controversy exists regarding the best agent to use, dosing regimens as well as mechanism for administration.

The most convincing evidence exists in the use of local anaesthetics – particularly bupivacaine for the management of acute peri-operative pain. [3, 23, 24, 39] Conflicting evidence regarding the use of morphine means that further investigation is required before it can be convincingly advocated as an alternative route to systemic or even intra-thecal routes. Corticosteroids remain useful in the management of chronic pain and inflammatory joint disease. [3]

### **Should Intra-articular Analgesia be Employed in our Current Practise?**

In keeping with the current South African and American Society of Anaesthesiologists acute pain guidelines this route may be employed as part of a multimodal analgesic strategy. [3, 4] There is evidence to support the use of intra-articular local anaesthetics but none to support instillation of opioids. [3] Local anaesthesia should be employed with caution in those joints where cartilage is conserved due to its chondro-toxicity.

### **CONCLUSION**

In conclusion, the intra-articular route is an infrequently considered option in the management of acute post-operative pain. It is of particular use in the fields of arthroscopy and arthroplasty that demand effective analgesia and accelerated post procedural rehabilitation. Local anaesthetic instillation shows particular promise for mitigating analgesia as part of a multi-modal approach to acute perioperative pain. However its use may be limited by recent demonstrations of chondro-toxicity. Much controversy and little consensus still exists within the field regarding opioid use, dosing ranges, mechanisms of administration and various other issues. Future research is required to clarify these points and guide clinical applications.

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