POST OPERATIVE PAIN MANAGEMENT

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Introduction :

IASP has described pain as "Unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage."

Surgical operation is a real and severe tissue damage and surgical pain or 'Post operative pain' (POP) is an universal phenomenon. Yet paradoxically after all the effort is taken to make intraoperative period pain free and stress free, the patient is left to fend for himsel f in the post operative period. P O P unfortunately is so grossly undertreated that it is usually relegated to a single line in the sugeon's postoperative instruction "Inj fortwin 1 ml IM. S.O.S."

This is due to traditional, though irrational fear of respiratory depression and addiction and also lack of understanding of the pharmacokinetics and pharmacodynamics of various analgesics.

Pathophysiology of POP.

Surgical trauma produces a combination of peripheral, neurogenic and humoral responses, spinal cord hyperactivity, pitutory, adrenal, sympathetic, renal and metabolic changes that are capable of causing considerable morbidity in the post operative period, adversely affecting the patients outocme from an operation.

This surgical stress response peaks during the post-operative period and has major effects on almost all of the body systems. Even though, effective pain relief and prevention of the stress responses are not directly coupled and analgesia alone does not guarantee that activation of stress response will be prevented, a pain free and a stress free post - operative period definitely, reduces morbidity and mortality of any sugical operation.

The following table No. 1 emphasizes the alterations occuring invarious organ systems and the resultant effects on the body.

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	Systems	Changes/Effects	Morbidity
1.	Cardio Vascular System	Sympathetic stimultion causing mycrdial work (02 demand) Coronry vasoconstriction. (02 supply)	Myocardial ischaemia, cardıac morbidity
2.	Respiratory System	Chest splınting Abnormal diaphragmatic function. Pulmonary compliance, inability to cough, V.C., FRC, T.V. FEV.	Hypoia Hypercabia
3.	G.I.T. & Urinary system	Paralytic Ileus Atony of bladder	Nausea, Vomiting Urinary retention
4.	Neuro endocrinal System.	catecholamines ACTH ADH Glucagon, AMP, Renin Anglotensin II Insulin.	Catabolism -VE N2 balance Sodium and water retention. Hyperglycalmia Anatolism lactate, Ketone FFA.
5.	Coagulation system.	Hypercoagulable state	Increased Vaso-occlusive and thrombo embolic events D.V.T.
6.	Immune function	Suppression of cellular and humoral immune function because of increased -cytokınes.	Increased postoperative tumour growth and metastasis
7.	Psychological function.	Restlessness Sweating, Palpitation etc.	Fear, anxiety and insomia.

Drug	Dosage mg/Kg	Side effects
Acetaminophen	8-10	Common side effects
Ibuprofen	6-10	- G. I. irritation
		- Increased bleeding
		- Decreased Renal blood flow
	0.5-1	- fluid retention.
Sulindac	3-4	
(Renal Sparing)		
Ketorolac	.3 - .6	
Diclofenac	1-4	
Piroxicam	1-4	
Nimesulide	1-2	
Naproxen	10-15	
Fenoprofen	1-4	
Ketoprofen	4-6	
M. fenamic acid	8-10	

Comments :

With short term use these side effects are generally manageable. Ketorolac and Diclofenac are the only NSAIDS available in parenteral form.

2) OPIOIDS :- They exert their effect by mimicking the action of endogenous opioids at receptors that are found in locations throughout the central nervous system, including the periaqueductal and periventricular grey matter and the dorsal horn of the spinal cord. These drugs can be given by various routes and either by intermittent injections or by continous infusion. The table below shows the commonly used opioids and their dosage, side effects etc.

Drugs	Dose Mg/Kg	Receptor	Duration (Hours)	Side effects
Morphine	0.1 - 0.2	Mu	3-4	- Nausea, Vomiting
				- Respiratory depression
Pethidine	1-1.5	Mu	3	- Urinary retention
				- Pruritis etc.
Pentazocine	0.6-.8	Sig & Delta	2-3	
Buprenorphine	0.04-0.06	Mu	8	
Fentanl	0.02	Mu	1-2	

Wolf has proposed a distinction between physiologic pain and clinical pain experienced after frank tissue injury such that associated with surgical operations Physiologic pain has a high threshold, is well localised and transient, has a stimulus response relationship similar to that of other sensations. Clinical pain can be broadly divided into that associated with inflammatory changes elicited by tissue damage (inflammatory pain) and that associated with nerve damage (neuropathic pain). However this distinction is probably artificial since it is difficult to carry out any operation without producing nerve damage, which then becomes sensitized by the inflammatory mediators. Clinical pain is characterised by both " peripheral sensitisation " and also " central sensitisation " of neurones in spinal cord. The end result of both of these processes is as follows :

1) An exaggerated responsiveness to noxious stimuli-Primary hyperalgesia.
2) A spread of hyper-responsiveness to non injured tissue -Secondary hyperalgesia.
3) A reduction in intensity of stimuli necessary to initiate pain so that stimuli that would normally never produce pain now do so-Allodynia.

It is the pupose of this symposium to discuss and highlight the analgesic efficacy, effect on stress response and adverse effects of commonly used as well as other less widely used analgesic techniques or combination of techniques. An attempt has also been made to throw light on recent concepts in POP management.

For the sake of convenience, the various methods of POP management can broadly be classified into pharmacological and non pharmacological methods.

I Pharmacological Methods

Various drugs used for the relief of POP are classified as

1. Non - steroidal Anti inflammatory drugs.
2. Opioids
3. Alpha - 2 agonists
4. Cholinesterase inhibitors
5. Drugs with mixed pharmacalogy
6. Ketamine
7. Nitrous Oxide

1) NONSTERIODAL ANTI INFLAMMATORY DRUGS NSAID)

In the perphery, injury is known to increase the release of prostaglandins and these lipidic acids by a local action, can enhance spontaneous activity and increase the excitability of peripheral afferent terminals. NSAIDS act by blocking the conversion of arachidonic acid to prostaglandins by the enzyme cyclooxyg enase.

The following table shows the list of NSAIDS, their dosages and side effects, etc.,

effective post operative pain management with a minimum of side effects required careful adjustment of the dose so that resultant plasma concentrations are near the minimum required to produce satisfactory analgesia.

This desire to tailor the administred dose of opioids carefully to meet the specific needs of each patient has led to the emergence of patient controlled analgesia (PCA) as an important conceptual frame work for the administration of analgesics. Through self administration patients can compensate for their own unique pharmacologic make up to achieve rapidly and mintain effective analgesic plasma concentration.

The components of PCA are:

1) Pump
2) Triggering mechanism
3) Timer
4) On demand analgesia computer.

Advantages of PCA

a) High degree of acceptance.
b) Lower total dose.
c) Decreased load of work on the nursing staff.
d) Decreased incidence of respiratory depression.

Disadvantages

a) Needs patient co operation & intelligence.
b) Decreasing dose delivery during sleep
c) High cost of apparatus

PCA schedule guideline

Drug	Bolus (mg)	Lockout interval (Minutes)
Morphine	1 - 3	5 - 25
Pethidine	5 - 30	5 - 15
Fentanyl	0.02 -0.1	3 - 10
Pentazoone	5 - 30	5 - 15
Buprenorphine	0.03 - 0.2	10 - 20

Patient controlled Epidural Analgesia (PCA) with combinations of opioids and local anaesthetics can be one of the most effective tools available for management of postopervative pain.

Non Pharmacological Methods

These methods though very effective, unfortunately are less commonly used.

A) BEHAVIOUR MODIFICATION:

A human being who is recovering from operation (Injury) will respond in a variety of ways which have been preset psychologically. Socially economically and physiologically.

The Anaesthesiologist who proposes provision of postoperative analgesia services will begin a routine of behaviour modification during the pre-operative visit, which will be the foundation for the successful management of patients with post operative pain.

A therapeutic relationship can be established so that trust develops between the patients and the doctor. Patients are

Comments :

Hydrophilic drugs such as morphine have longer duration of action because they tend to stay dissolved in the aqueous cerebrospinal fluid, which bathes the spinal cord and acts as a reservoir for the drug.

3) Alpha 2- Agonists:

Several clinical studies have shown that epidurally administered clonidine can be useful for management of post operative pain either alone or in combination with opiods and continous post operative intravenous administration of clonidine has been shown to decrease both pain and analgesic requirements. They act on the alpha 2 adrenergic receptors in the dorsal horn neurons and inhibit the release of substance P. These durgs have got synergistic effect with opiates and can be administered by various routes.

The side effects reported are sedation hypotension and bradycardia

4) Cholinesterase inhibitors :

After intrathecal injection, neostigmine, ablocker of acetylcholinesterase, produces antinociceptive effects. This effect has been shown to be additive or synergistic to the analgesia resulting from use of both opioids and clonidine.

5) Agents with mixed pharmacology :

Tramadol is formulated as a racemic mixture and is now known to possess both opioid and adrenergic activity.

6) Ketamine - Originally introduced as a dissociative anaesthetic. It has also been found to be useful in "subdissociative" doses as an analgesic. Suggested typical infusion rates are 3 to 4 mg/kg/hour following an initial bolus of 1 mg/kg.

7) Nitrous oxide : Entonox i.e. 50% Nitrous oxide with 50 % oxygen in pre - mixed cylinder can be a useful analgesic especially for acute painful procedures of short duration. The low solubility of Nitrous oxide provides rapid onset of analgeria and rapid ehmination upon the cessation of inhalation N_2O in 50% concentration is said to be as potent as 10 mg of IM Morphine with chronic administration of N_2O bone marrow depression leading to leukopenia may occur. This change is reversible when detected early.

ROUTES OF ADMINISTRATION

Various routes of administration of drugs used for pain relief are as below :

Oral:-	NSAIDS, Morphine, clonidine, Tramadol, Ketamine Transmucosal fentanyl (lollypop)
Sublingual -	Buprenorphine
Transdemal -	Fentanyl patch, Nimusulide, Diclofenac
Rectal -	M H S
I M / IV -	Ketorolac, tramadol Diclofenac, all opoids, clonidine ketamine.
Spinal and-Epidural	All opiods, ketamine, Neostigmine clonidine.
Intra articular-	Opioids, local anaesthetic.

Patient Controlled Analgesia (PCA)

Systemic administration of opioids produces both analgesia and side effects in a dose- dependent manner. Providing

d) Intestinal motility among patients having abdominal surgery is dramatically improved when epidural local anaesthetics is used instead of systemic opiates (Ahn H etal 1988). Although appropriate studies have not been done, it is our observation that intestinal activity would appear sooner with epidural local anaesthesia than for epidural opiates.

Disadvantages:

The use of post operative epidural blockade is limited by the side effects of a) Motor blockade b) Sympathetic blockade c) Local anaesthetic toxicity d) Urinary retention e) Failure to recognise and evolving compartment syndrome in a limb.

All of these problems can be minimised by practising segmental neuraxial blockade, thereby minimising the required local anaesthetic dose and the extent of the block. In our institution, we practice routinely continuous epidural anaesthesia for upper and lower abdominal surgery with local anaesthetic 1.5 xy locaine + adrenaline and continue the same along with either injection Buprenorphine 4-5 µg/kg or injection morphine 0.04-0.05 mg/kg on the first postoperative day and only narcotic analgesics in normal saline on the second postoperative day. This provides excellent postoperative analgesia not requiring any other medication by any other route.

ii) Other drugs :

a) Clonidine : Epidurally administrered clonidine exerts its analgesic action through stimulation of spinal delta receptors and when compared to epidural morphine it provides better analgesia in the first two hours. In our hospital we administer oral clonidine premedication which prolongs the xy locaine subarachnoid block.

b) Ketamine : Has received mixed reviews as postoperative analgesic. Low dose epidural administration has been shown to be very effective and devoid of side effects. There has been recent revival in interest for the drug since it is postulated to act by antagonism of N M D A receptors, activation of which by the excitatory amino acid glutamate is capable of providing a hyperalgesic state (Maruset A 1989).

c) Calcitonin : is another substance associated with non - opiate mediated analgesia when administered either spinally or systemically Intrathecal administration has been associated with reduced postoperative pain. It's mechanism of action is unknown.

2) Inter Pleural Analgesia :

It is a convenient method for producing continuous multilevel, partial blockade of intercostal nerves in the postoperative period. It appears very effective for controlling pain after cholecystectomy somewhat less effective for controlling post thoracotomy pain. Benefits in terms of improved ventilatory function are variable (Scott NB 1989, Schroeder D 1990.) Postoperative ileus, length of hospital stay, fatigue, weight, and protein losses were unaffected despite better analgesic scores when compared to opiate infusion for cholecystectomy pain. Pneumothorax, systemic toxicity and

encouraged to accept their physical and emotional limitations within reinforcements for activities which promote well being e.g. breathing exercises, artificial coughing etc. Having a friend or a family member present, who can share in the pre block question and answer session, eliminates later distress when the effects of local anaesthetic blockade result in more than analgesia.

When used in combination with behaviour modification and restoration of *full range of movement, local anaesthetic* axonal blockade can impact positively on the recovery and rehabilitation of patients suffering from pain.

B) REGIONAL ANALEGESIA TECHNIQUES :

1) Non - Opiate Neuraxial Analgesia :

i) Local Anaesthetic Agents : Epidural local anaethetic blockade commenced pre operatively and continued into post-operative period can have a significant effect on the surgical stress associated with lower abdominal and lower limb surgery Perhaps the most important effect is protein sparing since this appears to be clinically associated with postopertive fatique and prolonged convalescence due to loss of muscle tissue and function. In upper abdominal surgery, epidural local anaesthetic blockade has minimal to no effect on the surgical stress response when this technique is used by itself. Administration of a combination of low dose opiate and local anaesthetic via thoracic epidural catheter often provides vary effective and safe analgesia following major upper abdominal thoracic surgary.

The most effective nociceptive blockade, interms of reduced adrenocortical response to major abdominal surgery has been continuous spinal anaesthesia or combined spinal and epidural anaesthesia, probably because of the more efficient afferent neural blokade. However there is extraordinary inter individual variation in response to this regimen so that some patients fail to obtain adequate analgesia. The addition of a parenteral NSAID can reduce an essentially pain free postoperative period in virtually all patients.

Advantages:

a) Postoperative epiduralanalgesia with local anaesthetic agent for 24 hours prevents the usual endocrine metabolic responses to surgery, reduces lymphopenia and granulocytosis and improves nitrogen balance (Torda TA 1983)

b) Following upperabdominal and thoracic surgery epidural local anesthetic infusion has been shown to reverse a portion of the pulmonary dysfunction that occurs postoperatively. T.V. FEV, and PEFR have all been shown to be resorted towards normal. (Torda TA 1983).

c) There is a growing evidence that epidural local anaesthetic administration significantly reduces the risk of thromboembolic events. Local anaesthetics themselves are known to have a primary antithrombotic action and the use of epidural bupivacaine is associated with an increase in calf blood flow and enhancement of fibrinolysis (Wildsmith J. 1989).

D) CRYOANALGESIA :

The practie of freezing nerves to provide prolonged postoperative analgesia has been popular in a few centres for post thoracotomy pain. It can be performed intra operatively by surgical exposure of the appropriate intercostal nerve or postoperatively with assistance of nerve stimulator. Few controlled studies assessing the efficacy of this modality are available and results of other studies are mixed. It is ideal for post thoracotomy and sub costal or flank incision. It is done by a liquid nitrogen probe wherein, the intercostal nerve is exposed intraoperatively and cooled to -20 C. It causes axon destruction with preservation of nerve sheath. The nerve regenerates over the next few weeks Advantages of this technique are excellent with analgesia lasting for days with no side effects. Some of the disadvantages are 1) no analgesia to surgical drain sites, 2) prolonged anaesthetic patch may cause disturbance to patient. 3) Specialised sophisticated equipment is required.

E) ELECTRO ANALGESIA : (Electro Acupuncture) needs specialised equipment and technical skill. Analgesia may be inadequate.

Recent Advances

Concepts of Preemptive Analgesia

Preemptive analgesic strategy emphasises taking measures, to treat pain even before its occurrence. The concept of preemptive analgesia is being discussed in the clinical literature and is currently influencing the manner in which pain releiving agents are used in the periopertive setting Peripheral injury causes cascade of changes in CNS. Various chemicals are released at periphery. Noxious stimuli carried in c fibres excite spinothalamic tract cells. Changed signalling in these cells could contribute to the pain, primary and secondary hyperalgesia and mechanical allodynia. Effect on neurons can outlast the stimulus. This is pathological. It is sustained by A beta fibres. Intracellulor second messenger system also plays a role. Preemptive strategies should be aimed at three sites, periphery, sensory inflow in neurons and central nervous system.

Inhibitors, like NSAIDS, etc of myriad substances released at the periphery block sensitisation.

Spinal wind up and facilitation i.e., prolonged hyperexcitiability by c fibres is suppressed by spinal opiods. Preemptive analgesia supresses stress response to surgical trauma.

Pharmacokinetics

Advances in pharmacokinetics is critically important to anaesthesiologist.

Simple pharmacokinetic parameters like half life etc offer little insight, can lead to misleading conclusions.

pleural effusion are the most commonly reported complications. Pleural infections and broken catheters are also reported. We practice in our institute the same with passage of epidural cathteter through an epidural needle via 4th - 9th intercostal space. We use 30 ml of 1.5% solution with adrenaline and there is a fear of LA toxicity.

3) Continuous peripheral blocks :-

Have been used successfully for postoperative analgesia. These techniques potentially denervate the painful area without the degree of sympathetic blockade experienced with epidural anaesthesia. Injection of a single intercostal nerve with high volume of local anesthetic solution (e.g. 15 ml) results in blockade of multiple thoracic segments (Bigler D 1989) and catheter insertion into the subcostal or paravertebral region alows for continuous anaesthetic infusion, although the extent of blockade diminishes with time. Intercostal catheters can be passed intra operatively during thoracotomy. Superior pain scores, reduction in analgesic requirements and improvements in pulmonory function have been demonstrated with this technique. Continuous lumbar plexus block have been described and appear to offer better analgesia than systemic narcotics.

4) Infiltration blocks:-

Continuous perfusion of surgical wounds provides varying analgesic results. One study (Patrridge 1990) demonstrated reduced pain scores, lower analgesic requirements, shorter PACU stays and better 02 saturation among patients treated with bupivacaine infiltration of abdominal wounds. Other studies failed to show significant benefits. There are concerns among some surgeons regarding potential for wound infection and delayed wound healing as a result of cathelters placed in operative field.

5) Intra-articular injections :-

Intraarticular local anaesthetic agents can produce temporary analgesia when injected at the time of joint closure among arthrotomy patients. Continuous infusion of joints has not gained popularity because of the risk of infection and cartilage damage from contnuous presence of catheter in the joint.

C) TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION (TENS)

TENS has been assessed in a variety of postoperative settings. Sterile self adhering disposable electrodes are placed on either side of the wound. Stimulation at high frequencies (50 - 100Hz) is carried out for several days. Side effects are negligible. Most studies also fail to show any improvement in respiratory function with postoperative TENS use. There is little data available regarding the effect of TENS on endocrine / metabolic stress response in postoperative period and the possible effect of TENS on wound healing,bowel motility, stress responses and sensitised pain projection neurones need to be effectively studied. Mechanism of action: Gate control mechanism as proposed by Melzack and Wall.

Advantages : Low cost, minimal side effects like respiratory depression or sedation.

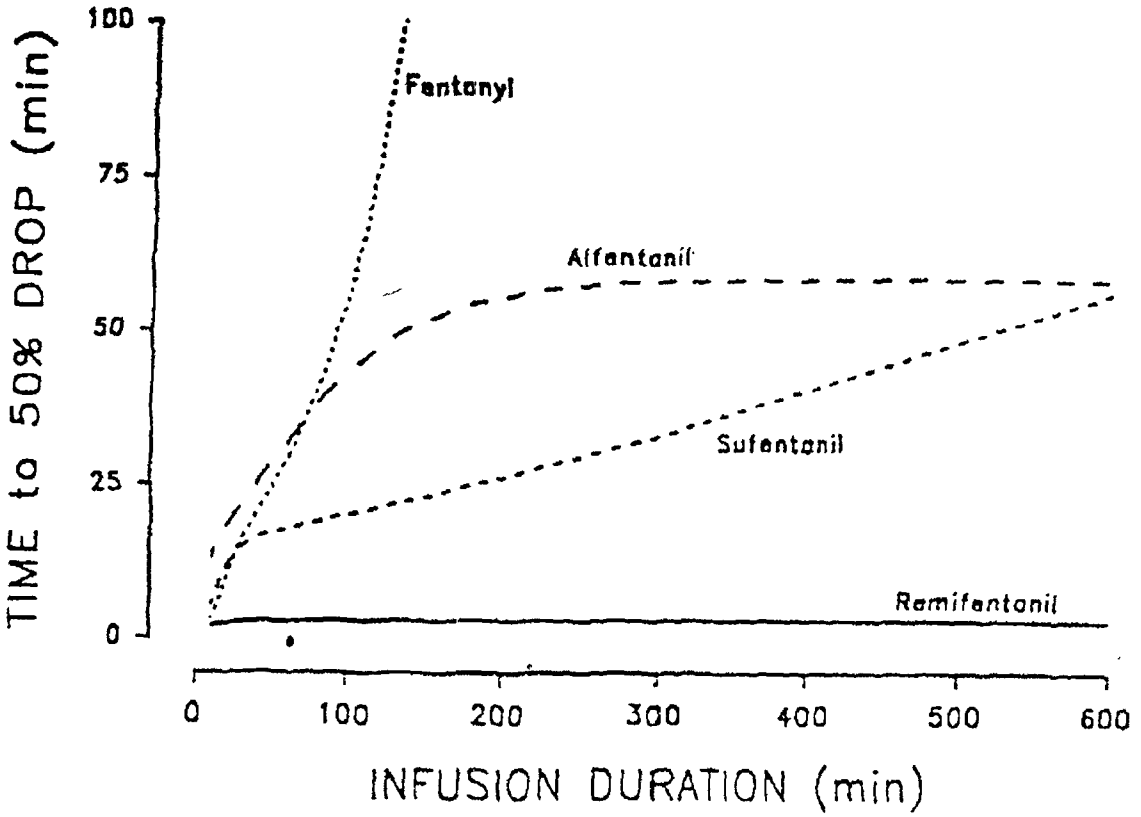

Fig 2. is a graphical representation of the context sensitive half time of the opioids. Contrary to the contemporary belief sufentanyl appears to have more favourable pharmacokinetic profile for infusions of 8 hours or less when the goal is to achieve a rapid 50% decrease in concentration.

Fentanyl exhibits an early time dependent increase in context sensitive half time. In clinical situations when prolonged opioid effect is the goal fentanyl might be the drug of choice. For very brief duration these durgs behave similarly as shown. Remifentanyl due to its ester structure exhibits context sensitive half time independent of infusion duration and extremely evaenescent pharmacokinetics after termination of continuous infusion.

Analgesia and outcome:- 2 studies by Yeager et al and Tumon et al (1987) demonstrated decrease in postoperative complications, intensive care unit stays, total cost in elderly high risk patients, with preemptive analgesia.

Christopher et al (1993) found that epidural anaesthesia significantly decreased incidence of reoperation in vascular surgery possibly due to decreased incidence of thrombosis. In hip arthroplasty Modig et al (1983) showed decreased postoperative deep vein thrombosis and pumlonary embolism.

Epidural analgesia in upper abdominal surgery decreases pulmonary morbidity.

This is due to complex time dependent interplay of various parameters, like age, various disease states etc.

Computer simulation has emerged as an important research and clinical tool, despite various limitations. Through computer simulation based on a drug's population, pharmacockinetic parameters it is possible to graphically visualise the concentration vs time profile that results from any type of dosing regimen. Context sensitive half time a recently introduced pharmacokinetic concept based on computer simulation, predicts the time necessary to achieve a 50% decrease in drug concentration after termination of a variable length continuous infusion It brings intuitively appreciable meaning to modern pharmacokinetic analysis.

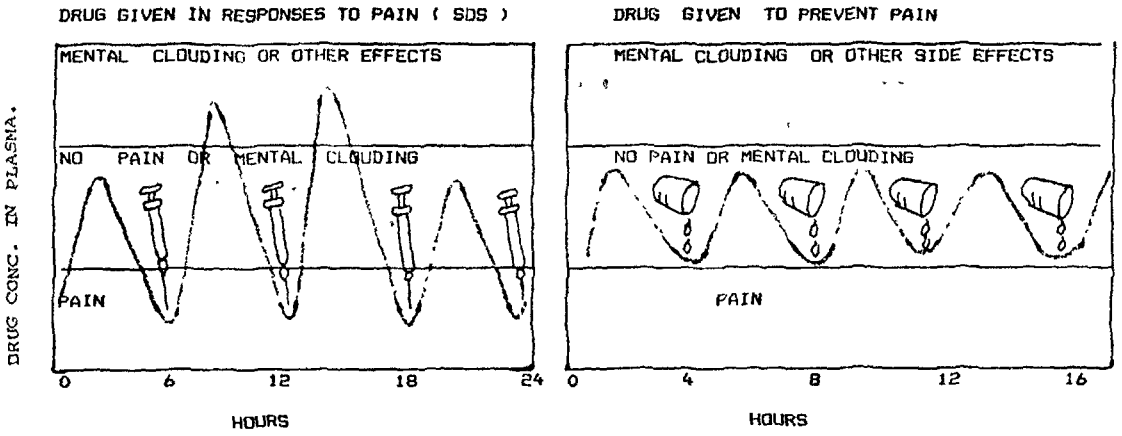

Fig 1. Standard approach to morphine therapy for ongoing pain (Left) is to administer it SOS (meaning, as needed) i.e. only in response to pain. Patient has to wait for help when the pain returns after 4-6 hrs. At that time, pain may be so severe that large dose may be needed which can cause mental clouding and other side effects like nausea.

A more enlightened approach (right) is to prevent pain. Morphine is administered every four hours or more frequently orally, IM or by continous infuion to keep plasma concentration in the analgesia range. This helps to keep the dosage low reducing the incidence of side effects.

Opioids. :

Wall is critical that tremendous benefit of opiods is not properly utilised. There is increasing evidence that opioids used for pain relief are less likely to cause drug dependency. Opiods act via C fibre pathway and not on A delta fibres.

Optimal pre emptive dose of narcotic is not determined 0.1 mg/kg morphine is effective.

Intrathecal requirement is less than 1% IV dose. Break through pain due to *increased severity of pain can occur via* A - delta fibres. This can be treated with 0.025 mg/kg IV Bolus morphine.

Innovative biocompatible materials, pharmaceutical and delivery systems will improve focussed drug delivery.

Major concern with PCA is misprogramming and equipment failure. Novel delivery systems like sustained release oral morphine, transdermal fentanyl transmucosal fentanyl citrate are like old wine in new bottle. Newer agents such as NMDA antagonists and Alpha adrenoceptor agonists (Ketamine, clonidine) are promising.

Advances in drug addication.

Fear of addiction may be a deterrent for many a clinicians to prescribe opioids for the patient havingagonising pain. In the words of Ronald Melzac, (Scientific American February 1990) "I do not suggest that morphine be prescribed indiscriminately. I do urge law makers, law enforcement agencies healthcare workers to distinguish between the addict who craves morphine for mood altering properties and pschologically healthy patient who takes the durg only to releive pain " Knowledge of mechanisms of addiction and withdrawal syndrome is growing with the latest research techniques probing the workings of the brain like, PET scan, molecular biological insights into receptors, studies of gene activations and expressions, antisence RNA strategies and unnravelling of the mystery of reward path way, the limbocortical system responsible for nature's rewards of pleasure and euphoria into which pain pathways have additional projections. Researches in these fields can lead to mindboggling possibilities of newer drugs devoid of addiction problems or to combat addiction. Naltrexone is one of the drugs binding to receptors in the reward pathway.

Conclusion :-

The pain relief techniques can be tailored to individual patient needs. With the technology available and proper utilisation of pharmacological principles and non pharmacological methods, surgical patients can have painfree post operative course. There is little disagreement that usual methods of providing post operative pain relief are less than adequate for many, if not most patients and hence it is always advantageous to combine various drugs / methods / techniques to achieve the goal - i.e. the concept of balanced analgesia.

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Suppression of stress response is more effective with opioid premedication along with blockade with local a nalgesiscs compared with general anaesthesia alone.

Geriatric and paediatric considerations :

In elderly patients intravenous opiods as more effective than intramuscular dose. Increasing age is associated with decreasing clearance. Dose has to be carefully titrated.

Comfort and humanitarian considerations justify analgesia in children. Early institution of pain therapy enhances survival in children. Ability of the child to experience pain is as real as adult.

During weeks 7 - 20 of gestation nociceptive pathways develop. Simple physiological pain measurement tool is not available in children. Documentary pain experience in neonates and children is different. Behavioral and physiological scoring mechanisms are used. Analgesic medicaaion in children is highly neglected. Neonates achieve adult level of morphine clearance at 3 months of age.

Foetus lacks well developed delta receptors. Development of drugs aimed at delta receptors will help their use in obstetrics to avoid neonatal respiratory depression. Investigators are searching for biological pain markers. Some of the pain markers are endorphins, lactate, C-reactive protein, prealbumin and antioxidant activity.

Role of NSAIDS :

They have variety of side effects, consequent upon their inhibition of prostaglandins.

Reasons for reconsidering the role of NSAIDS :

1. An increased understanding of pain mechanism.
2. Pain problem can be multifactorial and combination therapy may be more beneficial. The drug ketorolac can be given intravenously.

To avoid side effects, NSAIDS should be given in lowest effectve dose. Transition to oral route has to be made at the earliest and duration has to be as short as possible. There is ceiling of analgesic efficacy of NSAIDS. There is apparent delay in their effects due to already released prostaglandins exerting their action.

Target specific prostaglandins aiming to avoid, side effects have not yet reached the threshold of clinical development. Isoenzymes of prostoglandins, PGHS - 1 and PGHS -2 responsible for pain and inflammation can be blocked. The blocking agents are being developed, NSAIDS in combination with opioids offer superior analgesia.

Local Anaesthtetics :

They re also useful as part of combination analgesia strategy. They have in addition anti inflammatory activity.

Bupivacaine is known to be cardiotoxic than other commonly used agents like lignocaine, and the toxicity can be successfully treated by adrenaline 1 mg/kg and Amrinone 3mg/kg followed by 20 mcg / kg / min.