A study on side effects of post-operative analgesia with intravenous paracetamol versus dexmedetomidine in patients undergoing laparoscopic cholecystectomy

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Abstract

Several theories have been proposed, the most consistent being that it acts in a similar fashion to NSAIDs by the inhibition of the cyclo-oxygenase pathways. However, paracetamol lacks both the peripheral anti-inflammatory and anti-platelet response seen with NSAIDs[28]. More recently, it has been suggested that paracetamol may also be linked with both direct and indirect stimulation of the cannabinoid, nitric oxide synthase, and serotonergic pathways. Patients satisfying the inclusion criteria were selected during the study period from the operation register on a daily basis. After obtaining a written informed consent, sixty patients were recruited for this study. They were allocated into two groups of 30 each. 10 patients in group D and 08 patients in group P complained of nausea, none of the patients in either group had vomiting, bradycardia, and hypotension.

Keywords: Post-operative analgesia, intravenous paracetamol, dexmedetomidine

Introduction

Dexmedetomidine is a new alpha-2 agonist. Alpha-2 agonists provide sedation, analgesia, muscle relaxation and anxiolysis. Dexmedetomidine is selective for alpha 2 receptors but at higher doses it also has alpha 1 action. Dexmedetomidine has action also on muscarinic, dopaminergic, adrenergic and serotonin receptors [1].

The alpha 2-adrenoceptor selectivity of dexmedetomidine is dose-dependent. At low to medium doses or at slow rates of infusion, high levels of alpha 2-adrenoceptor selectivity are observed, while high doses or rapid infusions of low doses are associated with both alpha 1 and alpha 2 activities [2].

A biphasic cardiovascular response is been described after dexmedetomidine. The

administration of a bolus dose of 1μg/kg dexmedetomidine initially results in a transient increase of the blood pressure and a reflex decrease in heart rate, especially in younger, healthy patients. The initial increase in blood pressure is probably due to the vasoconstrictive effects of dexmedetomidine when stimulating peripheral α2B receptors. The response lasts for 5 to 10 minutes and is followed by a decrease in blood pressure of approximately 10% to 20% below baseline and a stabilization of the heart rate, also below baseline values; both of these effects are caused by the inhibition of the central sympathetic outflow overriding the direct stimulating effects [3].

Acetaminophen (Also known as paracetamol, N-acetyl-p-aminophenol) is a popular antipyretic and analgesic with little anti-inflammatory action.

Despite its popularity, the exact mechanism of action of paracetamol is still a matter of debate. Several theories have been proposed, the most consistent being that it acts in a similar fashion to NSAIDs by the inhibition of the cyclo-oxygenase pathways. However, paracetamol lacks both the peripheral anti-inflammatory and anti-platelet response seen with NSAIDs [4]. More recently, it has been suggested that paracetamol may also be linked with both direct and indirect stimulation of the cannabinoid, nitric oxide synthase, and serotonergic pathways. The overall consensus is that paracetamol has a central site of action with little if any peripheral effect. It is likely that paracetamol has a multifactorial mechanism of action, which may include the activation of different pain pathways hence the difficulty in elucidating its precise mechanism of action. Nevertheless, at the recommended doses, paracetamol possess effective antipyretic and analgesic effects with limited adverse events. For these reasons, it is considered safe for public use [5, 6].

Methodology
Type of study

A prospective, randomized, double blinded study.

Inclusion criteria

1. Patients aged between 18 to 50 years of age.
2. ASA grade I and II patient.

Exclusion criteria

1. Patient refusal.
2. Patients taking non-steroidal anti-inflammatory drugs, opioids.
3. Patients with hypersensitivity to paracetamol and dexmedetomidine.

Method of collection of data

Patients satisfying the inclusion criteria were selected during the study period from the operation register on a daily basis. After obtaining a written informed consent, sixty patients were recruited for this study. They were allocated into two groups of 30 each. Preoperatively, the patients were made familiar of their role in the study and the use of 10 cm VAS with end point to be labeled as 0 = no pain and 10 = excruciating worst possible pain.

On receiving patient in operating room, the patient monitoring included electrocardiogram (ECG), noninvasive blood pressure (NIBP), heart rate (HR), oxygen saturation (SPO2). The baseline HR, NIBP, SpO2 scores were recorded.

Computer based randomization was done and allocation concealment was done by sealed

envelope method. An anesthesiologist not involved in the management of the case opened a sealed envelope randomly and loaded drugs as per the drugs in the envelope:

D group:
1.   Dexmedetomidine 1µg/kg in 100 ml normal saline and connected to an infusion pump.
2.   Dexmedetomidine 2µg/ml in 50 ml normal saline and connected to a syringe pump.

P group:
1.   Paracetamol 1g in 100 ml normal saline and connected to an infusion pump.
2.   Normal saline in a 50 ml syringe and connected to a syringe pump.

The anesthesiologist in the theatre was blinded to the test drug conducted in the intraoperative anesthetic management and monitoring.
Group D (Dexmedetomidine)-received dexmedetomidine 1µg/kg in 100 ml of normal saline through infusion pump over 10 min. This was followed by an infusion of dexmedetomidine through syringe pump at 0.25ml/kg/h (0.25ml = 0.5µg) of prepared concentration.
Group P (Paracetamol)-received 1 g paracetamol in 100ml solution through infusion pump over 10 min. This was followed by an infusion of normal saline administered through syringe pump at 0.25ml/kg/h.

Results

The mean age in group D & group P were 34.93±9.91 and 34.67±11.01 respectively. There was no significant difference in the age of patients between the groups. Both the groups were similar with respect to age distribution.
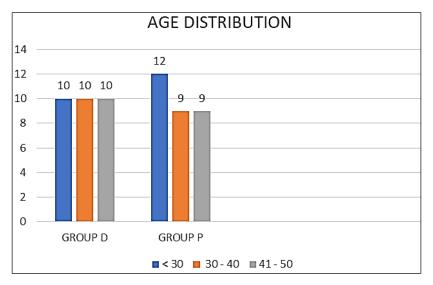

Fig 1: Age distribution

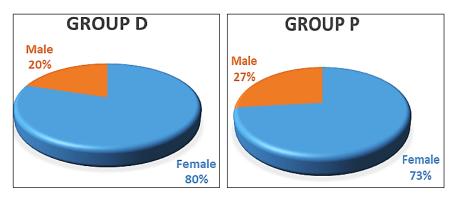Both the groups were similar with respect to gender distribution.

Fig 2: Gender distribution

The mean weight in group D & P; were 62.50±10.05 & 63.40±14.39 respectively. Both the groups were similar with respect to weight (p > 0.05).
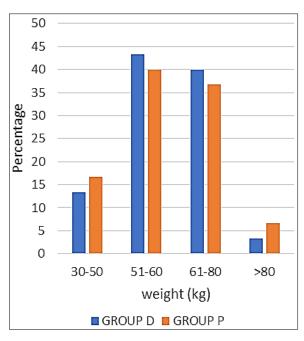

Fig 3: weight distribution

It was similar in both the groups and was not statistically significant.
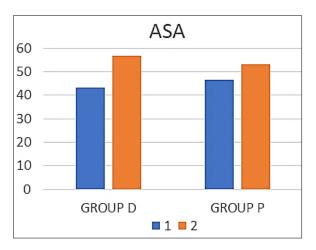ASA grade distribution was statistically similar in two groups.

Fig 4: ASA Grade distribution

10 patients in group D and 08 patients in group P complained of nausea, none of the patients in either group had vomiting, bradycardia and hypotension.
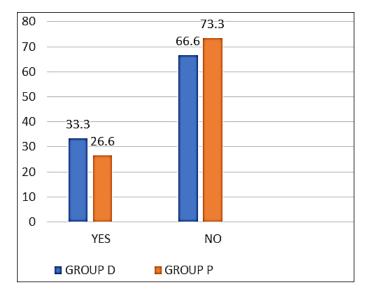

Fig 5: Incidence of Nausea

Discussion

Paracetamol is well absorbed in the gastrointestinal tract. Oral bioavailability is dose dependent: with larger doses, the hepatic first pass effect is reduced due to overwhelming of the liver enzymatic capacity; and therefore, bioavailability is increased. Rectal administration of paracetamol is also feasible. In this case, bioavailability is inconsistent and in overall reduced, due to incomplete dissolution of the suppository in the rectum. Finally, rectal administration can be considered unpleasant, inconvenient and intrusive. As a result of these limitations, a major advancement in the clinical use of paracetamol has been the introduction of the IV formulations, all of which have a bioavailability of 100%. The binding of paracetamol to plasma proteins is negligible [7].

Paracetamol is essentially metabolized in the liver by conjugation with glucuronic acid (55%) and sulfuric acid (35%). Hepatotoxic metabolites are produced in small amounts by the cytochrome P450 (isoenzyme CYP2E1). In the therapeutic plasma concentration range, this metabolite is detoxified by conjugation with glutathione. In case of intoxication the amount of this toxic metabolite increases and outweighs the amount of available glutathione, which can lead to hepatic failure and renal tubular necrosis [8].

Acetaminophen has low incidence of GI side effects. In acetaminophen overdose liver damage occurs by acetaminophen's metabolites, N-acetyl-p-benzoquinoneimine (NAPQI). NAPQI leads to liver failure by directly damaging liver cells and depleting the liver's natural antioxidant glutathione, leading to liver failure.

Treatment is aimed at removing the paracetamol from the body and replacing glutathione. In early presentation of overdose ingestion of acetaminophen can be treated by activated charcoal to decrease absorption of acetaminophen. Hemodialysis may be useful if started within 12 hours after ingestion of huge doses [9].

Acetylcysteine and Methionine is administered as an antidote which acts as a precursor for glutathione and can neutralize NAPQI metabolite directly. Patients treated early after ingestion has a good prognosis [10].

Conclusion

10 patients in group D and 08 patients in group P complained of nausea, none of the patients in either group had vomiting.

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