ASIAN JOURNAL OF BIOMEDICAL & PHARMACEUTICAL SCIENCES

e-ISSN: 2249-622X

RESEARCH ARTICLE

Comparative efficacy and safety study of analgesic effect of Fentanyl I.V. and Paracetamol I.V. in postoperative patients in Multidisciplinary Hospital.

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Received:
13th JULY 2013
Received in revised form:
25th July 2013
Accepted:
30th July 2013
Available online:
10th Aug 2013

OPEN ACCESS

Online ISSN 2249–622X
http://www.jbiopharm.com

ABSTRACT

Background: Intravenous acetaminophen is widely used in the management of postoperative pain. Opioids remain the agents of choice for severe pain; however, this class of analgesics is associated with dose dependent side effects and negative postoperative outcomes. Non-opioid analgesics are commonly used alone or as adjuncts to opioid-based analgesia to treat moderate to severe pain. The oral route for administration of drugs may be denied because of the nature of the surgery and drugs may have to be given by injection.

Aims & Objectives: A single-dose, parallel group study was performed to evaluate the analgesic efficacy and safety of intravenous acetaminophen as compared with intravenous Fentanyl. The aim of this study was to evaluate the analgesic efficacy and safety of a single dose of 1 g of intravenous acetaminophen in comparison with 100 mcg of intravenous Fentanyl in patients experiencing pain after surgery.

Methods: Patients (112) were selected who has received acetaminophen or Fentanyl. Pain intensity was assessed using WOMAC scale at 4 h after either of the drug administration. The secondary end point was Quality of Recovery (QoR) which was also assessed at 4 h after either of the drug administration. Safety was monitored through Side-effects reporting by patients.

Results: The intravenous acetaminophen and intravenous Fentanyl groups differed significantly regarding Pain intensity score after single dose administration and at 4 h reading. As far as safety concern, Dry mouth is the major side-effect reported by patients in both the groups but it was higher Fentanyl group.

Conclusion: Although acetaminophen is having low incidence of side effect as compared Fentanyl group but analgesic efficacy was much better in Fentanyl group than acetaminophen group. There were no significant differences in the QoR scale between two groups. We summarize how better postoperative pain management can be achieved with minimal side-effects and better recovery process.

Keywords: Post-operative pain management, Analgesics, Safety, Efficacy, Quality of Recovery.

1. INTRODUCTION:

Effective Pain management is an important component of Post surgical care. Postoperative pain is considered a form of acute pain due to surgical trauma with inflammatory reaction and initiation of an afferent neuronal barrage. Pain being a subjective phenomenon is perceived only by the sufferer. The adequacy of postoperative pain control is one of the most important factors in determining when a patient can be safely discharged. Because inadequately treated pain is a major cause of prolonged stays or unanticipated hospital admissions after surgery, thus

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introduction of multimodal analgesia including opioids and non-opioids, either alone or in combination with other drugs have greatly improved the efficacy of pain control.

Opioids remain the agents of choice for severe pain; however, this class of analgesics is associated with dose dependent side effects and negative postoperative outcomes. [1, 2] Non-opioid analgesics are commonly used alone or as adjuncts to opioid-based analgesia to treat moderate to severe pain. The oral route for administration of drugs may be denied because of the nature of the surgery and drugs may have to be given by injection. Normally, postoperative pain should decrease with time and the need for drugs to be given by injection should cease. Strong opioids may no longer be required and adequate analgesia can be obtained by using non-opioids alone or in combination with weak opioids. Whilst opioids are the mainstay for relief of severe pain, they are far from perfect analgesics as they have many significant side effects. [3]

Acetaminophen has a well established safety and analgesic profile. Until recently, there has not been an intravenous acetaminophen solution available because it is poorly soluble in water and not stable in solution. A ready-to-use formulation of intravenous acetaminophen has recently been developed that does not require reconstitution and is not associated with contact dermatitis or pain at injection site. The availability of intravenous acetaminophen preparation may aid accurate administration of drug to patients at higher risk of dose related hepatic toxicity, including neonates. [4]

The aim of this study was to evaluate the analgesic efficacy and safety of a single dose of 1 g of intravenous acetaminophen in comparison with 100 mcg of intravenous fentanyl in patients experiencing pain after surgery.

2. MATERIALS AND METHODS

2.1 Patients:

Patients aged at least 18 years who were recovering from surgery performed were eligible for study. Exclusion criteria included patients aged above 75 years. Patients were also excluded if combination of analgesics were given postoperatively. Patients in the I.C.U. were excluded because patients were kept in sedation state. The study was conducted in accordance with good clinical practice and was approved by institutional review board.

2.2 Study Design:

This study was parallel group study comparing 1g intravenous acetaminophen with 100 mcg intravenous fentanyl and was conducted in multi-disciplinary hospital of South Mumbai. Patients were studied over the first 4 hr after surgery.

Intravenous acetaminophen was chosen as a comparator because it is widely prescribed in hospital and is a recently marketed form for management of acute pain after surgery. So to study the efficacy and safety of this new form drug which is more frequently prescribed was chosen for study. Since it is available as 1g solution, dose chosen was 1 g for intravenous acetaminophen and 100 mcg for intravenous fentanyl.

All patients were closely monitored and patient's pain intensity was recorded. Patients reporting none to extreme pain intensity on a five-point verbal pain intensity categorical scale. (0= none, 1=slight, 2= moderate, 3= severe, 4= extreme).

The aim of this study was to judge good analgesia after surgery which depends upon type of surgery performed and recovery process. Patients reported quality of recovery score (QoR) on three point scale. (0= not at all, 1= some of the time, 2= most of the time). Both pain intensity and Quality of Recovery was measured after 4 hour of surgery.

2.3 Efficacy measurement:

Post operative pain relief was the major concern of this study. Intravenous Fentanyl and Intravenous acetaminophen both have similar half-life which is around 4 hours. Hence pain intensity was measured after 4 hour of surgery in which either of the drugs was prescribed postoperatively. Pain was measured on four-point categorical scale. (0= none, 1= slight, 2= moderate, 3= severe, 4=extreme). When the patient was asleep no attempts was made at arousal.

2.4 Safety Assessments*:*

Side-effects or adverse events were monitored throughout the study period. The following side effects were reported during study: Nausea, Vomiting, and Dry Mouth with either of the drugs.

2.5 Statistical Analysis:

Sample Size: Analysis on sample size of 56 patients per group was performed in the intention-to-treat patients. Data are expressed as mean and 95% confidence interval. Student's *t-test* was used to compare means and *P* value of equal to 0.05 was required to rule out the null hypothesis.

3.0. RESULTS

A total of 112 patients were included in study as per criteria and were considered for analysis, 56 in fentanyl group and 56 in acetaminophen group. Both the groups were comparable with respect to demographics and surgical procedures.

PATIENT CHARECTERISTIC DATA:

3.1 Efficiency Measures

Pain Intensity Score (Single Dose). The primary efficacy criterion was pain relief. For both active groups, Pain intensity Scores of intravenous acetaminophen were higher than those of fentanyl group with significant difference between the two active groups (P= 0.05).

The pain score in acetaminophen group was 2.410 (+/-) 1.30 as compared to fentanyl group which was 1.625 (+/-) 1.13 which was much lower as compared to previous group. In general, response was better in fentanyl group than acetaminophen group which was statistically significant.

Characteristics	Fentanyl group (n= 56)	Acetaminophen group (n=56)
Age (yr)	46.78 (+/-) 16.17	49.08 (+/-) 15.86
Men	24	19
Women	32	37
Pain score	1.625 (+/-) 1.13	2.410 (+/-) 1.30
QoR Score	15.78 (+/-) 1.68	15.21 (+/-) 1.82
Nausea	14 (25%)	17 (30.35%)
Vomiting	0	3 (5.35)
Dry mouth	33 (58.92%)	19 (33.92%)

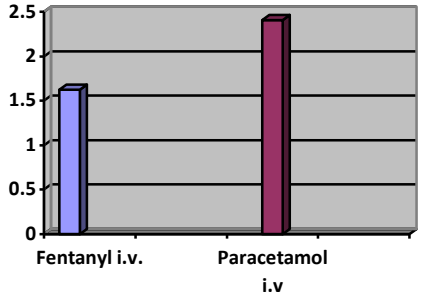

Figure 1: Average pain score of both active groups after single dose administration and 4 hour.

Quality of Recovery Score (QoR Score). Second end point of study was quality of recovery after surgery. The QoR score was 15.78 (+/-) 1.68 in fentanyl group which was higher as compared to 15.21 (+/-) 1.82 in Paracetamol group. In general there was difference in quality of recovery after surgery but it was not statistically significant.

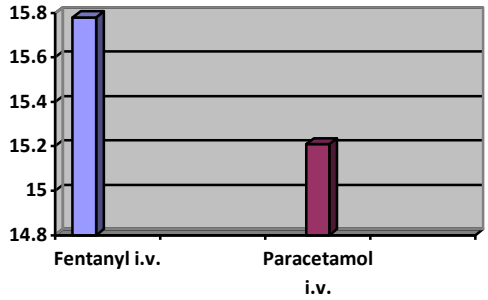

Figure 2: Average QoR score of both active groups after single dose administration and 4 hour.

At different age, pharmacokinetics and pharmacodynamics of drugs changes and hence efficacy of drug also changes. Below in table shows the age wise classification of average pain score of drugs in both the active groups.

Age	Fentanyl group (n=56)	Acetaminophen group (n=56)
18-30	1.16	2.33
31-45	1.85	2.35
46-60	1.56	2.06
61-75	1.85	2.86

3.2 Safety Assessments

Sideeffects were closely monitored during study and nausea, vomiting and dry mouth were reported. 14 patients (25%) reported Nausea in Fentanyl group as compared to 17 patients (30.35%) in Acetaminophen group.

3 patients (5.35%) reported vomiting in Acetaminophen group and no Vomiting reported in fentanyl group.

Dry mouth was the major concern in this study and it was frequently reported. 33 patients (58.92%) reported dry mouth in Fentanyl group whereas 19 patients (33.92%) reported dry mouth in Paracetamol group.

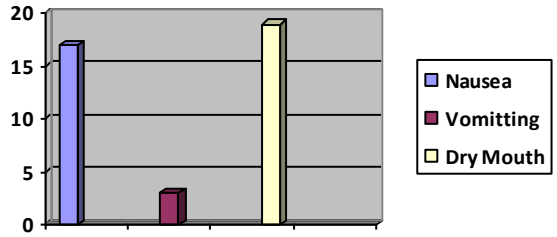

Figure 3: side-effect profile of Fentanyl group after single dose administration and 4 hour.

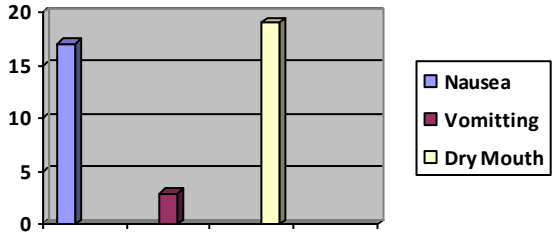

Figure 4: side-effect profile of Paracetamol group after single dose administration and 4 hour.

4. DISCUSSION

Phytochemicals are natural and non-nutritive bioactive compounds produced by plants that act as protective agents against external stress and pathogenic attack.[18] Secondary metabolite is a crucial for plant defenses (e.g. as an antioxidant or antimicrobial agent) which has enabled plants to survive. Based on their biosynthetic origin, phytochemicals can be divided into several categories: phenolics, alkaloids, steroids, terpenes, saponins, etc. Phytochemicals could also exhibit other bioactivities such as antimutagenic, anticarcinogenic, antioxidant, antimicrobial, and anti-inflammatory properties.[11] These plant-derived phytochemicals with

therapeutic properties could be used as single therapeutic agent or as combined formulations in drug development.[12] The present study is to investigate the phytochemical identification of ethanol extract of NC by GC-MS analysis, antioxidant ability and DNA protection by performing various *in vitro* assays and the results indicated a concentrated dependent antioxidant ability of NC. The phytochemical screening studies have been carried out by GC-MS analysis and we identified the sixteen chemical constituents present in the leaf extracts of NC. The results of our studies indicated that 60 µg/ml concentration of NC showed optimum protection against free radical induced oxidative damage. The DPPH and superoxide radical scavenging activity of NC can be attributed to the presence of phytol, squalene, β-tocopherol, vitamin E, campesterol, stigmasterol and β-amyrin which donates hydrogen and an electron to hydroxyl radicals, stabilizing them and giving rise to a relatively stable radical. Thus, the free hydroxyl group on the aromatic ring is responsible for the antioxidant properties.

The protective effect of DNA which might be due to the presence of vitamin E, campesterol, β-amyrin, stigmasterol, squalene, β-tocopherol and phytol present in the ethanol leaf extract of NC inhibit the oxidative stress induced DNA damage in cultured human lymphocytes.

5. CONCLUSION

This study provides supportive evidence on the safety and efficacy of i.v. fentanyl in comparison with ready-to-use i.v. acetaminophen after surgery. Although acetaminophen is having low incidence of side effect as compared Fentanyl group but analgesic efficacy was much better in Fentanyl group than acetaminophen group. There were no significant differences in the QoR scale between two groups. We summarize how better postoperative pain management can be achieved with minimal side-effects and better recovery process.

6. ACKNOWLEDGMENT

The authors wish to extend their gratitude and appreciation to team- nurses and other staff of hospital for their support and scrupulosity in conducting this study.

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Conflict of Interest: None Declared

Cite this article as:
Raval Divyesh, Patankar Zahoorahamad, Khety Zarine, Lavekar Swati. Comparative efficacy and safety study of analgesic effect of Fentanyl I.V. and Paracetamol I.V. in postoperative patients in Multidisciplinary Hospital. Asian Journal of Biomedical and Pharmaceutical Sciences, 2013, 3: (22), 66-70.

