

A survey of opioid analgesics used for treating pain of acute myocardial infarction (AMI): Need for promoting rational use of drugs

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Abstract

The study was aimed to find the drug of choice, pattern of opioid analgesic used and to promote the rationale use of Opioid analgesic in the treatment of pain of acute myocardial infarction. This was a planned survey in which 668 registered medical practitioners were interviewed by 122 trained medical personale with the help of a questioner. The study revealed that Morphine is the drug of choice according to 53% of different registered medical practionners as analgesic for pain of acute myocardial infarction. The actual analgesic used in clinical practice was Pentazocine by 55.24% of RMPs which has been well documented as an unsafe drug in patients of acute myocardial infarction. This study promotes use of safer and moreover cardio protective analgesics like Buprenorphine.

Key words: AMI (Acute Myocardial Infarction), Morphine, Pentazocine, Registered medical practitioners (RMPs)

Introduction

Acute myocardial infarction (AMI) is one of the most common diseases of the modern era. The Mortality rate with AMI is approximately 30% with more than half of these deaths occurring before the individual gets emergency care. In the emergency department, one of the goal for the management of patient with suspected AMI include control of cardiac pain^[1]. The alleviation or reduction of pain is a critical factor in the care of patients with acute myocardial infarction^[2] by parenterally administration of narcotic analgesics. The haemodynamic effects of these agents are quite different in patients with acute pain during the period of myocardial ischemia or in patients that are haemodynamically unstable^[3]. A wide verity of analgesics have been used in the treatment of pain associated with AMI including Meperidine, Pentazocine, Buprenorphine and Morphine; the last remained the drug of choice^[2,4]. Due to unavailability of Morphine, as Morphine comes under restricted drugs and has narcotic code other analgesics preferred are Pentazocine, Buprenorphine, Tramadol, Meperidine.^[3]

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Aims and objectives

- To study the pattern of opioid analgesic used in the treatment of AMI
- To find out differences in use of opioid analgesic in different registered medical practitioners treating AMI
- To promote the rationale use of Opioid analgesic in the treatment of pain of acute myocardial infarction.

Materials and methods

The survey was planned to interview registered medical practitioners from Maharashtra state to document the pattern of use of analgesics in the treatment of pain in Acute Myocardial Infarction.

- The registered medical practitioners qualified in modern medical sciences (MBBS, MD & super specialist) and those who were already treating patients of AMI were included in the survey.
- Practitioners from alternative medicine, unregistered, and those who were not involved in treatment of AMI were excluded from the survey.

- One hundred and twenty two trained, willing medical personale acted as interviewers.
- Interviews were conducted and samples were obtained from Mumbai, Poona, Nashik, Aurangabad, Dhule, Jalgoan (Khandesh), Ahmednagar districts of Maharashtra.

Interviewers recorded the following through a questioner:

- Name of the analgesic used in the treatment of pain in AMI by the RMP in his/ her routine clinical practice.
- Dose, route and frequency of use of analgesics
- According to medical practitioner, the analgesic of choice in AMI (drug of choice as an analgesic in AMI)
- Reason for using the above analgesic mentioned
- Medical Practitioners name, address, qualification, and signature with the stamp of hospital or clinic were obtained for authentication of information

Observations and Results

Total 976 medical practitioners were interviewed out of which 668 fulfilled the criteria fixed for the study survey. Rest were not included (thus n=668). Data was pooled and following observations were recorded.

1. The various analgesics used in clinical practice by medical practitioners of different status in treatment of pain of Acute Myocardial Infarction: (Table-1)
2. Region wise distribution of analgesics used in clinical practice by medical practitioners of different status in treatment of pain of Acute Myocardial Infarction: (Table-2)
3. The Drug of choice according to 53% registered medical practitioners (RMPs) in the treatment of pain of acute myocardial infarction was Morphine and 25% RMPs were in favour of Pentazocine. While Buprenorphine, Tramadol and Pethidine was the drug of choice for 9%, 7%, & 6% medical practitioners respectively.

Discussion

In the present study Morphine remained the drug of choice as an analgesic in the treatment of pain of AMI. Due to nonavailability of Morphine, as Morphine comes under restricted drugs and has narcotic code other analgesics are preferred like Pentazocine, Buprenorphine, Meperidine etc ^[3].

The present survey revealed surprisingly highly significant use of Pentazocine by 55.24% of registered medical practitioners in their clinical practice for the treatment of pain of AMI. This is not desirable as it is well documented that the use of Pentazocine as an analgesic in the treatment of pain due to AMI should be strictly avoided. ^[5, 6]

Pentazocine acts as a weak antagonist or a partial agonist at 'mu' receptor while it is agonist at Kappa. Pentazocine increases systemic and pulmonary arterial pressure, left

Table-1 Analgesics used by Medical Practitioners

Analgesic	General Practitioners	M.D. Medicine	Cardiologists	Total
Pentazocine	66	269	34	396 (55.24%)
Tramadol	08	45	09	62 (9.28%)
Pethidine	23	47	04	74 (11.08%)
Buprenorphine	22	51	25	98 (14.56%)
Morphine	17	17	10	44 (6.59%)
Others (Methadone, Fentanyl, etc)	06	08	07	21 (3.14%)
Total	142 (21.25%)	437 (65.42%)	89 (13.32%)	668

Table-2 Region wise distribution of analgesics used in AMI

Analgesic	Nashik	Poona	Aurangabad	Ahmednagar	Mumbai	Jalgaon	Total
Pentazocine	32	65	25	33	152	62	369 (55.24%)
Tramadol	11	6	8	11	21	5	62 (9.28%)
Pethidine	13	36	6	1	15	3	74 (11.08%)
Buprenorphine	1	19	7	21	40	10	98 (14.57%)
Morphine	0	10	2	7	25	0	44 (6.59%)
Others	0	5	0	1	15	0	21 (3.14%)
Total	57 (8.53%)	141(21.1%)	48 (7.19%)	74 (11.08%)	268 (40.12%)	80 (11.97%)	668

ventricular filling pressure, systemic vascular resistance, systolic and diastolic dimensions. Pentazocine decreases left ventricular ejection fraction and mean velocity of circumferential fiber shortening. These deleterious actions of Pentazocine appear due to peripheral vasoconstriction and negative inotropic properties. Thus Pentazocine increases peripheral as well as total systemic resistance and lowers cardiac index, it also increases pre and afterload along with oxygen demand. [6, 7, 8, 9]. All these can exacerbate myocardial ischemia in patients with AMI. [10]

Although opioid pharmacotherapy has been used for severe pain of AMI, not much research in the development of new opioid has translated into clinical practice. Probably because opioid pharmacotherapy has not been an integral part of mainstream medical practice [11]. However some authors in literature promotes the replacement of the hazardous Pentazocine as an analgesic in the treatment of AMI by the agonist antagonist opioids such as Butorphanol, Nalbuphine, and Buprenorphine. [12]

It has been mentioned in many studies that Buprenorphine is safe for use in pain therapy of patients with acute coronary heart disease. [13] Buprenorphine is described as mixed agonist antagonist acting mainly as partial agonist at mu receptors with some antagonistic activity at Kappa. Buprenorphine is used in some centers as an alternative to Morphine [13], since Buprenorphine is 25 – 50 times more potent than Morphine [6]. It produces more pain relief than

Morphine and appears to have longer duration of action, than both Morphine and Pethidine [14, 15].

Patient's subjective feelings also favor Buprenorphine than Morphine [16]. Buprenorphine has no narcotic code and can be administered by intermittent intravenous injection whereas Morphine requires special handling as a restricted drug and has to be administered as continuous intravenous infusion for better pain relief [3]. Buprenorphine has no effect over left atrial pressure and cardiac output. It has no effect on myocardial contractility as assessed by stroke volume, cardiac work and left ventricular force of contraction. Changes in systemic circulation are such as to possibly decrease the contractile effort, the oxygen need of left ventricle, and the size of infarction in patients presenting with myocardial infarction. [9] Buprenorphine has been shown to be safe and more potent than Pentazocine. [17].

Recent study of Keith J et al on opioids receptors and myocardial protection states the following salient features [18]

- In an *in vivo* rat model of AMI, opioid receptor stimulation has been observed to result in a reduction in infarct size similar to ischemic preconditioning and was due to involvement of myocardial ATP – Sensitive potassium channel (K_{ATP}). Further it was suggested that opening of K_{ATP} channel may be an endogenous protective mechanism in humans also.
- Opening of K_{ATP} channel is differentially involved in antinociceptive effects of some opioids including Buprenorphine, Morphine and Methadone but not in others such as Pentazocine, Fentanyl or Levorphanol.

- On the basis of analysis of these *in vivo* data, it was speculated that Buprenorphine possesses previously unrecognized beneficial cardioprotective effects in patients including those undergoing bypass surgery and those experiencing an AMI.
- Importantly data from antinociceptive studies indicated that differences have existed between opioids for antinociception with Buprenorphine having greatest cardioprotective potential while in contrast Pentazocine having least or no cardioprotective potential.
- Further it has been reported that Buprenorphine at doses that induce antinociception also provides protection against myocardial ischemia.

Conclusion

Morphine is the drug of choice in treatment of Acute Myocardial Infarction pain but Pentazocine is the most commonly used analgesic in clinical practice.

In view of the aforementioned beneficial pharmacological actions of Buprenorphine & detrimental adverse reactions of Pentazocine in the management of pain in AMI. We promote the use of safer & cardio protective opioid analgesics like Buprenorphine

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