Section: Anaesthesiology

Original Research Article

EFFICACY OF SUSTAINED RELEASE MORPHINE AND IMMEDIATE RELEASE MORPHINE FOR TREATMENT OF CANCER PAIN: A COMPARATIVE STUDY

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Abstract

Background: Pain is one of the most common and troublesome symptoms affecting patients with cancer. A lack of effective pain control can adversely affect treatment outcomes and quality of life. According to current NCCN guidelines, opioids are recommended for the management of cancer-related pain, in combination with other analgesics. Immediate-release morphine formulations must be given every 3-4hrs' to maintain adequate pain control. This results in interruption of sleep and inconvenience for the patient, and the potential for noncompliance and medication error. Extended-release formulations are preferred now due to the numerous potential advantages, such as convenient dosing schedules, sustained analgesia and uninterrupted sleep. The dose intervals recommended for these formulations vary from 8 or 12 to 24 hours. **Materials and Methods:** A Prospective Randomized Comparative Study was conducted in Department of Anaesthesiology and Critical Care. A sample size of 24 patients was taken. All patients included in the study were divided into 2 groups after titration. **Result:** On day 1, the titration of the drug dosing was done with Inj. Morphine for 24 hours to calculate oral dose of immediate release morphine. Each patient received either (a) SR morphine tablets or (b) IR morphine tablets. • IR dose = 24-hour oral dose of morphine / 6 (4 hourly dosing for 24 hours to the nearest approximate value) • SR dose = 24 hour dose of oral morphine / 2 (12 hourly dosing for 24 hours to nearest approximate value). **Conclusion:** A twice-daily regimen of SR-morphine is as effective as 4- hourly IR morphine regimen for the control of chronic severe cancer pain.

INTRODUCTION

Pain is one of the most common and troublesome symptom affecting patients with cancer.[1,2] Although effective pain relief can be achieved in up to 90% of patients with cancer,[2] numerous studies have shown pain remains inadequately controlled in many patients with cancer.[2,3] A lack of effective pain control can adversely affect treatment outcomes and quality of life.[4]The current National Comprehensive Cancer Network (NCCN) guidelines for the management of cancer-related pain in adults consider severe uncontrolled pain to be a medical emergency requiring immediate assessment and treatment.[5] According to current NCCN guidelines, opioids are recommended for the management of cancer-related pain, potentially in combination with other analgesics, NSAIDs or acetaminophen. Morphine is considered as prototype of all pure mu agonist opioids used for the management of severe pain. Oral morphine is available in both immediate release and extended-release formulations. Treatment with an immediate release oral formulation of morphine can relieve chronic pain from cancer in the majority of patients.[6] Immediate-release morphine formulations must be given every 3-4hrs' to maintain adequate pain control. This results in interruption of sleep and inconvenience for the patient, and the potential for noncompliance and

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medication error.[7] Extended-release formulations are preferred these days due to the numerous potential advantages, such as convenient dosing schedules, sustained analgesia and uninterrupted sleep.[8,9] The dose intervals recommended for these formulations vary from eight or 12 to 24 hours. We hypothesize that sustained-release morphine provides the similar pain relief as immediate-release morphine.

MATERIALSANDMETHODS

A Prospective Randomized Comparative Study was conducted in Department of Anaesthesiology and Critical Care. A sample size of 24 patients was taken for a study duration of 18 months.

Inclusion Criteria

1. Patients 19- 60 years of age undergoing treatment for cancer with moderate to severe pain
2. Analgesic regimen ≥ 60mg/day of orally given morphine
3. Life expectancy < 6 months

Exclusion Criteria

1. Patient refusal for consent.
2. Chemotherapy or radiotherapy that didn't allow accurate dose titration of morphine
3. Impaired bowel mobility or intractable vomiting
4. Inability to swallow whole capsule
5. History of respiratory depression
6. History of allergy to proposed/used drugs in the study
7. Patients with multiple organ failure
8. Inability to comply with protocol.

After approval of Institutional Ethical Committee. Informed written consent was taken from all patients included in the study and they were divided into 2 groups after titration. On day 1, the titration of the drug dosing was done with Inj. Morphine for 24 hours to calculate oral dose of immediate release morphine.

Oral dose of morphine = 3 x total intravenous dose of morphine over 24 hours

The patients were allocated into two groups S and I using closed envelope technique.

- GROUP S: sustained release
- GROUP I: Immediate release

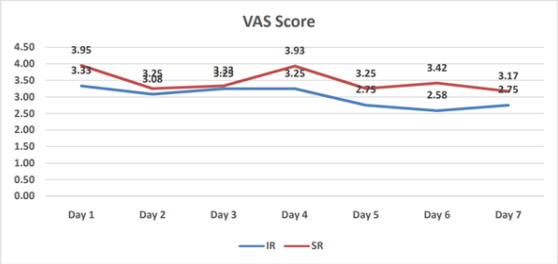
The first 12 envelopes were categorized as Group I and the following 12 envelopes were categorized as Group S.Each patient received either (a) SR morphine tablets or (b) IR morphine tablets. • IR dose = 24 hour oral dose of morphine / 6 (4 hourly dosing for 24 hours to the nearest approximate value) • SR dose = 24 hour dose of oral morphine / 2 (12 hourly dosing for 24 hours to nearest approximate value)

Each group received either SR or IR formulations for a period of 1 week During this study, patients continue to receive their regular pre-study regimen of non-opioid drugs {Tab PCM 500mg TDS, Tab Gabapentin 300mg OD (day 1) 300mg BD (day 2) and 300mg TDS (day 3), Syrup Cremaffin 2tsf HS, Tab Ondansetron, Tab Pantoprazole, Tab Cetrizine (if itching occurs)}.

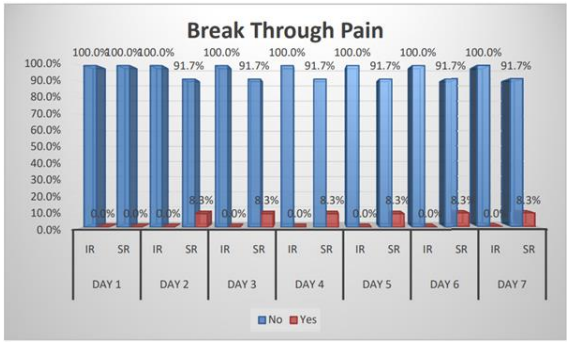
For any episode of breakthrough pain, oral IR morphine (1/6th of the daily dose of oral morphine) was prescribed to the patient. If any patient required more than 2 doses of IR morphine for breakthrough pain, he/she was excluded from the study. The incidences of breakthrough pain per patient day were recorded. Patients were given a chart to mark the daily dose of IR morphine required for any episodes of breakthrough pain according to him and were asked to bring the same at the end of 7 days for assessment.

RESULTS

During the follow up period of 7 days, Mean pain score as computed using VAS scale was comparable between both instant and sustained release morphine groups (p>0.05).Mean VAS score comparison among study groups.



VAS Score	Group	N	Mean	SD	p- value
Day 1	IR	12	3.33	0.89	0.09
	SR	12	3.95	0.97	
Day 2	IR	12	3.08	0.67	0.72
	SR	12	3.25	1.42	
Day 3	IR	12	3.25	1.14	0.89
	SR	12	3.33	1.92	
Day 4	IR	12	3.25	1.29	0.08
	SR	12	3.93	1.61	
Day 5	IR	12	2.75	0.62	0.24
	SR	12	3.25	1.29	
Day 6	IR	12	2.58	0.51	0.06
	SR	12	3.42	1.31	
Day 7	IR	12	2.75	0.45	0.34
	SR	12	3.17	1.40	



During the period of 7 days of follow up, a single patient complained of break through pain in sustained release morphine group while none of the

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patients had similar complaints in instant release morphine group (p>0.05).

Day	Group	Break Through Pain				p-value
		No		Yes		
Day 1	IR	12	100.0%	0	0.0%	NA
	SR	12	100.0%	0	0.0%	
Day 2	IR	12	100.0%	0	0.0%	1.00
	SR	11	91.7%	1	8.3%	
Day 3	IR	12	100.0%	0	0.0%	1.00
	SR	11	91.7%	1	8.3%	
Day 4	IR	12	100.0%	0	0.0%	1.00
	SR	11	91.7%	1	8.3%	
Day 5	IR	12	100.0%	0	0.0%	1.00
	SR	11	91.7%	1	8.3%	
Day 6	IR	12	100.0%	0	0.0%	1.00
	SR	11	91.7%	1	8.3%	
Day 7	IR	12	100.0%	0	0.0%	1.00
	SR	11	91.7%	1	8.3%	

DISCUSSION

We thus conclude that both immediate and sustained release (IR and SR) morphine provide effective pain control. There was no significant difference between morphine preparations in overall pain scores or in incidence of break through pain during the therapy. However, incidence of most of the associated adverse reactions like Nausea/ vomiting, sedation, confusion, constipation and decreased appetite was observed to be more with immediate release formulation.

CONCLUSION

In conclusion, a twice-daily regimen of SR-morphine is as effective as 4- hourly IR morphine regimen for the control of chronic severe cancer pain.

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