IRA-International Journal of Applied Sciences
ISSN 2455-4499; Vol.04, Issue 02 (2016)
Institute of Research Advances
Pg. no. 264-274
http://research-advances.org/index.php/IRAJAS

Morphine Use in Domiciliary Care under Supervision of Palliative Cancer Clinic in a Medical College: A Demographic Study

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Type of Review: Peer Reviewed.
DOI: http://dx.doi.org/10.21013/jas.v4.n2.p7

How to cite this paper:
Chakrabarty, A., Dasgupta, P., Choudhury, K., Chakrabarty, K., Roy, B., Choudhury, D., & Das, V. (2016). Morphine Use in Domiciliary Care under Supervision of Palliative Cancer Clinic in a Medical College: A Demographic Study. *IRA-International Journal of Applied Sciences* (ISSN 2455-4499), 4(2), 264-274. doi:http://dx.doi.org/10.21013/jas.v4.n2.p7

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Literature search	✓			✓	✓	✓	✓
Clinical studies	✓		✓	✓		✓	✓
Experimental studies		✓	✓		✓	✓	✓
Data acquisition		✓	✓	✓	✓	✓	✓
Data analysis	✓	✓	✓			✓	✓
Statistical analysis				✓			
Manuscript preparation	✓	✓	✓	✓	✓	✓	✓
Manuscript editing	✓	✓	✓	✓	✓	✓	✓
Manuscript review	✓	✓	✓	✓	✓	✓	✓
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ABSTRACT

AIMS and OBJECTIVES:

Morphine, a government controlled drug, is not readily available in India. The myths of morphine, especially respiratory distress at high doses has restricted the use to low suboptimal doses in both hospitals and in domiciliary set ups. The present study was done to determine the demographic profiles for patients treated with morphine on domiciliary care under the supervision of medical college palliative care centre.

MATERIAL and METHODS:

A prospective longitudinal study was performed among patients attending palliative clinic at tertiary care hospital. Raised intracranial tension, severe respiratory distress with history of uncontrolled COPD, bronchial asthma with severe lung impairment and renal and hepatic impairments were contraindications to morphine prescriptions.

RESULTS:

During October, 2013 to March, 2016, 523 patients were started on oral morphine after fulfilling the requirements of pain treatment protocol. In 48.2% of male patients head and neck (32.1%) and lung (27.8%) and in females patients cervical cancer(36.2%) and breast cancer at 33.2% were most common malignancies. 31.7% of patients had evidence of metastases. Palliative radiation was used in 37.3% patients. 19.3% patients had no use of opioids at the time of recruitment which meant that they were started at level WHO ladder step3 on oral morphine directly for control of severe pain. Codeine and tramadol were commonly used opioids either in single drug formulations or in combinations with NSAIDS. Commonly used NSAIDS were ibuprofen (400 -600 mg, QDS) , diclofenac (60mg, QDS) and paracetamol (500mg-1gm, QDS). 15.1% of patients had morphine threshold below 75 mg /day while 26.27% patients had dose in excess of 150 mg/day. None of the patients received dose > 300mg OME according to AQA. Adverse events were not significantly different among the 3 groups of patients.

CONCLUSION:

Morphine availability still remains a problem and training of health personals pertaining to cancer pain treatment and domiciliary morphine use should be mandatory.

KEYWORDS: Morphine, Oral Domiciliary use, Palliative care.

CONFLICT OF INETERST: NIL.

INTRODUCTION:

Pain management in Indian scenario for malignant and non-malignant patients are still beyond the scope of majority of patients and remains largely accessible at tertiary cancer centres and handful of dedicated hospice and palliative institutes.[1] The reasons are diverse ranging from poor socioeconomic conditions and poor compliance onus of which lies with patients, to logistics problem of hospitals, non availability of designated palliative and hospice centres and many more.[2-4] Pain management in oncology is integrated interface among oncologists, anaesthetists, and dedicated palliative care physicians, surgeons, nursing staff, non-government organizations and family members. With an ever increasing number of malignant patients being diagnosed every year, majority present in stage 3 / 4 disease, i.e requiring palliative care at onset. Analgesics and adjuvant drugs are

used according to WHO Pain Ladder which is an integral part of palliative care.[5] Opioids range from low dose codeine to intermediate tramadol to morphine. Non-morphine opioids are readily available, relatively costly and in combinations with non opioid analgesics. Morphine, a government controlled drug, is available only at designated hospitals and government approved licensed medical shops against prescriptions of registered medical practitioners.[6] So use of this drug has largely remained elusive to many patients and physicians. The myths of morphine, especially respiratory distress at high doses has restricted the use to low suboptimal doses in both hospitals and in domiciliary set ups. [7] The present study was done to compile the demographic profiles for patients treated with morphine on domiciliary care under the supervision of palliative care centre in a medical college.

MATERIALS AND METHODS:

A prospective longitudinal study was performed between October, 2013 to March, 2016 among patients attending palliative clinic at tertiary care hospital. The palliative care team comprised of radiation oncologists, anaesthetists working with pain clinic, surgeons, a nurse, social workers and a psychologist. The patients recruited in the study were suffering from biopsy or cytology proven malignant conditions with known primary or unknown primary, irrespective of age, all stages, morphine naive, with no known contraindication to morphine and either capable of self care and or under supervision of responsible family member. Raised intracranial tension, severe respiratory distress with history of uncontrolled COPD, bronchial asthma with severe lung impairment and renal and hepatic impairment were contraindications to morphine prescriptions. [8, 9] All patients recruited in study would have to comply with standard guidelines for analgesics prescription.

On day 1, at the palliative clinic, “morphine naive patients” and responsible care givers were interviewed. The data were tabulated in predesigned excel chart, which included patients’ case history details and specific inputs on analgesics like NSAIDs, non-morphine opioids, and adjuvants. For patients receiving codeine, tramadol prior to recruitment in study, conversion to oral morphine equivalent (OME) was done by “Equianalgesics Opioid Conversion tables”.[10] The drug was prescribed after obtaining necessary licence from Narcotic department through our hospital authorities. All patients were asked to take first dose of oral morphine on Day 1 in front of physicians and vital signs were monitored for 1 hour to detect like idiosyncratic respiratory suppression. Telephonic conversions were used to communicate for weekly review of pain, adverse events and any additional data. Patients were re-assessed at monthly intervals. “Visual Analog Scale” was used for pain at the beginning and during the study period, however because the treatment comprised of palliative radiation, surgery and polypharmacy, no score was used in statistical analysis for correlation of opioid dose and pain relief. While Edmonton classification is generally used for stratification of maximum total daily morphine dose usage, we had stratified our patients into 3 groups based on Analgesic Quantification Algorithm (AQA) for use of strong opioids: Group A (≤<75mg/day), Group B (> 75 - 150 mg/day) and Group C(> 150 -300 mg/day) of Oral Morphine Equivalent (OME) for statistical analysis.

RESULTS:

During October, 2013 to March, 2016, 523 patients were started on oral morphine after fulfilling the requirements of pain treatment protocol. 48.2% of patients were males, in whom the most common cancers were head and neck (32.1%) and lung (27.8%) malignancies. This largely reflects the widespread use of tobacco smoke and tobacco containing chewing elements which remains a large scale public health inspite of anti-tobacco drive by government of India. In 51.8% females patients

cervical cancer still predominated as most common cancer (36.2%) followed by breast cancer at 33.2%. (Table 1) 71.9% of patients had evidence of metastases with majority having both bone and visceral involvements (166/523). Palliative radiation (20Gray in 5 fractions, 30Gray in 10 fractions or single fraction of 8Gray) was used in 37.3% patients for bone metastasis, brain metastases, cord compression and superior venal caval obstruction syndrome. 19.3% patients had no use of opioids at the time of recruitment which meant that they were started at level WHO ladder step3 on oral morphine directly for control of severe pain. Codeine and tramadol were commonly used opioids either in single drug formulations or in combinations with NSAIDS. (Table 2) Commonly used NSAIDS were ibuprofen (400 -600 mg, QDS) , diclofenac (60mg, QDS) and paracetamol (500mg-1gm, QDS). 15.1% of patients had morphine threshold below 75 mg /day while 26.27% patients had dose in excess of 150 mg/day. (table 3) None of the patients received dose > 300mg OME according to AQA. "Breakthrough pain dose" was prescribed in all patients, however only 60% of the patients followed the advice. None of the patients had respiratory repression after first dose. The adverse events were not significantly different among the 3 groups of patients. (table 4)

DISCUSSION:

The present day health problems in India are shifting from acute illness to chronic illness like cardiovascular diseases, diabetes, cancer, mental diseases and road traffic accidents. The estimated new cancer cases are likely to cross 17.3 lakhs with 8.8 lalkh deaths in 2020. [11] Inspite of cancer detection and awareness, still 80% of patients would be diagnosed in advanced stages.[12] For majority of these subset of population palliative care might just the appropriate intervention available. Palliative care as defined by World Health Organization in 2006 is "is an approach that improves the quality of life of patients and their families facing problems associated with life threatening illness." [13] Palliative care comprises of early detection and assessment and management of pain and other problems of spiritual, physical and psychosocial magnitude. Pain was defined way back in 1979 derived from concept of Harold Merskey (1964) by International Association for the Study of Pain (IASP) as "unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage".[14] Even for patients treated with curative intent pain is often an initial symptom and pain management is based on same principles of WHO Ladder combined with definitive curative treatment. Pain is divided into 2 categories: a)physiologic pain and b) pathologic pain. Cancer "pathologic" pain is further divided into neuropathic, somatic and visceral subtypes. It is very difficult to distinguish the subtypes as considerable overlaps a classic example of which is cord compression due vertebral body metastases. In our study due logistic problems of arranging nerve conduction velocity tests for all patients, distinguishing among pain subtypes was not possible and hence omitted from the data analysis.

Morphine use in cancer patients treated with palliative care has always been an under-reported in India. In an article published in 2009 by *Barathi et.al*, internal auditing on use of oral morphine for management of severe pain in 20 patients concluded that training of doctors and nurses significantly improved the quality of pain control. The author was of opinion that "breakthrough pain management" was an important integral part of morphine dosage and both nurses and doctors were reluctant to use this for fear of overdosing patients might lead to respiratory distress, harm kidneys and cause addiction.[15] In our study similar problems existed because of logistic issues as well as non-compliance of the patients. *Bercovitch et.al* in a retrospective study on 435 patients on "home-care hospice service" concluded adverse effects were similar with good safety profile in the three groups receiving regular (5-299 mg of morphine per day), high (300-599 mg of morphine per day), and very high doses (≥600 mg of morphine per day). The authors concluded domiciliary use of ≥ 300

mg morphine doses was safe and does not adversely affect the patients' life expectancy, hospice team should not be apprehensive of adverse events.[16]

CONCLUSIONS:

Drawbacks of the study were 1) pain score was not used in statistical analysis, 2) subset analysis of role of morphine for relief in neuropathic and visceral pain was not available because it was difficult to distinguish between them, and 3) due to logistic problems it was not possible for assessing the patients at OPD frequently for dose modifications. Morphine remains the ultimate analgesic for terminally ill cancer patients suffering from severe pain. With no ceiling effect or optimum schedule for morphine dosage, all health personals remain cautious when prescribing the drug.[17] Our experience from a tertiary medical college definitively goes on to prove that high dose morphine use is safe and efficacious even when used in domiciliary setting control cancer pain.

REFEERENCES

1. McDermott E, Selman L, Wright M, Clark D. Hospice and palliative care development in India: A multimethod review of services and experiences. J Pain Symptom Manage. 2008;35:583–93.
2. Rajagopal MR, Joranson DE, Gilson AM. Medical use, misuse, and diversion of opioids in India. Lancet.2001;358:139–43.
3. Rajagopal MR, Venkateswaran C. Palliative care in India: Successes and limitations. J Pain Palliat Care Pharmacother. 2003;17:121–8.
4. Rajagopal MR. Access to palliative care: insights into ground realities post-2014 amendment to NDPS Act. *Indian J Med Ethics*. 2016;NS1(1): 25-30.
5. Gordin V, Weaver MA, Hahn MB. Acute and chronic pain management in palliative care. Best Pract Res Clin Obstet Gynaecol. 2001;15:203-34.
6. The Narcotic Drugs and Psychotropic Substances Act,1985 [Internet]. Narcotic Control Bureau: Government of India; Available from: http:// narcoticsindia. nic.in / legislations.php/NDPS Act, 1985.pdf. [Last accessed in 2016 June 8].
7. Bosnjak S, Maurer MA, Ryan KM, Leon MX, Madiye G. Improving the availability and accessibility of opioids for the treatment of pain: The International Pain Policy Fellowship. Support Care Cancer 2011;19:1239-47.
8. Sinatra R.S, Jonathan S.J, J. Michael W.P. The Essence of Analgesia And Analgesics. Cambridge, UK: Cambridge University Press, 2011, Print.
9. Rowe, A. H, Rowe, A. Bronchial asthma in adults—Causes and Treatment. California Medicine. 1950:72(4):228–33.
10. https://www.nhms.org/sites/default/files/Pdfs/Opioid-Comparison-Chart-Prescriber-Letter-2012.pdf.
11. http://www.mid-day.com/articles /over-17-lakhs-new-cancer-cases-in-India-by-2020-icmr/17248152.
12. Nair M. Krishnan, Varghese C, R. Swaminathan. "Cancer: current scenario, intervention strategies and projections for 2015." *NCHM Background papers-Burden of Disease in India.* 2005:219-25.
13. Definition of palliative care. Available from www.who.int/cancer/palliative/definition/en/. [last accessed on 2016, 23rd July.]
14. Definition of palliative care. Available from International Association for the Study of Pain/ Welcome to IASP.

15. Barathi B. Oral Morphine Prescribing Practices in Severe Cancer Pain. *Indian Journal of Palliative Care*. 2009;15(2):127-31.
16. Bercovitch M, Adunsky A. Patterns of high-dose morphine use in a home-care hospice service: should we be afraid of it? Cancer. 2004;101(6):1473-7.
17. Morphine in cancer pain: modes of administration. Expert Working Group of the European Association for Palliative Care. *BMJ : British Medical Journal*. 1996;312(7034):823-26.

(Tables & Figures)

Table 1. Demographic profile comparisons of patients receiving oral morphine (10mg)

Demographic profiles		Morphine dose stratification (based on AQA)					
		<75mg/day (N=79)		75-150 mg/day (N=388)		>150-300mg/day (N= 106)	
		N	%	N	%	N	%
GENDER	*Males (N=252)*	39	15.5%	173	68.7%	40	15.9%
	Females (N=271)	40	14.8%	165	60.9%	66	24.4%
AGE (in years)	*Mean ± S.D*	46.87 ± 12.57		46.81 ± 11.63		46.29 ± 12.30	
	Median	45.00		49.00		46.00	
	Range(Min, Max)	23,68		23,69		23,68	
MARITAL STATUS	*Married*	69	14.7%	298	63.5%	102	21.7%
	Unmarried	10	18.5%	40	74.1%	4	7.4%
RURAL – URBAN	*Rural*	46	15.2%	195	64.4%	62	20.5%
	Urban	33	15.0%	143	65.0%	44	20.0%
PRIMARY SITES	*Breast*	12	13.3%	54	60.0%	24	26.7%
	Head and Neck	14	12.6%	74	66.7%	23	20.7%
	Lung	17	20.5%	53	63.9%	13	15.7%
	Cervix	16	16.3%	57	58.2%	25	25.5%
	Gastrointestinal	3	11.5%	18	69.2%	5	19.2%
	Prostate	4	10.8%	28	75.7%	5	13.5%
	Others	13	16.7%	54	69.2%	11	14.1%
METASTASES	*Bone*	8	10.1%	58	73.4%	13	16.5%
	Visceral	21	16.0%	86	65.6%	24	18.3%
	Both	28	16.9%	104	62.7%	34	20.5%
	Nil	22	15.0%	90	61.2%	35	23.8%

Table 2. Opioids use among patients at the start of study								
Opioids use among patients at the start of study		Morphine dose stratification						P value
		<75mg/day		75-150 mg/day		>150-300mg/day		
		N	%	N	%	N	%	
OPIOIDS	No opioids	14	17.7%	65	19.2%	22	20.8%	0.539
	Codeine	37	46.8%	174	51.5%	59	55.7%	
	Tramadol	28	35.4%	99	29.3%	25	23.6%	
ADJUVANTS	Steroids	21	26.6%	103	30.5%	23	21.7%	0.500
	Antiepileptics	19	24.1%	81	24.0%	27	25.5%	
	Antidepressants	21	26.6%	77	22.8%	34	32.1%	
	All	18	22.8%	77	22.8%	22	20.8%	
PALLIATIVE RADIATION	Yes	27	34.2%	128	37.9%	40	37.7%	0.825
	No	52	65.8%	210	62.1%	66	62.3%	

Table 3. Maximum daily dose of morphine (10mg formulation P.O)						
MORPHINE DOSE STRATIFICATION	N	Mean	Std. Deviation	Median	Minimum	Maximum
<75mg/day	79	56.08	9.187	50.00	40	70
75-150 mg/day	338	104.64	18.247	100.00	80	150
>150-300mg/day	106	187.17	31.915	170.00	160	260
Total	523	114.03	45.652	100.00	40	260

Table 4. Complication rates stratified according to maximum dose of oral morphine								
CTCAEv4 adverse events		Morphine dose stratification						P value
		<75mg/day (N=79)		75-150 mg/day (N=388)		>150-300mg/day (N= 106)		
		Count	N %	Count	N %	Count	N %	
CONSTIPATION	*G0*	15	19.0%	80	23.7%	20	18.9%	0.280
	G1	48	60.8%	157	46.4%	49	46.2%	
	G2	13	16.5%	83	24.6%	30	28.3%	
	G3	3	3.8%	18	5.3%	7	6.6%	
NAUSEA VOMINTING	*G0*	32	40.5%	124	36.7%	40	37.7%	0.956
	G1	31	39.2%	130	38.5%	43	40.6%	
	G2	16	20.3%	83	24.6%	23	21.7%	
	G3	0	.0%	1	.3%	0	.0%	
FATIGUE	*G0*	48	60.8%	172	50.9%	59	55.7%	0.160
	G1	21	26.6%	134	39.6%	33	31.1%	
	G2	10	12.7%	32	9.5%	14	13.2%	
DIZZINESS	*G0*	63	79.7%	254	75.1%	83	78.3%	0.837
	G1	0	.0%	0	.0%	0	.0%	
	G2	16	20.3%	83	24.6%	23	21.7%	
	G3	0	.0%	1	.3%	0	.0%	
SOMNOLENCE	*G0*	32	40.5%	124	36.7%	40	37.7%	0.956
	G1	31	39.2%	130	38.5%	43	40.6%	
	G2	16	20.3%	83	24.6%	23	21.7%	
	G3	0	.0%	1	.3%	0	.0%	