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Palliative care: Inclusion of pregabalin in the pain management of terminal cancer patients in a national level cancer treatment institute of Nepal

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Abstract

In palliative care, prevention approaches and pain management are used to help terminally ill patients and their family members cope with their sufferings. In terminally ill cancer patients, pain management is considered to be the most important. Cancer patients with neuropathic pain may be effectively treated with adjuvants such as pregabalin.

A retrospective study performed in the palliative care unit of BP Koirala Memorial Cancer Hospital, Nepal emphasizes upon the various patients with different types and stages of cancer with majority having pain as the common and profound symptom, and the inclusion of various drugs including pregabalin in pain management.

While opioids have remained the mainstay of pain management of oncotic patients, a number of patients with neuropathic pain found significant relief from pain after pregabalin was included in the treatment package.

Keywords: Palliative care, cancer, pain, opioids, pregabalin

Introduction

Palliative care is the assimilation of preventive approaches and management of sufferings, in terminally ill patients and their family members facing the problems, with early diagnosis and treatment of physical, psychological, and social problems including pain management. With regards to death as a normal process, it integrates the provision of relief from pain and other distressing symptoms providing a support system to the family and enhancing their quality of life [1].

Treatment focusing on enhancing the quality of life rather than the prolongation of suffering should be sought in patients with a terminal illness. Thus, developed the concept of palliative care by Cicel Saunders as the first hospice devoted in South-East London in 1967 [2]. When curative management of the patients becomes ineffective, the approach should shift to the enhancement of quality of life more than the prolongation of life. Patients with advanced cancer who refuse intensive care management, who pray, have a therapeutic association with their physicians, and who worry less have a better quality of life at the end stage [3].

A good death is linked with patients who are prepared for their death, dying a quick and imminent death, with minimal suffering, and having social relations together [4]. According to WHO, an estimated 40 million people are in need of palliative care with most of them residing in low-and middle-income countries, and only 14% of them receiving the required palliative care. The high level of restrictions on necessary palliative care medications including opioids presents a major problem in implementing palliative care [5].

Among the various approaches to palliative management, pain management is considered the most important issue in terminal patients. The International Association for the Study of Pain (IASP), defines pain as an unpleasant sensory and emotional experience associated with actual or potential tissue damage or is described in terms of such damage [6].

Cancer is one of the leading causes of morbidity and mortality among the population worldwide [7].

More than half of the patients being treated for cancer experience pain with the proportion rising to more than two-thirds in the people at an advanced stage, metastatic lesions, or in the terminal phase [8].

WHO originally recommended a three-step pain ladder management?

1. For mild pain: Non-opioid analgesics (Non-steroidal anti-inflammatory drugs (NSAIDs) or acetaminophen) with or without adjuvants
2. For moderate pain: Weak opioids (hydrocodone, codeine, tramadol) with or without non-opioid analgesics, and with or without adjuvants
3. For severe and persistent pain: Potent opioids (Morphine, methadone, fentanyl, oxycodone, buprenorphine, tapentadol, hydromorphone, oxymorphone) with or without non-opioid analgesics, and with or without adjuvants [9].

Experts however suggest against the use of weak opioids, as the second step in pain management, due to their limited effect in pain management and the use of potent opioids in lower dosages for moderate pain [10]. Opioids are the mainstay in the management of pain in cancer patients. But patients usually develop tolerance to the analgesic and central side effects of these drugs like drowsiness, while the peripheral side effects like constipation persist. Incomplete cross-tolerance between the opioids allows the use of other opioids at a lower dosage during significant side effects like constipation, renal failure secondary to particular opioid use, or in-adherence to any opioid. A dose reduction of 25% is recommended while switching to other opioids [11].

According to the International Association for the Study of Pain (IASP), any pain originating or resulting from lesions or defects in the nervous system is neuropathic pain (NP) [12].

Adjuvants or co-analgesics are the vast majority of drugs from different classes, although primarily used to treat various medical conditions, are also effective in the treatment of painful conditions. These drugs include tricyclic antidepressants (TCAs) such as amitriptyline and nortriptyline, serotonin-norepinephrine reuptake inhibitors (SNRIs) such as duloxetine and venlafaxine, anticonvulsants like gabapentin and pregabalin, topical anesthetics (e.g., lidocaine patch), topical therapies (e.g., capsaicin), corticosteroids, bisphosphonates, and cannabinoids.

Gabapentin and newer generation pregabalin both inhibit the release of glutamate, norepinephrine and substance P by binding and acting on the $\alpha 2\text{-}\delta$ sub-unit of voltage-gated

Calcium channels. RCTs have demonstrated their effectiveness in neuropathic cancer pain, post-herpetic neuralgia, painful diabetic neuropathy, phantom limb pain, Guillain-Barre' syndrome, and acute and chronic spinal cord injury pain [13].

Pregabalin has a more rapid onset of action on pain relief than gabapentin with a starting dose of 150 mg/day given in divided dosages with benefits seen maximally at the treatment dosage of 300–600 mg/day [14].

Materials and Methods

Patients

A retrospective study approved by Department of Pain and Palliative Care, BP Koirala Memorial Cancer Hospital, Bharatpur, Nepal. The review of records did not require patient approval or required consent.

All the cases admitted for palliative care at this hospital from December 2020 to March 2022 were abstracted from medical record sections in the Hospital based cancer registry of BPKMCH. Patient's name, age, sex, address along with clinical diagnosis, symptoms and drugs used were recorded.

Methods

Data were entered and analyzed using SPSS and relative frequency were obtained.

Results

Age

Mean \pm SD=57.5 \pm 16.5 years (Range=2-93 years)

Age distribution

Table 1: Age distribution

Age group (in years)	Number	Percent
Upto 20	2	.7
21-40	48	16.1
41-60	120	40.3
61-80	104	34.9
More than 80	24	8.1
Total	298	100.0

Table 2: Sex

Sex			
		Frequency	Percent
Valid	FE	152	51.0
	M	146	49.0
	Total	298	100.0

Table 3: Address

Address					
		Frequency	Percent	Valid percent	Cumulative percent
Valid	Arghakhanchi	5	1.7	1.7	1.7
	Baglung	3	1.0	1.0	2.7
	Baitadi	2	.7	.7	3.4
	Bajura	1	.3	.3	3.7
	Banke	2	.7	.7	4.4
	Bara	3	1.0	1.0	5.4
	Bardiya	1	.3	.3	5.7
	Bhojpur	1	.3	.3	6.0
	Chitwan	72	24.2	24.2	30.2
	Dadeldhura	1	.3	.3	30.5
	Dailekh	3	1.0	1.0	31.5
	Dang	1	.3	.3	31.9

	Dhading	1	.3	.3	32.2
	Dhangadi	1	.3	.3	32.6
	Dhanusha	1	.3	.3	32.9
	Gulmi	5	1.7	1.7	34.6
	Ilam	4	1.3	1.3	35.9
	India	10	3.4	3.4	39.3
	Jajarkot	2	.7	.7	39.9
	Jhapa	3	1.0	1.0	40.9
	Jumla	5	1.7	1.7	42.6
	Kailali	5	1.7	1.7	44.3
	Kanchanpur	1	.3	.3	44.6
	Kapilvastu	4	1.3	1.3	46.0
	Kaski	5	1.7	1.7	47.7
	Ktm	1	.3	.3	48.0
	Lamjung	8	2.7	2.7	50.7
	Mahottari	3	1.0	1.0	51.7
	Makwanpur	17	5.7	5.7	57.4
	Morang	10	3.4	3.4	60.7
	Myagdi	1	.3	.3	61.1
	Mygdi	1	.3	.3	61.4
	Nawalparasi	22	7.4	7.4	68.8
	Nuwakot	1	.3	.3	69.1
	Palpa	1	.3	.3	69.5
	Panchthar	1	.3	.3	69.8
	Parbat	4	1.3	1.3	71.1
	Parsa	5	1.7	1.7	72.8
	Pyuthan	3	1.0	1.0	73.8
	Rautahat	12	4.0	4.0	77.9
	Rolpa	2	.7	.7	78.5
	Rupandehi	4	1.3	1.3	79.9
	Sankhuwasava	1	.3	.3	80.2
	Saptari	3	1.0	1.0	81.2
	Sarlahi	20	6.7	6.7	87.9
	Sindhuli	1	.3	.3	88.3
	Siraha	4	1.3	1.3	89.6
	Sunsari	7	2.3	2.3	91.9
	Surkhet	6	2.0	2.0	94.0
	Syanja	6	2.0	2.0	96.0
	Tanahun	10	3.4	3.4	99.3
	Udaypur	2	.7	.7	100.0
	Total	298	100.0	100.0	

Table 4: Diagnosis

Diagnosis		Frequency	Percent
Valid		3	1.0
	Adnexal ca.	1	.3
	Adnexal mass	3	1.0
	Anaplastic thyroid	1	.3
	B/l lung mets	1	.3
	Ca. Base of tongue	1	.3
	Ca. Bm	8	2.7
	Ca. Bm right	1	.3
	Ca. Bot	1	.3
	Ca. Breast	8	2.7
	Ca. Breast with bone mets	3	1.0
	Ca. Breast with liver mets	1	.3
	Ca. Cervix	12	4.0
	Ca. Colon	2	.7
	Ca. Cx	2	.7
	Ca. Fom	2	.7
	Ca. Gb	2	.7
	Ca. Gbm	1	.3
	Ca. Gbs	6	2.0
	Ca. Gej	1	.3
	Ca. Glottis	1	.3
	Ca. Hop	4	1.3
	Ca. Hyopharynx	2	.7

Ca. Left alveolus	1	.3
Ca. Left breast	1	.3
Ca. Left breast with lung mets	1	.3
Ca. Left check	1	.3
Ca. Left conjunctiva	4	1.3
Ca. Left conjunctiva	1	.3
Ca. Left gbm	2	.7
Ca. Left lungs	1	.3
Ca. Left maxilla	2	.7
Ca. Left pfs	1	.3
Ca. Left upper alveolus	1	.3
Ca. Lip	3	1.0
Ca. Lower alveolus	5	1.7
Ca. Lower lip	10	3.4
Ca. Lung	10	3.4
Ca. Lungs	5	1.7
Ca. Lungs with brain mets	2	.7
Ca. Mandible	2	.7
Ca. Maxillia	3	1.0
Ca. Nasopharynx	5	1.7
Ca. Nasophyrnex	1	.3
Ca. Npx	2	.7
Ca. Orbital	1	.3
Ca. Oropharynax	1	.3
Ca. Ovary	1	.3
Ca. Parotid	3	1.0
Ca. Penis	2	.7
Ca. Pfs	4	1.3
Ca. Pfs right	1	.3
Ca. Prenis	1	.3
Ca. Prostate	12	4.0
Ca. Rectum	1	.3
Ca. Right alveolus	1	.3
Ca. Right bm	5	1.7
Ca. Right breast	7	2.3
Ca. Right gbs	2	.7
Ca. Right gbs s	1	.3
Ca. Right lower alveolus	1	.3
Ca. Right lower gbs	1	.3
Ca. Right lung	4	1.3
Ca. Right lungs	1	.3
Ca. Right maxilla	4	1.3
Ca. Right parotid	4	1.3
Ca. Right uretic	2	.7
Ca. Rmt	3	1.0
Ca. Sinonasal	1	.3
Ca. Supraglottis	6	2.0
Ca. Supraorbital	1	.3
Ca. Thyroid	16	5.4
Ca. Tongue	29	9.7
Ca. Ub	4	1.3
Ca. Uretus	1	.3
Ca.bm	1	.3
Ca.cx	1	.3
Ca. gbm	1	.3
Ca. left conjunctiva	1	.3
Ca. lower lip	1	.3
Ca. npx	1	.3
Ca. pfs	1	.3
Ca.prostate with bone mests	1	.3
Chest wall mass	4	1.3
Cystic neoplasm	1	.3
Ewing sarcoma	2	.7
Left check mass	1	.3
Left rcc	4	1.3
Left renal neoplasm	1	.3
Neck mass	2	.7
Neuroblastoma	1	.3

	Nhl	3	1.0
	Ogs	1	.3
	Ogs left humerous	1	.3
	Osteosarcoma	1	.3
	Right rcc	7	2.3
	Sccl left conjunctiva	2	.7
	Sccl left leg	1	.3
	Sccl right temporal region	1	.3
	Sinonasal ca.	2	.7
	Spindle cell ca.	1	.3
	Swelling left check	1	.3
	Vertebral mets	1	.3
	Total	298	100.0

Table 5: Major Symptoms

Symptoms	Number	Percent
Pain	297	99.7
Nausea/vomiting	3	1.0
Anorexia	1	.3
Constipation	3	1.0

Table 6: Medications

Medications	Number	Percent
Tramadol	32	10.7
Morphine pr	246	82.6
Plain mor	251	84.2
Nsaid	185	62.1
Pentoprazole	207	69.5
Amitriptyline	227	76.2
Lactulose	239	80.2
Zoledronic acid	3	1.0
Pregabalin	110	36.9
Antiemetic	26	8.7

Discussion

Palliative care was the concept developed to relieve sufferings in the patient that were terminally ill and at the end stage of life by combining various approaches from the care providers [2]. Pain is one of the important aspects to alleviate in palliative care to provide a good quality of life during the terminal period. Even though palliative care is required in a large population, only a small proportion have the ability to get these cares [5]. Terminal cancer, among the various diseases, requires a well-planned palliative care. Management of pain is challenging among the terminal cancer patients with more than two thirds of them experiencing pain at several scale [8]. Opioids stay the mainstay of pain management in cancer patients. Non-opioids or weak opioids can be used to manage the mild to moderate pain, however the more severe pain requires potent opioids [11]. Opioids can be combined with adjuvants medications to treat the recalcitrant pain that are difficult to manage with opioids alone. The prevalence of neuropathic pain is higher in these patients and agents like pregabalin is included to treat the condition along with other adjuvants [13].

BP Koirala Memorial Cancer Hospital, Bharatpur is a central level hospital of Nepal established as the national referral center for cancer patients. Patients not only from Nepal but also from neighboring countries visit the hospital to seek onco-care. Patients with different and at various stages of cancer get medical care from this hospital. The hospital has a well-managed palliative care division being managed by medical professionals from all the levels. Study was conducted among the patients that were admitted in the

palliative care division and have diverse geographical background. Mostly the patients were in the age of 40-60 years, with pain as a universal symptom. Management of pain was tactical. Opioids stayed the mainstay of management. Inclusion of adjuvant as pregabalin in the treatment package provided significant relief from neuropathic pain in a number of patients. Thus, pregabalin had a crucial role in pain management for oncotic neuropathic pain.

The study could have been more detrimental if was to be conducted to study the pain management among the patients of several health institutions. The study has also its limitations as the expression of pain is differs from individual to individual and is to be monitored and managed relatively. And in the absence of a proper protocol for palliative care and the management varying among the different health care professionals, pain management still has its limitations in this institution.

This study points out the need to formulate a well-defined and more inclusive palliative care protocols with different adjuvant drugs that is required to treat the several debilitating conditions deteriorating the quality of life in the terminal stage of patient.

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