The Prevalence And Management Of Pain In Gynaecological Malignancy Within The Outpatient Setting

J Yen, A Gubbay, S Kandikattu, S Chapman, J Williams

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Abstract

Objectives: Despite pain being a common symptom in gynaecological malignancies there is limited literature on accurate rates of prevalence or current management. Our aim was to investigate these issues to establish integrated pain pathways with our oncology colleagues. This information would also be considered in future research for the development of cancer specific pain pathways.Method: We recorded pain scores from those attending gynaecology outpatient clinics in our tertiary cancer referral hospital. The characteristics of the pain and its management were assessed using the Brief Pain Inventory, the self-assessed Leeds Assessment of Neuropathic Symptoms and Signs pain scale and the Pain Management Index. We also investigated associated risk factors (age, tumor site, cancer treatment types) in presence and severity of pain.Results: Of all patients investigated, 38% were in pain from any cause with 80% of these patients scoring their pain as moderate to severe. Background pain lasted for more than three months in 75% of patients with pain whilst 42% complained of breakthrough pains of similar duration. Just under half of patients in pain suffered from neuropathic involvement. A negative PMI signifying under-treatment was seen in 63% of patients with pain. Surprisingly the most common cause of pain was from non-cancer causes. Over half of patients in pain accepted post-study assistance when offered. We could not identify any associated risk factors.Conclusions: Patients with gynaecological malignancies in the outpatient setting commonly experience pain which is chronic and undertreated. Many also have complicating neuropathies which would benefit from specialist input. We recommend that all patients attending gynaecological cancer outpatient clinics should be routinely assessed for pain to improve cancer management. This information is to be incorporated in future cancer specific pain pathways.

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INTRODUCTION

With advances in anticancer treatment patients with gynaecological malignancy have witnessed an increase in the likelihood of survival yet as a by-product of this success the suffering of pain may continue. This complicates an already well-established incidence within other stages of the disease particularly the incurable phase [1,2]. Pain is often related to the cancer or from its treatments and bears a significant reduction in quality of life [3]. A recent systematic review reported a moderate to severe pain prevalence of 60% in this population but found only six published papers over a 40 year period up to 2007 to quantify this [4]. Other estimations range from 40% to 100% in those with uterine, cervical or ovarian cancers and this lack of accurate prevalence score is surprising given gynaecological malignancies are a common cause of cancer with treatment strategies strongly associated with pain [5,6].

Cancer pain involves mechanisms of inflammation, compression and ischaemia causing a combination of nociceptive, neuropathic and visceral symptoms and this neuropathic component has been adjudged to affect at least one-third of all assessed cancer patients [7,8,9]. Risk factors for cancer pain are also confusing – age [10], gender [11,12], type of cancer [4,13], stage of cancer [14,15,16], presence of metastases [9,14,15,16,17], presence of breakthrough pain and decreased performance status [9] have all been indicated as predictors although none have been fully validated.

The objective of this study was to determine the problem of pain in gynaecological malignancies by measuring prevalence, intensity and severity as well as highlighting the adequacy of its management. The identification of risk factors with a better understanding of breakthrough pain,

neuropathic pain, and the phenomenon of non-malignant pain in cancer patients were also investigated. It is hoped that the study will raise awareness of these issues within this population and facilitate the production of integrated pain treatment pathways with our oncological colleagues.

METHOD

STUDY SETTING

The Ethics Committee of approved the study and it was registered with the Hospital Committee for Clinical Research. Good Clinical Practice Guidelines and recommendations in the Declaration of Helsinki were correctly adhered to [18, 19]

Patients were recruited from gynaecological oncology outpatient clinics from November 2008 to March 2009 at the Royal Marsden Hospital, a large tertiary referral cancer hospital in the United Kingdom. The clinics attended focused on a mixture of medical (radiotherapy and chemotherapy) and surgical treatments.

Patient characteristics

Inclusion criteria for the study were:

Study subjects included patients: i) who had received anticancer treatment (surgery, radiotherapy, and chemotherapy) ii) patients currently receiving anticancer therapy and iii) patients characterised as having advanced/metastatic/terminal disease. The only exclusion criterion was whether the patient's health would be compromised by participation in the study.

RECRUITMENT

Consecutive patients attending any of the Royal Marsden Hospital gynaecological oncology outpatient's clinics were recruited. A week before their outpatient appointment eligible patients were contacted by post or telephone and informed of the study. On the clinic date these patients were approached and if they agreed informed consent was obtained. The screening questionnaire was then filled out by the patient. Members of the research team who assisted throughout the process were independent from hospital clinical staff.

SCREENING TOOLS

The following screening tools were used:

Demographic information. Age, tumour site and treatment history were obtained by access to the patients' electronic records.

Prevalence and aetiology of pain. All patients were asked if they had pain and for their regime of analgesic medication. Patients scoring positive for pain were assessed to determine possible causes, subdividing into pain due to tumour pressure/infiltration, from anticancer treatment or from non-cancer related pain.

Pain assessment. Patients with pain were asked to fill out two validated and reliable self-assessment pain tools; the Brief Pain Inventory (BPI) which is a collection of Visual Analogue Scales (VAS) assessing pain severity and impact on daily function and the self-assessment version of the Leeds Assessment of Neuropathic Symptoms and Signs pain scale (S-LANSS) which uses multiple questions to assess the presence of neuropathic pain [20,21].

Adequacy of pain management. This was assessed using the Pain Management Index (PMI). The PMI is a simple tool to determine if the patient is receiving adequate analgesia for cancer-related pain [22]. It compares the patient's worst score on the BPI to the potency of the prescribed analgesia according to the World Health Organisation (WHO) analgesic ladder [23]. Negative scores indicate inadequate analgesia.

RISK FACTORS

We aimed to determine whether:

POST-STUDY TRACKING

As a pain assessment had been completed as part of the screening process, some patients were offered advice on their pain management. With ethics committee approval and the agreement of the clinicians responsible for the patient, the researcher referred willing patients to the pain team to institute follow up. This could be either a) to give advice and contact details, b) to prescribe appropriate analgesia and/or c) to book an appointment for the patient into their local pain management clinic. When any of these were instigated, a note was made on the patient's questionnaire.

RESULTS AND ANALYSIS

DESCRIPTION OF SAMPLE

Of the 268 eligible patients, 151 patients consented to the study. A total of 117 patients did not participate in the study for various reasons as listed in Table 1. Patients were recruited from a total of 20 outpatient clinics over the five month period; eight medical oncology, two chemotherapy, three radiotherapy and seven surgical clinics. The age range

of the patients was 23-91 years old, with a mean age of 60. The identified sites of the tumours are shown in Table 2.

Figure 1

Table 1. Reasons for non-participating patients

Reason for non-participation	Number of patients
Cancelled appointment	17
Did not attend	14
Refusal	83 (31%)
Incomplete data	3
Total	**117 (of 268)**

Figure 2

Table 2. Identified tumour site

Tumour site	'Any Pain in the last 7 days?'		Total
	No	Yes	
Cervix	13	8	21
Endometrium	18	12	30
Ovary	47	29	76
Vagina	4	0	4
Vulva	2	1	3
Other	10	7	17
			151

PAIN CHARACTERISTICS

PREVALENCE AND SEVERITY

Of the 151 patients surveyed, 57 patients (38%) reported pain due to any cause within the previous seven days. In these patients, the VAS ranged from 2 to 10. A total of 11 patients (7% of 151 patients) reported their pain as mild (VAS score 2-3). Moderate pain (VAS 4-6) was reported in 24 patients (16% of 151 patients), while 22 patients (15% of 151 patients) had severe pain (VAS score 7-10). A total of 46 patients (30% of 151 patients) therefore had moderate to severe pain, i.e. a VAS score of 4 or greater.

CHRONICITY

Out of the 57 patients with pain, 43 (75%) had pain present for more than three months, while the remaining 14 had pain of less than three months.

AETIOLOGY

Pain secondary to anticancer treatments was seen in 16/57 (28%) while tumour-related pain was present in 15 patients (26%). Pain due to non-cancer causes was present in 26 cases (46%) although only four had an appropriate diagnosis; three with musculoskeletal pain, one patient complaining of migraines.

NEUROPATHIC PAIN

The researchers identified 23 patients to have neuropathic pain yet only 12 patients demonstrated accepted criteria for neuropathic pain on the S-LANSS by scoring more than or equal to 12/20. Of these 12 patients one described their pain as mild, four as moderate and seven as severe.

Post-study tracking was performed in nine out of these 12 patients with neuropathic pain; advice and contact details were given to three patients, analgesia was prescribed in one patient while five patients were given an outpatient appointment at the pain management clinic.

BREAKTHROUGH PAIN

Breakthrough analgesic medication was required in 33/57 (58%) patients. Of these, five patients described the need for breakthrough analgesia for longer than seven days, but less than three months. One of the five had had surgery three weeks before his outpatient appointment. These five patients all had some form of post-study tracking with two of them requiring further analgesia and the remaining three booking appointments at the pain management clinic.

The remaining 27 patients (42%) reported to require breakthrough analgesia for more than 3 months.

ADEQUACY OF ANALGESIC TREATMENT

A negative score on the PMI was found in 36/57 patients (63%) suggesting undertreatment in terms of analgesia. Of those that screened positive for neuropathic pain, the PMI showed inadequate analgesia in 23 patients.

RISK FACTORS

Binary logistic regression was used to identify any predictors or risk factors for reporting pain. The variables tested were i) surgery, ii) chemotherapy, iii) radiotherapy, and iv) tumour site. These variables were tested against patients reporting any pain in the previous seven days (Table 3), and against the severity of pain, i.e. comparison of patients with mild/moderate pain versus patients reporting severe pain. (Table 4). There were no statistically significant associations between potential risk factors and the reporting of any pain or the severity of pain.

POST-STUDY SURVEILLANCE

Post-study tracking was carried out in 39/57 (68%) who

complained of pain during the previous seven days. Advice and contact details of the pain team were given to 16 patients while six patients were prescribed analgesia. Pain clinic outpatient appointments were made for 16 patients with one patient advised to liaise with his existing pain service.

Figure 3

Table 3. Risk factors i) – iv) and association with in the previous 7 days. (p-value denoted by * indicates that the Fisher exact test was performed instead due to low sample numbers).

Risk Factor		'Any Pain in the last 7 days?'		Chi-Squared p-value unless indicated by *
		No	Yes	
i) Previous Surgery	No	7	1	
	Yes	87	56	0.26*
ii) Previous Chemotherapy	No	40	22	
	Yes	54	35	0.733*
iii) Previous Radiotherapy	No	73	38	
	Yes	21	19	0.183*
iv) Tumour Site	Cervix	13	8	0.760
	Endometrium	18	12	
	Ovary	47	29	
	Vagina	4	0	
	Vulva	2	1	
	Other	10	17	

Figure 4

Table 4. Risk factors i) – iv) and association with . (p-value denoted by * indicates that the Fisher exact test was performed instead due to low sample numbers).

Risk Factors		Pain Severity		Chi-Squared p-value unless indicated by *
		Mild/Moderate	Severe	
i) Previous Surgery	No	0	1	
	Yes	35	21	0.386*
ii) Chemotherapy	No	13	9	
	Yes	22	13	0.776
iii) Radiotherapy	No	21	17	
	Yes	14	5	0.178
iv) Tumour Site	Cervix	4	4	0.429*
	Endometrium	8	4	
	Ovary	20	9	
	Vagina	0	0	
	Vulva	0	1	
	Other	3	4	

DISCUSSION

Our study has shown that the prevalence of pain in gynaecological cancer is approximately 38% and when the pain is moderate to severe the prevalence is 30%. This is considerably lower than the 60% quoted by van den Beuken-van Everdingen MHJ et al in their systematic review of six similar studies concerning 372 patients with moderate to severe pain (95% CI: 50-71%) [4]. However their studies describe hospice and hospital inpatients with advanced or terminal disease which are strongly associated with cancer related pain [2]. A majority of these studies also focus on a specific tissue type (ovarian or cervical cancer) whereas ours includes all gynaecological malignancy.

A negative PMI was seen in 63% of the patients in pain and this is considerably higher than the 43% in Deandra's review of 26 studies [11]. Although our study takes into account those seeking help from alternative therapies such as acupuncture, massage or shiatsu, it clearly indicates that nearly two-thirds of patients remain undertreated. Research indicates that inadequate treatment leads to huge socioeconomic costs particularly in those of working age [13,24,25,26] as well as an assortment of morbidities ranging from the psychosocial; depression, anxiety [24,27] and poor personal interactions [28], to the physiological; poor sleep [29,30], neuroplasticity, chronic pain syndromes and immune suppression [31]. This will inevitably lead to increased hospitalisations [32].

In an attempt to identify 'at-risk' patients a number of variables were investigated to observe their influence in pain prevalence. Studies with other cancer groups have reported increased pain from radiotherapy, post-surgery, related to the specific tumour type and in those with poorly controlled acute pain [33,34,35,36,37,38]. In our study no positive associations were found between the risk factors and the presence or severity of pain. Conceivably prevalence may be related to other variables which were not assessed but as pain appears unpredictable, it should be anticipated for all cancer patients. Further studies continue to discover any potential associations to pain [39].

Whilst a discrepancy was noted between the researchers and the S-LANSS in the prevalence of diagnosed neuropathy, it was still found that at least a third of patients suffered from this pain, seven of whom were affected severely. Clearly a difficulty in diagnosing this abnormality exists yet this still proves that neuropathic pain is strongly associated with cancer pain and should be considered. Neuropathic pain is best managed with adjuvants such as anticonvulsants and antidepressants though opioids can be used in resistant cases [40].

Interestingly half of our patients' causes of pain were non-cancer related whilst tumour and treatment causes each shared a quarter of the total. This is contrary to literature on cancer pain which has found that around 25% of general oncology outpatients have non-cancer related pain [41]. It is

unclear as to the reason for this discrepancy.

For symptoms to continue for more than three months suggests a shift from an acute to a chronic pathophysiology and this inevitably becomes harder to manage. 75% of our patients complained of pain of more than three months. Additionally 57% of the patients in pain required breakthrough analgesia and just under three-quarters of these patients endured this for more than three months. The presence of breakthrough pain needs to be assessed because it is reported that inadequate management results in reduced function, higher incidences of depression and a need for hospital admission [32,42]. It has a reported prevalence of 65% in other large scale studies and is an indicator of poor prognosis [9,43]. The traditional treatment of breakthrough pain is immediate release formulations of oral opioids however, there is increasing use of oral transmucosal routes to administer opioids [44]. A recent Cochrane review reported that oral transmucosal fentanyl citrate was an effective treatment for breakthrough pain [45].

A significant proportion of our patients with pain wished to be followed up with assessment or advice suggesting that whilst patients may grumble on, when confronted more would accept help. This is important when considering the overall care of the cancer patient. Currently a multimodal approach to cancer pain management is recommended with the use of adjunct pharmacology and a multi-disciplinary team [7].

CONCLUSION

Our findings confirm that a significant number of gynaecological cancer patients suffer with moderate to severe chronic pain that may have some neuropathic involvement and is often undertreated. It is important to systematically enquire about pain so as to commence an appropriate management plan incorporating pain team assistance. Whilst no specific risk factors for developing pain were established further studies are needed in this area. A further study might also assess the value of using a routine screening tool such as the BPI and S-LANSS followed by an immediate treatment protocol.

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Author Information

Jonathan T.C Yen, MB ChB
Advanced pain trainee, Royal Marsden Hospital

Anthony N Gubbay, MB ChB
Pain Research Fellow, Royal Marsden Hospital

Subhash Kandikattu
Advanced pain trainee, Royal Marsden Hospital

Suzanne Chapman, MSc
Clinical nurse specialist, Royal Marsden Hospital

John E. Williams, MBBS
Consultant in cancer related pain management, Royal Marsden Hospital