

Opioid Consumption before and after the Establishment of a Palliative Medicine Unit in an Egyptian Cancer Centre

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Abstract / Opioid consumption before and after the establishment of a palliative medicine unit (PMU) in an Egyptian cancer centre was reviewed. A comparison of consumption during the year before the PMU was established to consumption during the third year after the PMU's establishment revealed that morphine consumption increased by 698 percent, fentanyl by 217 percent, and tramadol by 230 percent. Expressed in defined daily dose (DDD) and adjusted for 1,000 new cancer patients, consumption increased by 460 percent, from 4,678 DDD/1,000 new patients to 26,175 DDD/1,000 new patients. Expressed in grams of oral morphine equivalent (g OME), consumption increased by 644 percent, from 233 g OME/1,000 new patients to 1,731 g OME/1,000 new patients. The establishment of the PMU was associated with an increase in opioid consumption, especially morphine, which is an indicator of improvement in cancer pain control. The expression of opioid consumption in OME in addition to DDD may provide further information, especially when weak opioids are included in the analysis.

Résumé / Cette étude avait pour objectif de mesurer le niveau de consommation d'opioïdes dans un centre de cancer en Egypte, avant et après l'établissement d'un service de médecine palliative. En comparant la consommation d'opioïdes au cours de l'année ayant précédé la création du service de médecine palliative, avec la consommation d'opioïde au cours de la troisième année ayant suivi la mise sur pied du service, on note les augmentations suivantes: morphine 698 pourcent, fentanyl 217 pourcent et tramadol 230 pourcent. Exprimée en doses quotidiennes déterminées (DQD) et ajustée en fonction de 1,000 nouveaux patients atteints du cancer, la consommation a augmenté de 460 pourcent, elle est passée de 4,678 DQD/1000 nouveaux patients à 26,175 DQD/1000 nouveaux patients. Par ailleurs, exprimée en tant que gramme de morphine orale équivalente (gMOE) la consommation a augmenté de 644 pourcent, soit de 233 gMOE/1000 nouveaux patients à 1731g/1000 nou-

veaux patients. La mise sur pied de ce service de médecine palliative a été associée à une augmentation de la consommation d'opioïdes, plus particulièrement la morphine, laquelle est un indicateur d'une amélioration dans le contrôle de la douleur. L'expression de la consommation d'opioïde en dose de morphine orale équivalente, ajoutée à la dose quotidienne déterminée fournira peut-être des renseignements supplémentaires particulièrement lorsque les opioïdes moins puissants font partie de l'analyse.

INTRODUCTION

The World Health Organization (WHO) defines palliative care as "an approach that improves the quality of life of patients and their families facing the problem associated with life-threatening illness" (1).¹ Many studies have provided evidence of the effectiveness of palliative care (PC) in improving quality of life for cancer patients and their families (2). One of the outcomes measured in these studies is cancer pain control (2). The WHO recognizes consumption levels of morphine and other opioids as a possible indicator of PC accessibility and improvement in cancer pain control in different countries (1); similarly, opioid consumption data have been used to evaluate the quality of cancer pain control at an institutional level (3, 4).

In Egypt, PC and cancer pain control are at an early stage of development. Very few services are available (5, 6), and there are many barriers to be faced, such as limited opioid accessibility and availability for medical use (7, 8).

The palliative medicine unit (PMU) of the Kasr Al-Ainy Center of Clinical Oncology and Nuclear

¹The data given in this paper were partially presented at the sixth research congress of the European Association for Palliative Care, Glasgow, Scotland, UK, June 10-12, 2010.

Medicine (NEMROCK), Kasr Al-Ainy School of Medicine, Cairo University was established in September 2008. A priority action for the unit was to overcome barriers to cancer pain control, using available resources (7). The aim of our research was to demonstrate, using opioid consumption figures as a surrogate indicator, the efficacy of establishing a specialized PC service in an Egyptian cancer centre to improve cancer pain control and quality of life for Egyptian cancer patients.

METHODS

Our study was a retrospective one of opioid consumption at NEMROCK conducted over a five-year period; data were collected starting two years before the PMU was established (from September 2006 to August 2008) and for three years after its establishment (from September 2008 to August 2011). The PMU staff includes four physicians: three palliative medicine physicians (two full time and one part time) and one rotating clinical oncology resident. PMU physicians are aided by the nurses and social workers of NEMROCK. The PC service is provided through a tri-weekly outpatient clinic, eight in-patient beds, and a limited home care activity (6). Opioid consumption data were retrieved from the computer system of NEMROCK's pharmacy.

During the study period, the strong opioids available were fentanyl (25 and 50 µg/h transdermal fentanyl [TDF] patches), morphine (30 mg slow-release morphine [SRM] tablets), and tra-

madol (50, 100, 150, and 200 mg tablets/capsules and 100 mg ampoules). The opioid consumption was expressed in oral morphine equivalent (OME) and defined daily dose (DDD). Annual consumption was then adjusted for the number of new cancer patients registered at NEMROCK per year.

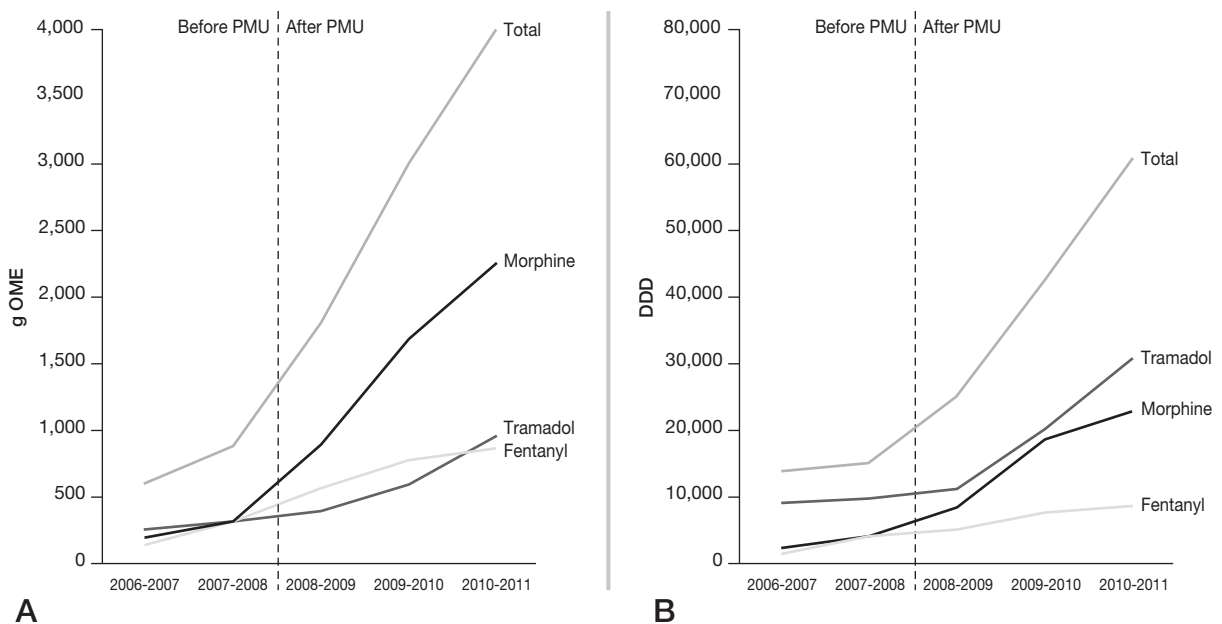
To calculate the OME, we used conversion ratios of 1:100 to convert from TDF to oral morphine (9), and 10:1 to convert from tramadol to oral morphine (10). The DDD is "the assumed average maintenance dose per day for a drug used for its main indication in adults"; it is 1.2 mg for TDF, 100 mg for oral morphine, and 300 mg for oral and parenteral tramadol (11). In calculating the OME and the DDD of fentanyl, the actual dose released when TDF was applied for 72 hours was the one taken into consideration and not the actual content of the patch.

RESULTS

The yearly absolute consumption of opioids during the five years of the study in g OME and DDD is illustrated in figure 1. Table 1 shows the absolute consumption of opioids in g OME and DDD and their contribution to the total consumption during the year before PMU establishment compared to the third year after.

Comparing the consumption during the year before PMU establishment and the third year after and using the OME method, we determined that the increase in total consumption (3,207 g OME) was due to the increase in morphine con-

Figure 1 / Yearly Absolute Consumption of Opioids before and after Establishment of the Palliative Medicine Unit (PMU)^{a, b}



^a Part A is expressed in grams of oral morphine equivalent (g OME).

^b Part B is expressed in defined daily dose (DDD).

Table 1 / Absolute Consumption of Opioids and Their Percent Contribution to Total Consumption during the Year before Establishing the Palliative Medicine Unit and the Third Year After

		Absolute consumption			% contribution to total consumption	
		Before	After	% change	Before	After
Strong opioids						
Fentanyl	g OME ^a	260	826	+217%	31%	21%
	DDD ^b	2,169	6,885		15%	11%
Morphine	g OME	284	2,266	+698%	34%	56%
	DDD	2,838	22,655		20%	37%
Weak opioid						
Tramadol	g OME	286	946	+230%	35%	23%
	DDD	9,544	31,526		66%	52%
Total						
	g OME	830	4,037	+386%	100%	100%
	DDD	14,551	61,066	+320%	100%	100%

^a Grams of oral morphine equivalent.

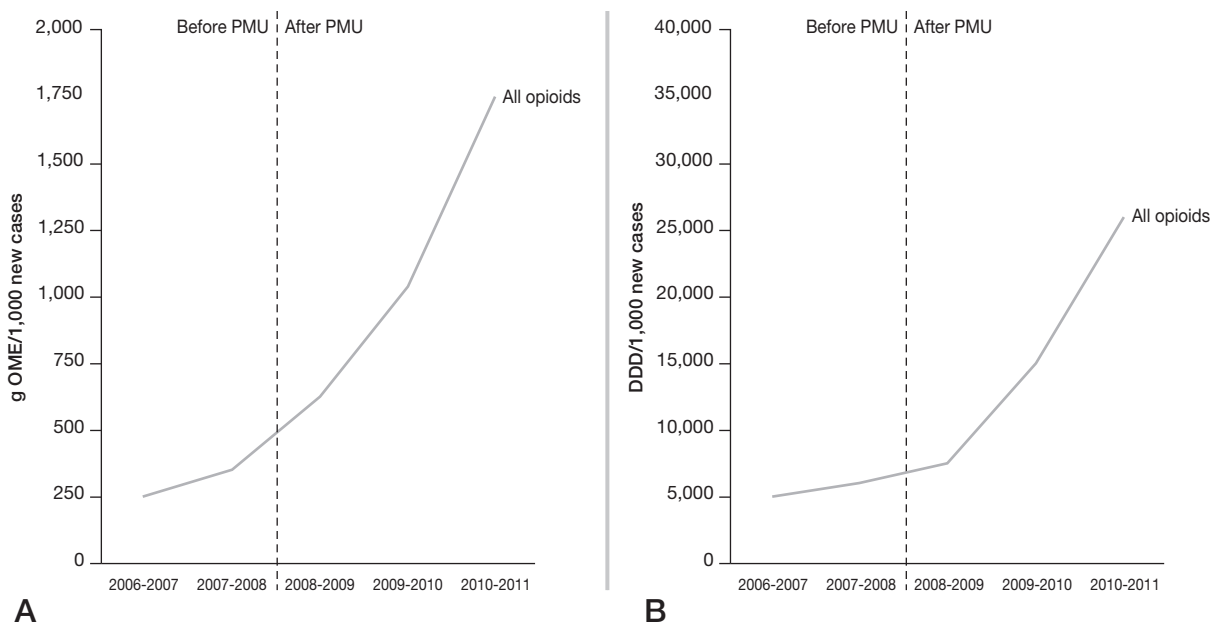
^b Defined daily dose.

sumption (1,982 g OME, 61.8 percent), followed by that of tramadol (660 g OME, 20.6 percent) and fentanyl (566 g OME, 17.7 percent). Using the DDD method, we determined that the increase in total consumption (46,515 DDD) was due to the increase in tramadol consumption (21,982 DDD, 47.3 percent), followed by that of morphine (19,817 DDD, 42.6 percent) and fentanyl (4,716 DDD, 10.1 percent).

The numbers of new cancer patients registered at NEMROCK in each of the five years were, respectively, 2,698, 2,434, 2,607, 2,874, and 2,333.

The yearly total opioid consumption corrected for 1,000 new cancer cases per year and expressed in g OME and DDD is illustrated in figure 2. Expressed in g OME, opioid consumption increased from 233 g OME/1,000 new patients during the year before PMU establishment to 1,731 g OME/1,000 new patients during the third year after (a 644 percent increase). Expressed in DDD for the same periods, opioid consumption increased from 4,678 DDD/1,000 new patients to 26,175 DDD/1,000 new patients (a 460 percent increase).

Figure 2 / Yearly Consumption of All Opioids Adjusted for 1,000 New Cancer Patients before and after Establishment of the Palliative Medicine Unit (PMU)^{a, b}



^a Part A is expressed in grams of oral morphine equivalent (g OME).

^b Part B is expressed in defined daily dose (DDD).

DISCUSSION

There is an ongoing effort to demonstrate the positive impact of PC on the quality of life of cancer patients and their families (2). The available evidence is derived from studies done in high-income nations, such as Australia and some European and North American countries (2). To the best of our knowledge, the current study is the first conducted in a lower-income country to address the issue of PC effectiveness.

The measured outcomes differed among studies investigating the effectiveness of PC — they included, for example, quality of life and control of cancer pain and other symptoms (2). In our institution, opioid consumption is probably the only measurable parameter that can be assessed before and after PMU establishment to indicate improvement in cancer pain control.

In Egypt, the control of cancer pain remains inadequate, as indicated by the low opioid consumption figures (12). The average consumption of narcotic drugs in Egypt for the period 2007–2009 in DDD per million inhabitants per day was only 49, and on this measure Egypt ranked 112th among other countries. In comparison, the figures were 20,632 for Canada, 8,013 for Australia, and 3,655 for the United Kingdom (12). Egypt's inadequate cancer pain control is largely due to restrictive regulations that limit access to opioids (8, 13). By applying the WHO guidelines to improve cancer pain control while remaining within the limits of Egyptian narcotics law, the PMU succeeded in providing patients with enough opioids to control their pain (7). This had a significant positive impact on opioid consumption (especially morphine) in our centre; total opioid consumption increased more than sevenfold, indicating improved cancer pain control.

Our results confirm those of Centeno and colleagues (4), who used opioid consumption data to assess the effectiveness of a PC service in a Spanish university hospital. In their study, the total opioid prescription increased from 240 to 558 DDD per 1,000 hospital stays per year in the oncology department after the establishment of a PC unit; the increase was mainly due to greater morphine utilization (4). Similarly, the inauguration of a hospice was associated with an increase in total opioid consumption in a study conducted in Italy (3).

Globally, the growth in fentanyl consumption far exceeds that of morphine. From 1989 to 2009, there was a hundredfold increase in fentanyl consumption compared to a sevenfold increase in morphine consumption (12). In Egypt, over a 10-year period (1999 to 2008), fentanyl consumption increased by 2,180 percent, while morphine con-

sumption increased by only 9 percent (14, 15). This discrepancy between fentanyl and morphine consumption trends may be attributed to many factors — for example, the impact of marketing (16). A major cause of this discrepancy in Egypt may be regulations that limit access to morphine more stringently than to fentanyl. Egyptian narcotics law limits the amount of morphine in a single prescription to 420 mg, and the usual practice in centres where SRM is available is to allow a single prescription on weekly basis (17). As a result of these regulations, Egyptian cancer patients in need of strong opioids have access to only 60 mg of morphine per day, which is not enough for the majority (74 percent) (8).

However, there is no dose limit for fentanyl per prescription in the narcotics law, and the usual practice is to dispense one pack containing five TDF patches per prescription. For example, using a single prescription, a patient can get one pack of TDF 100 µgm/h patches containing a total of 84 mg fentanyl, an amount equivalent to that allowed with 20 morphine prescriptions. As a result, the practical choice for patients who are in need of a strong daily opioid dose of over 60 mg OME is TDF. In addition, most cancer patients in our setting die at home (6), and the only available option for those who need strong opioids and cannot take oral medication is TDF, because access to parenteral morphine is very limited. The maximum dose of parenteral morphine in a single prescription is only 60 mg, which, as it is dispensed on weekly basis, is not enough for any patient requiring strong opioids (8).

After the PMU was established, we managed to change the practice of prescribing opioids without violating the narcotics law and thus supply patients with sufficient amounts of oral morphine (7). As a result of this more rational utilization of morphine, there was an eightfold increase in morphine consumption compared to a threefold increase in fentanyl consumption. In addition, the contribution of morphine to total opioid consumption (in g OME) increased from 34 to 56 percent after the PMU was established, while that of fentanyl decreased from 31 to 21 percent. This indicates that morphine was underutilized due to limited accessibility in our setting. Our results coincide with those of Centeno and colleagues (4), which linked the initiation of PC services to an increase in morphine consumption, reflecting a more rational use of morphine. However, in that study, the increase was in parenteral rather than oral morphine consumption. Furthermore, unlike that study, which reported a decrease in TDF consumption following PC initiation, our study reported an increase in TDF consumption. This

may have been due to the unavailability of parenteral morphine in our setting; we instead had to use TDF for patients unable to take oral medications.

Unless Egypt's narcotics law is revised, consumption of fentanyl will increase at a greater rate than that of morphine. Being forced to resort to the relatively expensive TDF rather than much cheaper immediate-release morphine will place an economic burden on Egypt, a lower-income country.

Including a weak opioid, tramadol, in our calculation of opioid consumption may be seen as a limitation of this study because tramadol is mainly used to treat mild-to-moderate pain. However, we believe that it was important to do so for several reasons. Tramadol is the only immediate-release oral opioid registered in Egypt. We use tramadol as a breakthrough analgesic and for dose titration when appropriate for patients with moderate-to-severe pain. Also, for opioid-naïve patients with moderate-to-severe pain, we do not skip the second step of the WHO cancer pain relief ladder, which is to administer an opioid for mild-to-moderate pain (18). The patient is treated with tramadol, the dose is titrated to the maximum allowed, and then the patient is switched to a strong opioid. Although there is evidence to support the decision to skip that second ladder step (19, 20), it is not feasible in our setting because of the unavailability of strong opioids in lower concentrations.

A recent study showed that measuring opioid consumption using OME reflects the clinical use of opioids better than doing so using DDD (21). That study reported that the increase in opioid consumption between 2004 and 2008 in Norway was 23.6 percent using OME and only 6.7 percent using DDD (21). The results of the current study confirm that measuring opioid consumption using OME in addition to DDD provides further valuable information. Utilizing OME rather than DDD may work better to reflect changes in cancer pain management over time. Our study reported a 644 percent increase in adjusted opioid consumption using OME compared to a 460 percent increase using DDD. This is mainly due to the fact that we included tramadol in our analysis. Using DDD, we determined that tramadol comprised 66 percent and 52 percent of total consumption before and after PMU establishment, respectively. Due to the major contribution of tramadol to total consumption when measured using DDD, the change in strong opioid consumption was less noticeable. However, when OME was used, the contribution of tramadol was much less (35 percent before, and 23 percent after PMU estab-

lishment), reflecting a more realistic assessment of the contribution of strong opioids.

DDD and OME are complementary. DDD provides a standardized common language, while OME tends to change due to the wide variability in equianalgesic ratios (22). Still, from a clinical point of view, OME is more informative than DDD, which is not based on equipotency (21).

CONCLUSION

The establishment of a PMU in an Egyptian cancer centre was associated with a significant increase in the consumption of opioids, especially morphine. This indicates improvement in cancer pain control and a more rationale use of morphine. There is a need to spread similar models to other Egyptian cancer centres. Further research is recommended to identify and overcome barriers to cancer pain control and PC development in Egypt. The expression of opioid consumption using OME in addition to DDD yields valuable information.

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