Contents

P2  Report on Annual Scientific Meeting 2009... Dr. RSK Lo
P4  Message from Chairman... Dr. AOL Kwok
P5  Farewell to Dr. KK Lam... Dr. M Sham
P6  Editor’s Column: Advance directives - More than an advance refusal in need... Dr. DMW Tse
P8  Advance Directives: their role in clinical practice and their difficulties... Dr. CY Tse
P10 Major airway obstruction... Dr. CM Ma
P12 Drug interactions in palliative care... Dr. CWS Yau
P16 Any breakthrough for breakthrough pain?... Dr. JTM Chan
P19 Beheaded souls: The psychological distress faced by neck and neck cancer patients... Dr. RKW Woo
P25 Opioid switching... Dr. MH Khemlani
P26 Malignant intestinal obstruction... Dr. BCW Li
P27 Diarrhoea in acute radiation proctitis... Dr. KY Chan
P30 Total parenteral nutrition in malignant intestinal obstruction... Dr. BHW Cheng
P33 Death rattle: A brief review... Dr. AKW Mok
P35 Understanding dignity in the light of Chochinov... Dr. RKW Woo
P38 Spring dinner of HKSPM and HKHNA
P40 Membership Information
P41 Education Seminars & Meetings
P42 7th Hong Kong Palliative Care Symposium - Call for abstract
P43 News from Society for the Promotion of Hospice Care... Ms Faye Chan
Dear Colleagues,

It is my great honour to serve as the new Chairman of the Hong Kong Society of Palliative Medicine. I would like to express by great gratitude to all my predecessors, Dr. Michael Sham, Dr. KS Chan, Dr. Doris Tse, Dr. KS Lau and Dr. KH Wong, as they have laid a solid foundation for our Society to reach its current level of success.

I became one of the council members of Hong Kong Society of Palliative Medicine since 2004. During these six years, I experienced the passion of all our council members in serving patients and families during their last journey and in promoting palliative care in Hong Kong. I also learned how devoted one should be before one could instill any change and progress in the community. As we look back, we would proudly identify the important milestones in the development of palliative care in Hong Kong – the establishment of our Society in 1997, the recognition of Palliative Medicine as a subspecialty under the Hong Kong College of Physician since 1998 and the Hong Kong College of Radiologist since 2002, and the extension of palliative care beyond cancer to other chronic debilitating diseases. However, all these significant progress would not be possible without the perseverance of my predecessors, who had shed a lot of time, blood, sweat and tears during the course.

In the coming year, our Society will continue to organize academic and educational activities including the regular Palliative Medicine Doctors’ Meetings, the Multidisciplinary Meetings, the Hong Kong Palliative Care Symposium, and the Annual Scientific Meeting to promote the highest standard in clinical practice in palliative medicine.

With the release of the consultation paper on advance directive from the Food and Health Bureau of the Government of HKSAR, our Society shall respond to the paper in advocacy for equity to quality palliative and end-of-life care for our local citizens. Our Society, in collaboration with City University of Hong Kong, Hong Kong Hospice Nurses’ Association and Society for the Promotion of Hospice Care, will conduct a public forum to introduce the concept of advance directive and advance care planning.

Lastly I would like to welcome Dr. WM Lam and Dr. PT Lam to join our big family. I would also like to take this opportunity to thank Dr. Doris Tse. Under her editorial leadership, we have a beautiful and informative newsletter to act as a platform for sharing our experience, activities and education programmes with our members.

With the concerted effort of our teams and all our members who are committed to promote palliative care in Hong Kong, it is beyond my doubt that more achievements are yet to come.

Dr. Kwok Oi Ling, Annie
Dr. KK Lam has been working with us in the palliative care community, since the establishment of the Hong Kong Society of Palliative Medicine. He retired at the end of last year. After retirement, to the surprise of many people, he went on to study theology in London.

One of the major contributions of Dr. Lam is in palliative care consultative service, especially our collaboration with the gynaecologists in Queen Mary Hospital. Together, we have been awarded repeatedly as an outstanding team of Hong Kong West Cluster. Before retirement, Dr. Lam often wore the badge of the award on his white coat, confirming how much he values the collaboration.

Why did Dr. Lam decide to study theology? He told me that suffering, which disrupts one’s world view, would demand meaning making. Theology, including Christianity and other religions, would help to address suffering, illness and death. Learning and practicing theological reflection would facilitate his own meaning making and spiritual growth.

I agree with him, and I believe there are many ways in which palliative care could stimulate spiritual growth in the workers.

Palliative medicine is never a glamorous specialty. We look after dying patients, not saving life with highly sophisticated technologies. Modern societies, unfortunately, are often preoccupied with efficiency, and regard dying people as intolerable and burdensome. Palliative care doctors are, therefore, never great heroes, but humble servants, accompanying patients in their last journey. Humility, however, may bring a person to God, who is Himself gentle and lowly in heart. Where there is true humility, He will give peace.

Sharing patients’ darkness, palliative care workers also suffer, by taking up the patients’ suffering in such a way that it becomes theirs also. Who can help the worker then? For Christians, our Lord has descended to the valley of death, conquered death, and returned to us, to reassure us that, together with Him, we can find a way through.

I am convinced that palliative care workers are invariably wounded. Humility is the ointment for our wounds. Hence, it is just natural for a humble palliative care doctor to seek God and even further his studies in theology.

Let us hope that Dr. Lam will come back later, to enrich us with the theology he learnt, and the insights he gained.
Advance Directive: More than an advance refusal in need

Dr. Tse Man Wah, Doris, Editor-in-Chief.

With the release of the consultative paper on advance directives (AD) by the Food and Health Bureau HKSAR in Dec 2009, it is timely to have more open discussions on AD and its related process – advance care planning (ACP).

A public forum on advance directives was held on 6th March 2010 in the City University of Hong Kong. This forum is co-organized by Society for the Promotion of Hospice Care; Governance in Asia Research Centre, City University of Hong Kong; Hong Kong Hospice Nurses’ Association; Hong Kong Society of Palliative Medicine.

The forum included a comprehensive program with talks delivered by Dr. Chan Ho-man on “Ethical consideration of advance directives”; Dr. Doris Tse on “Advance care planning”; Dr. Tse Chun-yan on “Practical difficulties in executing advance directives”; Ms Faye Chan on “Promotion of advance care planning and advance directives in the community”. The organizers see this as a good opportunity to clarify the issues related AD, and to facilitate open discussion on a topic that is relevant to all citizens of Hong Kong.

Albeit a new concept to the public in Hong Kong, advance care planning in the form of discussion on preferences of life sustaining treatments is not totally new in health care. Years ago, the Hospital Authority had promoted the use of DNR form. The DNR form, in analogy to the AD form, is just a tool. Recent local studies have shown that patients with advanced cancer had DNR order established in near 99% if they ever received palliative care and in 86.3% of those who did not receive any palliative care. Another study on local patients who died from cancer and chronic non-cancer diseases showed that 95.6% of cancer patients and 80.0% to 89.5% of patients with chronic diseases had DNR order in place. The discussion of CPR and DNR was conducted directly with patients in 40.1% and 11.5% with cancer and non-cancer respectively. Multiple factors could account for the quoted differences. Nonetheless, patients who have chronic non-cancer diseases also have significant palliative care needs and ACP is relevant and applicable in their model of care.

The development of palliative care in Hong Kong, the effort of Hospital Authority in setting guidelines on withholding and withdrawing life sustaining treatment and the promotion of the DNR form are factors that might have shaped these findings in various local studies. It also seems that the DNR form, a tool itself, has served beyond that. The concept has been incorporated into local clinical practice as many of these DNR orders and their discussions are conducted and documented without confining to the original form.

Photos of the Forum on AD
The audiences
The speakers & chairs

Ms Faye Chan, Dr. Doris Tse, Dr. CY Tse, Ms Ellen Yeung, Dr. Annie Kwok, Prof. HM Chan
Editors’ Column

Could one be just as optimistic in promotion of AD, which is a tool for advance care planning? Perhaps experience elsewhere could shed light on this.

AD has been promoted in other places with the main theme of promotion of patients’ autonomy. The Patient Self Determination Act (PSDA) enacted in US in 1990 was historic in this movement, and efforts have been given to improve end-of-life care. The SUPPORT study (Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments) included a 2-year prospective observational study (phase I) with 4301 patients followed by a 2-year controlled clinical trial (phase II) with 4804 patients and their physicians randomized by specialty group to the intervention group (n=2652) or control group (n=2152). The phase I observation of SUPPORT confirmed substantial shortcomings in care for seriously ill hospitalized adults - only 47% of physicians knew their patients prefer no CPR, 6% of DNR orders were written only 2 days before death, and 38% of deaths spent at least 10 days in ICU.

Despite an increase in recording of completed AD by the physician from 6%-35% to 78% at phase II post interventional study, there were no improvement in patient-physician communication, incidence or timing of written DNR orders, physicians’ knowledge of their patients’ preferences not to be resuscitated, number of days spent in an ICU, and the level of reported pain. The SUPPORT investigators concluded that in order to improve the experience of seriously ill and dying patients, greater individual and societal commitment and more proactive and forceful measures may be needed. Although the SUPPORT study yielded negative results in terms of the targeted outcomes after intervention, it does bring insights into planning for better end-of-life care.

The objectives of advance care planning are not limited to making an AD. The communication process of ACP can bring along better understanding and stronger relationships among the family members, and solace to all at the end-of-life when making decisions are often difficult and stressful. In traditional Chinese culture where family decisions are honoured, it is important that these goals are brought to light and not being over powered by that of enhancing patients’ autonomy.

Finally, an AD will fall short of enhancing patients’ autonomy if planning for better end-of-life care depends solely on advance refusal - the true nature of an AD form. Indeed, why should one find the AD form compelling in driving for better end-of-life careand not merely a statement of giving up opportunities? The answer to this question resides in what is fundamental in enhancing patients’ autonomy, that is to empower patients to make informed choices and quality palliative care should be among the options. Unless we have quality palliative care equitable to all, an AD could remain as a tool for achieving a narrow range of autonomy, and with withholding or withdrawal of life sustaining treatment portrayed as omission of care.

Palliative care in Hong Kong has moved beyond from the scope of cancer in public health care. We welcome the commitment of our Government to support the pilot of renal palliative program in Hong Kong. We hope this marks the first step in the strategic development of palliative care for non-cancer in Hong Kong.

References
2. Comparing non-cancer and cancer deaths in Hong Kong. A retrospective review. KS Lau, DMW Tse, WT Chen, PT Lam, WM Lam, KS Chan. Journal of Pain and Symptom Management (Accepted for publication 20 Jan 2010).
4.Experience of a Renal Palliative Care Program in a Hong Kong Center: Characteristics of Patients who Prefer Palliative Care to Dialysis. Tse DMW. Hong Kong Journal of Nephrology 2009; 11[2]:50-58.
5. A Controlled Trial to Improve Care for Seriously Ill Hospitalized Patients. The Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments (SUPPORT). The SUPPORT Principal Investigators. JAMA 1995;274[20]: 1591-98.
Advance Directives: their role in clinical practice and their difficulties

(Article reprinted from Medical Diary, with the permission of the Federation of Medical Societies of Hong Kong)

Dr. TSE Chun Yan,
Honorary Advisor, Hong Kong Society of Palliative Medicine.
Correspondence: tse_cy@hotmail.com

Background

In the Hong Kong context, the term “advance directive” (AD) usually refers to a set of instructions about what kind of life sustaining treatment (LST) that a patient wishes to refuse when he becomes mentally incapacitated under some specified circumstances. In Hong Kong, a proxy directive appointing another person to decide on the patient’s behalf does not have legal status. Under the common law framework in countries like UK, Australia, Canada and USA, a valid and applicable AD refusing LST is legally binding. The courts in Hong Kong would very likely take this view. In 2006, the Law Reform Commission published a report on AD recommending promotion of the concept of AD via non-legislative means in Hong Kong. However, there are different views on this in the community, and the Food and Health Bureau has issued a consultation paper in December 2009 asking for comments, among other questions, whether the concept of AD should be more widely promoted in Hong Kong or not.
Role of AD in clinical practice

Sometimes, AD as a legally binding tool in ACP has its role in clinical practice:

1. When there is a need to express the decision of the patient effectively to clinicians not familiar to the patient: For example, a terminally ill patient who plans to stay at home as much as possible may die at home. A statement that he declines CPR would be helpful. Another example is a severe COPD patient with repeated intubation for respiratory failure. If the patient does not want further intubation on his next admission for respiratory failure, a statement indicating his decision would be helpful.

2. When it is difficult to judge what is in the best interests of the patient: In some cases, a decision based on the best interests principle for an incompetent patient can be difficult, even if the patient’s values and wishes are known. A statement indicating his decision would be helpful.

3. When the wish of the patient appears not in the best interests of the patient: Occasionally, a patient may have idiosyncratic view on a particular LST, for example, a Jehovah Witness patient would not want transfusion. A statement indicating his decision would be helpful.

Difficulties

However, there are practical difficulties in executing an AD. Unlike contemporaneous refusals, a patient may have difficulty to make a rational advance decision before the actual scenario happens. On the other hand, the clinical team may have difficulty to judge whether the AD is valid or applicable. Also, unlike a contemporaneous refusal, the clinical team may find it difficult to accept an advance refusal which appears not in the best interests of the patient, without the chance of further discussing with the already incompetent patient. Such difficulties should be greater in patients without a terminal illness.

Another problematic area is an AD demanding withdrawal of artificial nutrition and hydration when PVS status is confirmed. This is highly controversial. Common law framework seems to support that such AD should be followed. However, many people think this is euthanasia.

Furthermore, without specific legislation in Hong Kong, there are legal uncertainties. Recently, doubts have been raised whether a valid and applicable AD can really override the best interests principle. For example, can a doctor transfuse a Jehovah Witness patient (with a valid AD refusing transfusion) dying of bleeding when he becomes unconscious, based on the best interests principle according to the Mental Health Ordinance Cap 136 Section 59Z?

The way forward

There are no easy answers to the above difficulties. In the 2006 report, taking reference mainly from the Singapore model, which has a rigid legislation with statutory forms and procedures, the Law Reform Commission considers that legislation would not help the promotion of AD in Hong Kong. However, there are some recent developments. In 2007, the Mental Capacity Act became operative in England and Wales. The legislation on AD there is just on the basic principles only, allowing flexibility in its execution, but it confirms the legal status of AD and its relationship to the best interests principle. I think Hong Kong should work towards legislation for AD along the UK approach, to confirm the legal status of AD, but to allow flexibility in its execution.

At this moment, I think AD should be promoted in selected patients as part of ACP in advanced incurable illnesses. However, it may be prudent to wait till enactment of specific legislation on AD before promoting AD to the general public in Hong Kong. Meanwhile, it would be useful to develop guidelines for clinicians on how to handle an AD.

Regardless of whether AD is promoted in Hong Kong or not, it should be noted that AD is not a panacea for the difficulties faced by dying patients. Firstly, an AD cannot (and should not) cover all possible future scenarios. Scenarios not covered by the AD should be managed along the best interests principle, taking into account the values and wishes of the patient. Secondly, AD is a legal tool only. In patients faced with an advanced incurable disease, AD should be part of ACP, and ACP should be part of the full spectrum of palliative care for a terminally ill patient.
Palliative Medicine Doctors’ Meeting

Major Airway Obstruction

Dr. Ma Chi Ming,
Department of Pulmonary and Palliative Care, Haven of Hope Hospital.
Correspondence: mcm985@ha.org.hk

ABSTRACT

Major airway obstruction (MAO) is often diagnosed too late for definitive intervention. High index of suspicion and early diagnosis are crucial for successful management. Common clinical presentations of MAO include dyspnoea, cough, mucus secretions and stridor. Spirometry, imaging and bronchoscopy are the main investigations for MAO. Management strategies include interim measures, treatment targeted on the aetiology, and symptom palliation. A brief review of these interventions will be presented.

HKSPM Newsletter 2010 Apr Issue No.1 p10-11.

Introduction

Major airway obstruction (MAO) poses a management challenge in palliative medicine. Often it is either too late or too difficult to reverse this life-threatening situation. Early diagnosis and management is the key for successful MAO management.

Case History

Madam C, a 58 year-old-lady, suffered from breast cancer with metastases to lung, peri-bronchial and hilar lymph nodes. She developed dyspnoea and stridor while she was hospitalized in Haven of Hope Hospital for symptom control. ENT surgeon was consulted. Flexible laryngoscopy showed left vocal cord palsy while right vocal cord was mobile. There was no obstruction seen below the glottis. Intrathoracic tracheal obstruction was suspected. She was given intravenous dexamethasone and low dose alprazolam. Her dyspnoea initially improved and she managed to spend some good time with her grandchildren in the ward garden. However, her condition suddenly deteriorated soon after, and she was too ill for transferral to the oncology clinic. Palliative sedation was started and she died peacefully after one day.

Pathophysiology and clinical features

Stridor, dyspnoea, cough and mucus secretion are the most common clinical features of MAO. Stridor is caused by turbulent air flow when gas molecules pass through the site of obstruction. Inspiratory stridor is more likely with extrathoracic obstruction. During inspiration, the surrounding atmospheric pressure of the extrathoracic airway is higher than the tracheal pressure, causing compression of the extrathoracic airway and inducing inspiratory stridor. Expiratory stridor is more likely to occur in intrathoracic obstruction. During expiration, the surrounding pleural pressure of intrathoracic airway is higher than the tracheal pressure, causing compression of the intrathoracic airway and inducing expiratory stridor. Cough and mucus secretion are related to the direct mechanical effect of the obstruction. Dyspnoea is related to the work of breathing, neuro-mechanical dissociation, and chemoreception of blood oxygen and carbon dioxide levels; all these are in turn related to the obstruction.

Pathology of MAO

MAO can be caused by endoluminal tumors, extrinsic compression by tumors or mediastinal masses, and bilateral vocal cord palsy. Common cancers causing MAO include head and neck cancer, lung cancer, and mediastinal lymph node or endobronchial metastasis due to primary malignancy in the breast, gastrointestinal tract, kidneys, ovaries, uterus, testis, thyroid gland, nasopharynx and adrenal gland. Less likely, it can be due to primary tracheal tumour.

Investigations

Spirometry, imaging and bronchoscopy are the mainstay of investigations for MAO. As spirometry can only detect airway resistance...
when its diameter is less than 8 mm, it is not a sensitive method until late in the course of MAO. The sensitivity of detecting upper MAO by Chest X-ray is only 66%. Helical computer tomography can detect intramucosal, submucosal and extra-luminal lesions with a sensitivity up to 97%. With 3-Dimension reconstruction, it allows better visualization of the extent of the disease and airway obstruction. MRI is inferior to CT scan for airway visualization but superior in visualizing vascular structures surrounding the airway.

**Management**

Factors affecting the clinical management of MAO include urgency of presentation, aetiology, localization, extent of obstruction and prognosis. Interim measures while waiting for definitive treatment and interventions with palliative intent include proper head positioning, oxygen supplement, helium-oxygen (Heliox) inhalation, systemic corticosteroids, securing the airway, cardiopulmonary bypass and palliative sedation.

Heliox, a gas with nitrogen replaced with helium, is a lower density gas that reduces airway resistance. In one case-control study, it reduces around 30% of breathing work.1 Systemic steroid mainly acts on the edema of inflamed tissue.2 Its effect is directly proportional to the local concentration of steroids in the inflamed tissue.

Measures targeted at the cause of obstruction include dilatation, resection techniques, stenting, brachytherapy, external irradiation and photodynamic therapy, depending on their availability.

Resection techniques include tissue removal with rigid bronchoscopy, laser - Neodymium yttrium aluminium garnet (Nd:YAG) and cryotherapy. A systematic review of more than 2500 patients undergoing Nd:YAG showed an 80% dyspnoea relief rate, and success rates of 70-95%, 40-60%, 57% for central lesions, lobar lesions and complete obstruction respectively. Mortality rate was around 0.4-3%.3 Cryotherapy induces tumor necrosis by freezing the tissue and inducing tissue death, followed by bronchoscopic examination to remove the resultant necrotic tissue. Repeated bronchoscopic treatment may be needed. In a systematic review of 411 patients, 65-68% showed symptom relief. Success rates of 60% and 35% for central and peripheral lesions were reported respectively.3

Metallic or silicone stents can be used for stenting. In one case study, 80% of patients showed immediate symptom relief with no immediate peri-operative death.4 However, 5-10% had stent migration, 4-8% had stent obstruction for those using silicone stents and 40% required repeated stenting.5

Brachytherapy delivers a relatively high dose of a radiation source via bronchoscopy. Follow-up bronchoscopy is needed for removal of necrotic tissue. It allows treatment for both endoluminal and extrinsic tumour. In a case study6, 60-90% showed symptom palliation, but 1-3% developed bronchovascular fistula and stenosis, 10% developed radiation bronchitis and 5-20% had massive hemoptysis. A Cochrane review7 showed no single regimen that could give greater palliation. In addition, high dose regimens led to more acute toxicity especially radiation oesophagitis. There was a modest increase in survival of 5% at 1 year and 3% at 2 years in patients with higher performance status and receiving higher dose radiotherapy. The risk of radiation myelitis is a concern.

Photodynamic therapy induces tumor necrosis by administration of a photosensitizing agent followed by activation of the agent with light of specific wavelength. Follow-up bronchoscopy is needed. Sunlight exposure should be avoided for 4 to 6 weeks.

**Conclusion**

Early diagnosis is required for successful management of MAO. Some measures can be used as interim measures before more definitive treatment, but none is consistently better than others. Treatment decision is mainly determined by the balance of risks and benefits, patient's goals and wishes, aetiology, disease trajectory and prognosis, and available resources.

**References**

Palliative Medicine Grand Round

Drug Interactions in Palliative Care

Dr. Yau Wai Shan, Cora, 
Palliative Care unit, Caritas Medical Centre. 
Correspondence: yws073@ha.org.hk

ABSTRACT

Advanced cancer patients are at risk of potential drug interactions because they are often on many medications. Drug-drug interactions can be kinetic, dynamic and pharmaceutical. Pharmacokinetic interactions mainly involved Cytochrome P450 enzymes system. Currently, more emphasis is placed on the newer information about its genetic polymorphism. It is important to recognize the potential drug interactions of commonly used medications, such as phenytoin, warfarin, anti-depressants and opioids to avoid possible side effect or toxicity.

HKSPM Newsletter 2010 Apr Issue No. 1 p12-16.

Introduction

Cancer patients often receive numerous medications for treating the cancer, co-morbid conditions or the associated symptoms. In the palliative care setting, drug-drug interactions are common. It can result in potential risks to patients.

Case 1

Madam C, a 52-year-old lady, was a known hepatitis B carrier. She was diagnosed to have adenocarcinoma of recto-sigmoid colon with laparoscopic anterior resection done in November 2006. The staging was T3N0 Duke’s B. In April 2009, she was found to have tumour recurrence with metastasis over the brain, scalp, manubrium, lung and lymph nodes. She received whole brain radiotherapy (RT) in June 2009. Later, she was found to have bone metastasis in the skull, manubrium, distal left femur and cervical spine. Palliative RT was given to the distal left femur.

Madam C was regularly followed up in oncology department and she was planned for palliative chemotherapy in July 2009. However, she was admitted to medical department for generalized tonic-clonic convulsion in late July. Computed tomography (CT) of brain showed a 2 cm heterogenous lesion with peri-focal edema in left frontal lobe and mass effect. The dose of dexamethasone was increased and phenytoin was started. She was clinically unfit for further chemotherapy.

She was then transferred to our palliative care unit. Her medications included diclofenac, phenytoin, dexamethasone, pantoprazole, lamivudine and senna. She developed convulsion in ward. Her phenytoin level was 29umol/L (reference range: 40-79umol/L). Phenytoin was increased from 300mg to 330 mg per day. There was no further convulsion and she was discharged.

In summary, this was a case of carcinoma of colon with brain metastasis. The drug level of phenytoin was suboptimal, suggesting the possibility of drug-drug interaction between phenytoin and dexamethasone.

Case 2

Mr. T, a 58-year-old gentleman, was a chronic smoker. He had history of paroxysmal atrial fibrillation, ischaemic heart disease and chronic rheumatic heart disease with mitral stenosis. Mitral valve replacement (MVR) and coronary artery bypass graft surgery were done in Jan 2009. His medications included digoxin, warfarin, isosorbide dinitrate and rabeprazole.

He presented with haemoptysis in May 2009. CT Thorax found right lower lobe carcinoma of lung with multiple lymph nodes metastasis. Emergency bronchoscopy with stenting was performed. He refused palliative radiotherapy and preferred Chinese medicine.

He was later admitted to the acute medical ward for fast atrial fibrillation. Amiodarone infusion was given for control of heart rate and oral amiodarone was given for maintenance. International normalized ratio (INR) was elevated to 3.14. In view of persistent haemoptysis and the interaction between warfarin and amiodarone, amiodarone was switched to sotalol. Serial INR was monitored and the level was around 1.6 while on sotalol. He was then discharged with stabilisation of the INR.
In summary, this was a case of carcinoma of lung with history of MVR on regular warfarin; subsequently complicated by haemoptysis. There was drug-drug interaction between warfarin and amiodarone. The potentiated effect of warfarin was dangerous by increasing the risk of haemoptysis.

**Discussion**

Drug interactions are defined as ‘the possibility that one drug may alter the intensity of pharmacological effects of another drug given concurrently’.1 It can involve interactions between drugs and disease, drugs and chemicals in the environment, drugs and drugs, and drugs and nutrients.

Drug-drug interactions can be classified into (1)pharmacokinetic, (2)pharmacodynamic and (3)pharmaceutical.2 Pharmacokinetic interactions refer to that in which one drug affects the disposition of another. The interaction can alter absorption, binding, distribution, transportation to the site of action, biotransformation, metabolism and excretion. Pharmacodynamic interaction arises when there is an interaction at the site of action – a receptor or physiologic system. The effect can be synergistic, additive, or antagonistic. Pharmaceutical interactions occur when there are physical incompatibilities between drugs.3

**Pharmacokinetic interactions**

Cytochrome P450 (CYP) hepatic enzymes are major sites of drug metabolism. It can be found in hepatocytes and other parts of body, such as the intestinal mucosa, brain, and kidney. The P450 system of enzymes consists of more than 20 families of enzymes. These families are defined by cDNA techniques.3,4 Several of these enzymes show genetic polymorphism.

The most extensively studied enzyme is isozyme CYP2D6. This enzyme is inherited in autosomal recessive pattern.5 Newer studies, using molecular techniques such as polymerase chain reaction and restriction fragment length polymorphism, have characterized more than 90% of the genetic defects in the CYP2D6. 6-9 Defects that give rise to loss of activity include complete gene deletion, splice site mutation, single base pair deletion and gene rearrangements. Three groups of individuals are identified: ultra-rapid, extensive and poor metabolizers. Most individuals are extensive metabolizers, but there is variation among different ethnic groups. For example, the percentage of poor metabolizers in the White is around 5-10%. In Asian and African Americans, the incidence of poor metabolizers is much lower, around 1-2%. For the West African, the poor metabolizers are up to 18%.5,7,10,11

The implication of recognition of different metabolizers is important in daily practice. Eichellbaum et al.5 suggested that if the standard dose of medications is used, extensive metabolizers may be under-treated. On the other hand, the poor metabolizers may be over-treated. In poor metabolizers, activation of the drug may be ineffective. There can be decreased elimination, prolonged half-life, and potential for drug accumulation that may cause toxicity. 5

**Prevalence of drug interaction in palliative care**

In general medical wards, the rate of potential drug interaction was approximately 60%.12-14 Studies conducted in emergency departments showed that the rate ranged from 16% to 47%.16-18 Davidson et al. concluded that almost 70% of ambulatory patients with variable clinical conditions were exposed to potential drug interactions.18

For cancer patients, drug interactions are also very common. In a retrospective study of 100 hospitalized cancer patients, 63% were exposed to at least one drug combination with the potential to interact.19 Another recent study of 405 ambulatory cancer patients receiving cancer-directed therapy found that one-third were at risk of drug interactions. 20

Riechelmann et al.21 conducted another study to describe the epidemiology of potential drug interactions in cancer patients receiving supportive care exclusively. Among 372 eligible patients, 250 potential drug interactions were identified in 115 patients (31%, 95% confidence interval 26%- 36%). The most commonly involved drugs were warfarin and phenytoin. Most interactions were classified as being of moderate severity (59%) and 42% of them were supported by levels 1-3 of evidence. In multivariate analysis, increasing age (P < 0.001), presence of co-morbidity (P < 0.001), cancer type (brain tumors, P < 0.001), and increasing number of drugs (P < 0.001) were associated with greater risk of drug interactions.21
Drug interactions in common individual drug groups in palliative care

Anticonvulsants
Phenytoin causes induction of CYP3A4. It is commonly used with dexamethasone in palliative setting for treating brain metastasis. Phenytoin increases the rate of metabolism of dexamethasone through induction of hepatic microsomal enzyme, thus decreasing its drug level. Dexamethasone can both increase and decrease the phenytoin level. However, the exact mechanisms are still not well known. Phenytoin should be stepped up to 600-1000 mg/day if dexamethasone is used concurrently. It is impossible to predict the levels of phenytoin in an individual patient who is also on dexamethasone. Therefore, careful monitoring of phenytoin levels is highly recommended. After successful control of the tumor-associated brain edema, both dexamethasone and phenytoin should be tailed down simultaneously according to close drug level monitoring.

Anticoagulants
Warfarin is well known to interact with different medications, diet or herbs. It is mainly metabolized by CYP2C9. Drugs, such as amiodarone, anti-fungal agents and anti-depressants, that inhibit the isozymes will potentiate the effect of warfarin. Another mechanism is related to the interruption of the vitamin K cycle. Acetaminophen inhibits vitamin K-dependent carboxylase, a key enzyme in the vitamin K cycle. Hence, it may have possibility of potentiating the effect of warfarin.

Tricyclic anti-depressants (TCAs)
Amitriptyline and clomipramine are metabolized by multiple isozymes of P450 cytochrome. Consequently, there is a significant risk of unfavourable pharmacokinetic interaction. Amitriptyline is metabolized by 2D6, 3A4, 1A2, 2C9 and 2C19 isozymes, while clomipramine by 3A4, 1A2, 2C19 isozymes. Drugs suppressing the activity of the above-mentioned isozymes will increase the risk of undesirable effects of TCAs. TCAs may increase the potency of sympathomimetics, causing an increase in blood pressure. Impaired absorption of oral drugs may occur because of the strong cholinolytic effect of TCAs that inhibits peristalsis of the digestive tract.

Selective Serotonin reuptake inhibitors (SSRIs)
Paroxetine and fluoxetine show the greatest inhibition of CYP2D6. Fluvoxamine has its greatest inhibitory effect on CYP1A2. Other drugs in this class have less effect on the enzymes. Clinically significant interactions of SSRIs can occur when it is used with agents that have a narrow therapeutic index e.g. TCAs. Poor metabolizers may also reduce its clearance and produce adverse drug effects.

Analgesics
Codeine is metabolized to morphine by CYP2D6. It is ineffective for pain control in patients lacking CYP2D6 or if CYP2D6 is inhibited by other drugs. Phenotyping for CYP2D6 should be considered, so that codeine can be avoided in those CYP2D6 inhibitors. Caraco et al. evaluated the effect of codeine phosphate in individuals who were known to be poor or extensive metabolizers in the CYP2D6 system. Clearance by the extensive metabolizers was 200-fold greater than poor metabolizers.

There are many drugs that can suppress the CYP2D6 and affect the metabolism of codeine. These include SSRIs e.g. fluoxetine; TCA, e.g. amitriptyline; metoclopramide; haloperidol; methadone and valproic acid. Caution should be taken when co-administering these groups of drugs.

Tramadol is another opioid that is metabolized by CYP2D6. Therefore, similar to codeine, the simultaneous administration of tramadol with drugs that inhibit the activity of CYP2D6 is not recommended. Apart from its influence on opioid receptors, tramadol also inhibits serotonin reuptake in the descending antinociceptive system. Combination of SSRIs and tramadol has an increased risk of serotonin syndrome.

Methadone is cleared by the CYP3A4 and it strongly inhibits CYP2D6. It also auto-induces its metabolism. Methadone toxicity may cause bradycardia, mood swings, depression of the respiratory centre and an increased risk of potentially lethal arrhythmia, due to QT prolongation on ECG.

Common drugs that suppress CYP3A4 include: SSRIs; antibiotics such as ciprofloxacin, clarithromycin; anti-fungal agents, such as ketoconazole; diltiazem; methadone and valproic acid. Methadone should be cautiously combined with benzodiazepine derivatives due to the significant toxicity of this combination. When
methadone is used with TCAs, methadone disturbs their metabolism, by inhibiting the activity of the CYP2D6 isozyme. Barbiturates, carbamazepine, rifampicin, risperidone and glucocorticosteroids suppress the analgesic action of methadone, probably because of interactions with CYP3A4.  

### Table 1.

<table>
<thead>
<tr>
<th>Enzyme</th>
<th>Substrate</th>
<th>Drugs suppressing the isozyme activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>CYP2D6</td>
<td>Codeine</td>
<td>Tramadol</td>
</tr>
<tr>
<td></td>
<td>SSRIs (e.g. fluoxetine)</td>
<td>TCAs (Amitriptyline)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Metoclopramide</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Haloperidol</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Methadone</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Valproic acid</td>
</tr>
<tr>
<td>CYP3A4</td>
<td>Methadone</td>
<td>SSRIs (e.g. ciprofloxacin, clarithromycin)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Anti-fungal agents (e.g. ketoconazole)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Diltiazem</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Methadone</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Valproic acid</td>
</tr>
<tr>
<td>CYP2C9</td>
<td>Warfarin</td>
<td>Amiodarone</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Anti-fungal agents</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SSRIs</td>
</tr>
</tbody>
</table>

### Conclusion

Poly-pharmacy in palliative care increases the potential risk of drug-drug interactions. Pharmacokinetic interactions involving the CYP enzymes and its genetic polymorphism play an important role in drug interactions. The common drug interactions occur with phenytoin, warfarin and common opioids (Fig. 1, Table 1). We should take great caution during co-administration of different groups of drugs.

### Fig. 1

A summary flow chart of the common drug interactions

---

**References**

Introduction

Breakthrough pain has been defined as a transitory increase in pain intensity on a baseline pain of moderate intensity, in patients on analgesic treatment being regularly administered\(^1\). Other terminologies used to describe breakthrough pain include “episodic pain”, “transient pain” and “pain flare” \(^2\). It is a distinct and common component of cancer pain which was reported by 64-90% of palliative care patients \(^1,3\). The origins of breakthrough pain are somatic (33%), neuropathic (27%), visceral (20%) and mixed organ (20%). Of those, deep somatic pain from bone metastasis is commonly encountered in our daily practice \(^3\).

Some people propose different subtypes of breakthrough pain \(^2\). Firstly, incident pain is pain precipitated by certain events such as movement and defaecation. Another type is spontaneous pain which occurs without identifiable precipitating event. Lastly, there is pain resulting from end-of-dose failure, inadequate analgesic dose or too long interval between administrations.

Why is breakthrough pain difficult to be treated? It is likely due to its changing frequency, unpredictability and high pain severity. Even worse, doses required to control incident pain may produce unacceptable adverse effects when the patient is at rest or pain spontaneously stops. Therefore, ideal medications are those of rapid onset, early peak effect, and duration of action of no more than 1-2 hours.

Pharmacological treatment - opioids

The commonly used medications for breakthrough pain are opioids in different forms:

**Oral short-onset opioids on as needed basis**

These include morphine, oxycodone and hydromorphone. However, optimal dose for breakthrough pain is controversial due to variability in presentation of pain flare.

**Normal release oral morphine (NRM)**

The Expert Working Group of the European Association for Palliative Care (EAPC) recommended the use of NRM as early as 1996. For initiation and titration, the dosage is modified every 4 hours according to patient’s need, with the NRM rescue dose being one-sixth (17%) of the total daily dose, every 2-4 hours as needed. In a consecutive sample of 159 morphine-naive patients, 50% and 75% of patients achieved pain reduction of at least 50% with respect to baseline pain score, within 8 and 24 hours after initiation of NRM \(^4\).

NRM is also said to be immediate release morphine (IRM). Is its immediate effect really achieved pain control immediately? When administrated through the oral route, onset of effect is 30-45 minutes and time to peak effect is one hour. While typical pain flare could last to the median time of 30 minutes, it may have subsided by the time IRM begins to work. Therefore, parenteral routes such as subcutaneous and intravenous routes are alternatives.
**Parenteral routes of opioid administration**

**Standard injection pen**

In two separate pilot studies, 58 patients used standard injection pen for self-administered subcutaneous rescue morphine involving hydromorphone (43 patients), morphine (11 patients) and sufentanil (4 patients). The median dose per injection was equianalgesic to 25 micrograms of subcutaneous morphine. Efficacy was rated “good” in 49 patients (84%), “moderate” in 8 patients (14%) and not noticeable in 1 patient (2%) 5.

**Patient controlled analgesia (PCA)**

Another subcutaneous measure is patient controlled analgesia (PCA) which involves continuous infusion with an initial bolus dose at 25% of the hourly dose and a lock-out interval of two hours. It allows treatment for fluctuating pain with its rapid adjustment of analgesic level to the degree of pain. However, drawbacks are invasiveness, limited mobility, technical demand and high cost 1.

**Intravenous opioid**

Apart from subcutaneous route, intravenous route has been proven to be safe and effective for breakthrough pain. The morphine IV dose was one-fifth of the oral daily dose, converted using an equi-analgesic ratio of 1/3 (IV/ oral). In 496 events of breakthrough pain, a decrease in pain intensity of more than 33% and 50% was observed in 287 (61.2%) and 115 (24.5%) events. No life-threatening event in most cases was reported 6.

There was another open-label study which verified the effectiveness of IV morphine for the treatment of episodic pain in patients receiving transdermal Buprenorphine. In 106 breakthrough pain events involving 29 patients, 98 episodes were successfully treated by pain reduction of more than 33% within 15mins and mean pain intensity was decreased to 2.9. Equivalent oral daily dose was calculated using a ratio of transdermal buprenorphine/ oral morphine of 1:75, and morphine IV/ oral ratio of 1:3 7.

**Transmucosal fentanyl**

Compared to morphine, oxycodone and hydromorphone, fentanyl series of drugs have higher lipid solubility, higher potency, shorter duration of action and better therapeutic index. Congeners of fentanyl are Alfentanil (less potent, rapid onset of action), Sufentanil (ten times more potent) and Remifentanil (faster onset and offset of effect).

**Oral transmucosal fentanyl citrate (OTFC)**

One of the popular options is oral transmucosal fentanyl citrate (OTFC) which is the first analgesics specifically investigated for breakthrough pain. Fentanyl is incorporated into the matrix and rubbed over the oral mucosa. It is administrated through the oral route with 25% fentanyl crosses the buccal mucosa, avoids the first-pass metabolism; remaining one third is swallowed giving bioavailability of 50% 2. Pain relief was similar to intravenous morphine in greater than 80% of 133 post-op non-cancer patients 8.

Truly, when OTFC was evaluated in opioid-tolerant cancer out-patients, it was suggested to be an effective alternative over intravenous morphine 9.

The Cochrane Database of Systemic Review 2009 reported four studies of 393 patients which showed that OTFC was superior to placebo, immediate-release oral morphine and previous rescue medication [2]. One point to note is that effective dose is independent of the basal opioid regime and should be titrated. A new preparation was proposed, it was the Fentanyl effervescent buccal tablets (FEBTs). Efficacy and safety has been evaluated in a double-blind, placebo-controlled study in opioid-tolerant cancer patient 10.

**Intranasal analgesia device**

Sufentanil is delivered by patient controlled intranasal (IN) analgesia device. It delivers 0.18ml as a fine spray with each depression of the nasal applicator (9 mcg). The side effects are drowsiness, nausea, facial flushing and sweating. It is published in a prospective, open-label, observational study involving 30 patients in three palliative care units in Australia. Significant reduction in pain scores at 15 and 30 minutes was reported. 77% of the study population rated IN sufentanil better than pre-study medication 11.

**Weak opioids and Non-opioids**

Non-steroidal anti-inflammatory drug (NSAID) has been commonly prescribed in incident pain due to bone metastases and mucositis while intended to avoid opioid use. The use of Tramadol for breakthrough pain was also suggested. Nevertheless, freedom from pain...
During movements is still difficulty to be achieved in patients with bone metastases.

**Non-pharmacological treatment**

It involves radioisotopes used with single dose samarium-153 (153-Sm) lexidronam intravenous infusion. The mechanism is not fully understood. Reduction of pain on movement, at rest and reduction of analgesic consumed within 4 weeks was shown 12.

**Discussion**

Breakthrough pain is a common and distinct component of cancer pain that have a negative impact on quality of life. Current approach involves giving an additional dose based on patient’s round-the-clock analgesia. An ideal medication should have a rapid onset and short duration of action.

Although a number of advanced treatment options for breakthrough pain are present in the market, there is limited availability of those new items in our daily practice. It is also said that whenever possible, breakthrough medications should be the same opioid as the round-the-clock opioid the patient is taking. However, there is still no common consensus about the choice for breakthrough pain when patients are taking certain analgesia such as Methadone and Tramadol.

In addition to the use of different treatment options for breakthrough pain, successful management depends on thorough assessment of pain characteristics. It is especially important due to high prevalence of breakthrough pain in the palliative care population. Temporal pattern of pain, which includes breakthrough pain in particular, was ranked as the second most important dimension. Nevertheless, only 16% of the pain assessment tools measure this dimension 13. Therefore, breakthrough pain may be under-detected.

**Conclusion**

OTFC is the drug specifically developed for management of breakthrough pain. Evidence exists for greater analgesic effect and better global satisfaction than the usual rescue medication. On the other hand, use of opioids such as morphine, hydromorphone and oxycodone still need to be compared. Further recommendations are also required for the use of non-opioids for breakthrough pain.

**References**

Beheaded Souls –
The psychosocial distress faced by head and neck cancer patients

Dr. Woo Kam Wing,
Palliative Care Unit, Our Lady of Maryknoll Hospital.
Correspondence: wookamwing@yahoo.com

ABSTRACT
Despite the advances in tumour targeted surgery, radiotherapy and chemotherapy, the palliative care needs of patients with head and neck cancers remain significant. The complex psychological and spiritual issues are often underestimated and underaddressed. We presented three patients with head and neck cancer, and recent studies in this area were reviewed.

HKSPM Newsletter 2010 Apr Issue No. 1 p19-22.

Story of Mr. A
Mr. A presented with hoarseness of voice in 2003 when he was 60. He was diagnosed to have laryngeal cancer with radiotherapy done at that time. He remained in remission until 2007. Tracheal stent was inserted as he was found to have recurrence below the vocal cords. The tumour continued to infiltrate and repeated stent revisions were required. Finally the mass grew around the trachea at the level of stent, inseparable from the lower cricoids cartilage and inferior pole of thyroid gland. It was decided that no further surgical nor oncological intervention would be possible.

Two days later he attempted suicide by cutting his wrist in the ward toilet. Bedside exploration and suturing was performed by the orthopedic surgeon. He was diagnosed as suffering from “situational reaction” by the psychiatrist. Tracheostomy was performed in view of potential airway obstruction, and he was transferred to our unit for palliative care.

An interview was arranged to explore the meaning of his act of deliberate self-harm. He expressed hopelessness and frustration after hearing that no more stent revision could be performed. He felt helpless after being told that nothing could be done to help him except “referring him to a hospice ward”. In fact he felt helpless that he might suffocate to death. His discomfort and mood were improved after placement of tracheostomy. He had intermittent episodes of suffocation due to blood clots, which could make him desaturate and cyanosed. He did not require any antidepressant. He was put on palliative sedation with his and his family members’ consent three months later, due to irreversible tracheostomy blockage by tumour. His morale remained positive during the last months in his journey with palliative care.

Story of Mr. B
Mr. B enjoyed good past health until 2004. He presented with left jaw swelling. Excision showed basal cell carcinoma. He received left supraomohyoid functional neck dissection and then radiotherapy. Tumour recurred in 2006 and he received radical neck dissection with another course of adjuvant radiotherapy. His disease recurred in 2007. He visited traditional Chinese medicine practitioner for follow up until December of 2008. He returned to his oncologist because of progressive neck pain with increasing discharge. He requested euthanasia because he thought that there was no further intervention which could alleviate the symptoms. He was referred to our Palliative Care Team for assessment.

During the first consultation, he admitted that his mood was low and affected by uncontrolled pain. The pain was neuropathic in nature. Examination showed a smelly fungating mass larger than 10cm encasing his neck with contact bleeding. Amitriptyline was started, both for low mood and neuropathic pain. He was also referred to Community Nursing Service for home dressing of the wound.

A few weeks later he was admitted for difficulty in swallowing. During the ward round he requested our assistance to send him to the Netherlands for euthanasia. Further exploration found that he worried he had become a burden to his sisters, who were very helpful and supportive carers during his illness. He also worried the mass would erode into his neck, causing severe bleeding. We took the opportunity to discuss
advanced care planning with him and his sisters. Emergency palliative sedation was agreed in case there was sudden carotid artery burst out. Respite hospice service was also suggested if his sisters were unable to cope and feeling overburdened. His worry of being a burden was reassured by his sisters also. He also decided not to initiate artificial nutrition by nasogastric tube or percutaneous gastrostomy in case oral feeding was not possible.

His morale and mood improved after the in-depth discussions. He was readmitted on a few more occasions later; some were for malignant wound care, some were for respite care. He finally passed away few months later with his family accompanying him at the end.

**Story of Mr. C**

Mr. C underwent partial glossectomy and selective neck dissection in 2007 due to squamous cell carcinoma of tongue at age 64. He received conformal radiotherapy but the tumour recurred few months afterwards. He then received modified radical neck dissection with right submandibular sialoadenectomy. After that he received another course of radiotherapy. Three months later he was found to have jaw recurrence. The positron emission tomography (PET) showed loco-regional recurrence and lung metastasis. He then received palliative chemotherapy starting from September 2009.

Mr. C attempted suicide by jumping from height in mid February 2009. Fortunately he was stopped by his social worker during a scheduled visit. He admitted that he trapped himself in electrical wires and suffered burns, causing multiple blisters and strangulation marks over the limbs. He was sent to hospital with amputation of left index finger and left thumb performed due to full-thickness burn complicated by infection. He was diagnosed to have depression by psychiatrist with sertraline and lorazepam started. He was put on nasogastric tube for feeding as the tumour had obstructed the whole oral cavity. Surgical resection was not possible and patient refused palliative radiotherapy. He was sent to our palliative care unit for further care.

Mr. C was a chronic smoker and drinker. However he lived alone and had no close relatives in Hong Kong. Upon arrival he was already bed-ridden and cachexic. There were multiple strangulation marks around his hands. The fungating tumour was obstructing the oral cavity. He could only communicate by nodding or shaking his head. Poor hygiene was noticed. We started morphine for pain control as he indicated severe cancer pain. We also applied metronidazole solution over the wounds. Our medical social worker contacted the NGO who would provide funeral service to patient. He passed away in the following morning.

**Beheaded Souls, are we ready?**

The physical and psychological needs of head and neck cancer (HNC) patients are challenging1. The palliative care needs of these patients are not decreased by advances in the surgical and oncological fields.

There are unique but under-addressed psychological burdens faced by HNC patients2.

1. Pre-morbid adaptive coping deficits

Smoking and alcohol use increase the prevalence and mortality of head and neck cancer. Duffy et al. screened 973 head and neck cancer patients, 46% were positive for depressive symptoms, 30% smoked and 16% were problem drinkers3. Depressive symptoms and smoking status were associated with negative quality of life. Problem drinking is more prevalent among HNC patients than the general population (16% vs. 8.5%) 3. Alcohol use itself increases the mortality of HNC patients4. Over one third of patients continue smoking even after the diagnosis5.

2. Higher reported rates of suicide

Analysis from the data of Surveillance, Epidemiology, and End Results (SEER) program found that HNC patients had higher suicide rates. Kendal found that among male cancer patients, HNC (p<0.001) and myeloma (p=0.02) had higher completed suicide rates.6 It was found that among HNC patients, being male, older, surgery being contraindicated, histology of cancer being of higher grade, suffering oropharyngeal cancer will have increased hazards ratio of completed suicide. Misono et al. studied 3,594,750 patients diagnosed with cancer from 1973 to 2002. They found that head and neck cancer patients had higher suicide rates comparing with the other cancer types as well as the general population7. While lung cancer and stomach cancer patients had the highest suicide rates with standardized mortality ratio (SMR, general US population suicidal rate =1) 5.74 and 4.68 respectively, oral cavity and pharyngeal cancer, and laryngeal cancer ranked third (SMR = 3.66) and fourth (SMR = 2.83) respectively.
3. Unique barriers of communication and emotional expression

HNC can distort facial expression, which is the most important part of emotional expression. The cancer itself, treatment and its complication can affect voice production. Patients can become dysphasic or aphasic. Tracheostomy, if performed, may further hinder the patients’ ability to communicate.

4. Unique stress of illness

The line between curative and palliative intervention in HNC is blur. The uncertainties make care planning in HNC patients difficult and may even produce ethical dilemmas. A Japanese study reviewed the dying process of 55 terminal HNC patients retrospectively and reported that 30% patients died suddenly, mainly due to haemorrhage. These illness trajectories pose significant psychological stress on our patients. More importantly, facial disfigurement and dysfunction will produce severe psychological trauma to HNC patients because of its visibility. The face has its specific role in human psychological being (see Table 1) and post HNC surgery patients often reported suffering psychological impairment due to distorted body image (Table 2). Dropkin defined body image as the perception of one’s body as a physiologic-psychologic-social unity, which is dependent upon: (i) individuals’ memory of his pre-surgical appearance and function, (ii) idealized self-appearance and function and (iii) his current status (Table 3). Callahan uses the concept of “internal conflicts vs. external conflicts” to describe the psychological distress. The external conflict is due to the large unsightly, oozing and smelly tumour which distorts the individual’s appearance. The internal conflicts stem from the heightened sense of shame, self-consciousness and hyper-vigilance. HNC patients are highly sensitive to perceived stares by passers-by.

Management of the psychological distress of HNC patients

The fundamental step of assessment and management of psychological distress in HNC patients is ASKING. The multi-disciplinary team, involving physicians, nurses, physiotherapists, occupational therapists, speech therapist, dietitians, social workers, spiritual counselors, volunteers and the larger social network is essential. The family and patient should be involved in managing the psychological distress. General intervention includes good symptom control and treating any associated depression is essential. Therapy should focus on patients’ sense of hopelessness and fracture of dignity. Discussions surrounding spirituality by skilled spiritual counselors would be helpful. Communication strategies and social network should be enhanced. Advance care planning with the patient may help to reduce patients’ uncertainty.

Table 1. Role of face
- Communicates ideas, perception, intensity of emotion, self-reflection and awareness
- Reflects self-concept and self-esteem
- Reflects feeling about the body
- Communicates pride or shame in one’s appearance
- Mirrors the lifestyle chosen
- Radiates one’s personality style

Table 2. Psychological distress reported by patients after HNC surgery
- Feeling of distress
- Negative changes in self-image
- Loss of self-esteem
- Perceptions of limited attractiveness
- Diminished feelings of sexuality due to embarrassment
- Increased isolation

Advances in technology have made communication easier. A survey found that one-third of head and neck cancer patients are interested in e-mailing their clinicians but only 9.5% reportedly did so. The most common issues addressed would be symptom management and prescription refills. However, direct e-mail communication between patients and health care staff is not popular in Hong Kong. In the Netherlands, an information support system is set up for the head and neck cancer patients to facilitate communication between professionals and patients. Patients can also contact other fellow patients and search for information related to their illness through the system. In case there is change in symptoms, the system assists in early detection by screening using tailored questions.

Recent studies have focused on the role of prophylactic antidepressants as well as behavioural modulating antidepressants in HNC patients. Lydiatt et al. randomized 23 non-depressed, non-psychotic, non-suicidal HNC patients undergoing treatment to either placebo or citalopram. After treatment for 12 weeks, only 2 out of 12 patients receiving citalopram met the...
criteria for depression using the Hamilton Rating Scale for Depression in comparison with 5 out of 10 patients in the placebo group. However the p-value is 0.17 only. Two patients in the placebo group became suicidal but none in citalopram group. The only statistically significant difference was found in the Clinical Global Impression – Severity rating – 60% patients in the placebo group rated at least “mildly ill” in comparison with only 15% in the citalopram group (p=0.04). Although limited by the small sample size, this study provides groundwork for future research in use of antidepressants.

Bupropion and varenicline are behavioural modulating antidepressants and are currently being prescribed for smoking addiction. Duffy et al. randomized 184 HNC patients into either usual care or a nurse-administered intervention protocol, which included cognitive behavioural therapy for 9 to 11 sessions plus appropriate medication. All participants were either smokers, problem drinkers or depressed patients. Bupropion would be used if the subject was either depressed or had been a smoker in whom the nicotine patch had failed. They found that the intervention group had decreased smoking rates by 50% (47% vs. 31%, p<0.05). The authors also claimed that there were clinically important but statistically insignificant reduction in alcohol use and depressive symptoms.

**Conclusion**

According to Eric Cassell, the obligation of physicians is to relieve human suffering. HNC patients face unique illness trajectories with specific problems affecting their intactness. How can we preserve human integrity for these beheaded souls?

### Table 3. Disfigurement/ Dysfunction Scale11

<table>
<thead>
<tr>
<th>A. Disfigurement</th>
<th>B. Dysfunction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minor</td>
<td></td>
</tr>
<tr>
<td>1. Radical Neck Dissection (RND)</td>
<td>1. Loss of smell</td>
</tr>
<tr>
<td>2. Cheek Resection with Forehead Flap Repair</td>
<td>2. Unilateral hearing loss</td>
</tr>
<tr>
<td>3. Total Parotidectomy with Facial nerve Sacrifice</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td></td>
</tr>
<tr>
<td>4. Total Laryngectomy</td>
<td>3. Impaired mastication</td>
</tr>
<tr>
<td>5. Bilateral Radical Neck Dissection</td>
<td>4. Speech impairment</td>
</tr>
<tr>
<td>6. Orbital Exenteration</td>
<td>5. Unilateral loss of vision</td>
</tr>
<tr>
<td>7. Hemimandibulectomy with RND</td>
<td>6. Impaired salivary control</td>
</tr>
<tr>
<td>8. Nasal Amputation</td>
<td>7. Impaired deglutition</td>
</tr>
<tr>
<td>Severe</td>
<td></td>
</tr>
<tr>
<td>9. Anterior Partial Mandibulectomy</td>
<td></td>
</tr>
<tr>
<td>10. Segmental Mandibulectomy with RND</td>
<td></td>
</tr>
<tr>
<td>11. Orbital exenteration with Radical Maxillectomy</td>
<td>8. Aphonia</td>
</tr>
</tbody>
</table>

### References

Opioid Switching

Dr. Mansha Hari Khemlani, Palliative Care Unit, Caritas Medical Centre.
Correspondence: manshahk@hotmail.com

ABSTRACT
Pain is one of the most common and often most feared symptom in cancer patients. Effective management of cancer pain remains a high priority and is an ongoing challenge in both the oncological and palliative care settings. The World Health Organization (WHO) recommends the use of strong opioids for management of moderate to severe cancer pain. The European Association of Palliative Care (EAPC) recommends morphine as the first-line strong opioid for these patients. Response to morphine varies significantly between patients and even within the same patient at different stages of the illness trajectory. Finding a morphine dose that provides adequate analgesia with tolerable side-effects can be difficult. While most cancer patients tolerate morphine well, about 10-30% of patients do not and suffer from inadequate analgesia, intolerable side-effects or a combination of both. The EAPC Research Network gathered evidence-based clinical practice recommendations on interventions to manage the side-effects of oral opioids, including dose reduction of the systemic opioids, symptomatic management of the side-effect and changing the route of administration. If all fails, opioid switching, the therapeutic strategy of switching one opioid for another, may be the only option for symptomatic relief. There is evidence to support the therapeutic maneuver of opioid switching in clinical practice, although the evidence is largely anecdotal or based on observational and uncontrolled studies. Opioid switching is not without intrinsic problems. Given the wide conversion ratios reported in literature, we risk under- or over-dosing. It is recommended that opioid switching should not be a mere mathematical calculation, but form part of a more comprehensive assessment of pain, side-effects, comorbid diseases, and concomitant drugs. Good cancer pain control remains a high priority for doctors and treatment should be highly individualized.

Introduction to cancer pain
Pain is recognized as an important but neglected public health issue. About 80% of patients with advanced cancer suffer from pain as the major symptom. In about 60% of these, the pain is moderate to severe in intensity. The World Health Organization (WHO) released a set of guidelines under the title Cancer Pain Relief in 1986, and is now widely translated and distributed. Promotion of the 3-step analgesic ladder is among the core components, and strong opioids are recommended for moderate to severe cancer pain (Step 3).

Morphine use in cancer pain
The European Association for Palliative Care (EAPC) published recommendations on the use of opioids in cancer pain in 2001. Morphine remains as the first choice of strong opioids for cancer pain, based on its relative ease of availability, familiarity to clinicians, established effectiveness, simplicity of administration and relative inexpensive cost.

It is generally stated that morphine has no ceiling dose; the appropriate dose of morphine is one that controls pain without causing significant side-effects. Escalation of morphine doses is an important consideration when pain control is suboptimal, subjected to limitation by intolerable side-effects. Management of opioid-related side-effects remains a major clinical challenge, and the recommended evidence-based clinical practices to minimize side-effects of opioids include: 1) dose reduction of the opioids, 2) symptomatic management of the side-effect, and 3) changing the route of administration.

However, there are limited studies which compare the actual effectiveness of these different interventions in reducing opioid-related side-effects. The pain control of a significant portion of patients on morphine is limited by either inadequate analgesia, intolerable side-effects or a combination of both. The later affects about 10-30% of patients on morphine, for whom opioid switching is recommended.

Opioid switching – definition
Opioid switching is a term given to the clinical practice of substituting one strong opioid for another in an attempt to achieve an optimal balance between analgesia and opioid-related side-effects. The term “opioid switching” is sometimes used interchangeably with “opioid rotation” or “opioid substitution”. However “opioid rotation” sometimes includes changing the route of administration of the same opioid.
The practice of opioid switching and the available alternative opioids used vary widely between different centers, depending on local experience and the available alternatives to morphine. For simplicity purposes, the term “opioid switching” will be used in the remaining of this article to represent the clinical practice of substituting one strong opioid for another. Opioid switching is gaining popularity as a therapeutic strategy. It has become established practice in pain management in helping to achieve a more favorable analgesia vs. side-effect profile.

**Incidence of opioid switching**

In a review article published in 2008, the incidence of opioid switching from retrospective trials ranged from 20 to 44%. Trials on opioid switching mainly focus on the positive results, and the condition for switching is not described in detail or standardized. In two recent prospective studies published in 2006 and 2009, 25% and 34.2% of cancer patients respectively required opioid switching after using their own local guidelines or protocols on pain management.

**Indications for opioid switching**

In a more recent prospective study published in 2009, the indications of opioid switching in 118 cancer patients in an acute palliative unit were evaluated. The reasons for switching in these 118 patients included uncontrolled pain in 15.2%, side-effects in 28.8% and combination of both uncontrolled pain and side-effects in 50.8%.

**Opioid switching: What does evidence say?**

Some studies on opioid switching have shown an improvement in the side-effect profile, especially with improvements in relation to side-effects related to the central nervous system and the gastrointestinal system. Whether there is a true difference among opioids in relation to the side-effect profile is subject to considerable debate. Some argue that the overall reduction in the morphine equivalent daily doses (MEDD), due to incomplete cross-tolerance, may have caused reduced opioid-related side-effects rather than actual differences between opioids at the same equianalgesic doses. Large, randomized, controlled trials have not been performed to directly compare opioids, and smaller individual trials are underpowered to demonstrate superiority of one opioid over another.

Some studies have reported factors associated with increased need for opioid-switching including terminal stages of cancer and longer length of stay. In a retrospective analysis including 273 cancer patients amongst whom 103 patients (37.7%) required opioid switching, an increased incidence of opioid switching was found to be associated with terminal stages of cancer. In another retrospective analysis including 191 terminal cancer patients, 80 patients (41.9%) of whom required opioid switching, a longer length of stay in a palliative care unit was found to be associated with an increased incidence of opioid switching.

The Cochrane review in 2004 identified 52 reports on opioid switching to improve pain relief and drug tolerability. This review included 23 case reports, 15 retrospective studies or audits, and 14 prospective uncontrolled studies. No randomized controlled trials on opioid switching were identified. All 52 reports, except one study, showed favorable outcomes in improving pain control and/or reducing opioid-related side-effects. Although the evidence supporting opioid switching is largely anecdotal, or based on observational and uncontrolled studies, the reviewers concluded that for patients with inadequate pain relief and intolerable opioid-related side-effects, a switch to an alternate opioid may be the only option for symptom relief.

Another systematic and critical review on opioid switching published in 2006 included 31 reports. This review reported that opioid switching resulted in clinical improvement in more than 50% of patients with chronic pain with poor response to one opioid. However, this data is also based on open studies and small case series.

**Interindividual variation & role of pharmacogenetics**

The concept that different individuals respond to morphine differently is not a new one. In the 1950s, Lasagna & Beecher reported a 65% “success rate” with morphine in an experimental pain model. Opioid switching is based on incomplete cross-tolerance and differences in pharmacokinetic and pharmacodynamic properties which account for inter-individual variation in response to opioids. Recent research in pharmacogenetics, based on animal and human models, has highlighted the
importance of a genetic influence on morphine responsiveness. Research has identified differences in μ-opioid receptor densities, variations of the gene coding for this receptor and differences in the process of receptor renewal. Genetic differences in factors affecting drug transportation and metabolism have also been identified.

Intrinsic limitations with opioid-switching

Despite the growing popularity of opioid switching as a therapeutic strategy in pain management, opioid switching is not without problems. The problems with opioid switching are related to:

1. Opioid availability. Opioid-switching is limited by the availability of alternate opioids, or availability of a particular preparation. Problems with opioid switching are related to:

2. Problems with conversion tables. In switching from one opioid to another, equianalgesic conversion tables are used to guide the dose conversion. However, there are intrinsic problems with equianalgesic dose conversion tables. Many available conversion tables were calculated in opioid-naïve patients. Some conversion data were derived from single-dose studies or studies not originally designed to evaluate equianalgesic dosing. This can result in under- or over-dosing. Furthermore, there is no one universally adopted conversion table. Different conversion ratios exist and often do not take into account for age, organ failure or polypharmacy, all of which may warrant adjusted doses. In some situations e.g. methadone to fentanyl, conversion tables do not exist. Opioid switching also has demonstrated directionality; that is a reciprocal ratio cannot be used for reverse switching.

Recommendations

Since opioid switching is not without intrinsic problems, it is recommended that clinicians thoroughly consider measures to control side-effects, re-evaluate the cancer pain, and consider use of adjuvant analgesic or non-pharmacological measures of pain control, before putting off a considerably effective therapy.

If opioid switching is the only available option, some authors emphasize that opioid switching should not be a mere mathematical calculation. They recommend that opioid switching should form part of a more comprehensive evaluation of pain, side-effect intensity, comorbidities and concomitant drugs. Therefore it is recommend that the process of reaching an optimal dose after opioid-switching should be highly individualized, particularly when patients are switched from high doses of opioids, given the wide variation of conversion ratios given in literature.

Summary

Opioid switching is a therapeutic intervention to help improve analgesia and side-effect profile. Existing equianalgesic conversion tables serve as a guide only. Given the wide variation of conversion ratios in literature, in reaching an optimal dose after opioid-switching, each case needs to be individualized.

References

Palliative Medicine Grand Round

Malignant Intestinal Obstruction

Dr Li, Cho Wing Bryan,
Palliative Medical Unit, Grantham Hospital.
Correspondence: lcw167@hotmail.com

ABSTRACT

Intestinal obstruction is not uncommon in patients with terminal cancer. Patients suffer from various physical and psychological distress associated with it. We presented a case of intestinal obstruction and outlined the various treatment options. Many of the treatments have limited efficacy. Multidisciplinary team approach is needed to facilitate care of patients suffering from such complex symptomatology.

HKSPM Newsletter 2010 Apr Issue No.1 p26-27.

Case History

Madam C, 45 years old, suffered from metastatic cancer of ovaries. She underwent de-bulking surgery followed by 10 cycles of chemotherapy. However, the disease progressed despite treatment. She developed malignant ascites requiring repeated peritoneocentesis. She was admitted for repeated vomiting, abdominal distention and colicky abdominal pain. Abdominal X-rays showed small bowel obstruction at multiple sites with fluid levels. Trials of dexamethasone and hyoscine butylbromide were not successful. Surgical treatment was not possible. She was then transferred to our palliative care unit.

She was married for 5 years, and she gave birth to her only baby 3 years ago before her disease onset. She was living with her husband. As a result of intestinal obstruction, she could not take care of her son. She was upset for the separation from her son. She complained of colicky abdominal pain and vomiting which disturbed her sleep. Her husband was well aware of the patient’s terminal disease, but felt sad and uneasy to share his feelings with the patient because he used to be an introverted person.

Continuous subcutaneous infusion of octreotide was given for intestinal obstruction. Haloperidol was given for nausea and vomiting. Morphine was given for abdominal pain. However, despite 2 weeks of medical treatment, there was no resolution of intestinal obstruction. Vomiting was partially relieved by haloperidol.

Our nurses and our clinical psychologist offered psychological support to her. Family gatherings were arranged in ward, together with her husband and son. Photos and video were taken to record the messages that she would like to pass to her family. Her condition went downhill gradually and she passed away after one month of hospitalization.

Discussion

Intestinal obstruction is not uncommon in terminal cancer. Up to 40% of terminal ovarian cancer patients developed intestinal obstruction.1 It is a symptom that poses great challenge to physicians.

Patients suffer various physical and psychological distress resulted from intestinal obstruction. They lost the very basic enjoyment of life, eating. Good taste of food and the feeling of a full stomach are lost. There are common associated physical discomforts including colicky pain, nausea, vomiting and weakness. It can result in frustration and fear. Long duration of symptoms together with unpredictability of symptoms makes prolonged hospitalization common and home leave difficult.

Various medical treatments are used for palliation of intestinal obstruction. For continuous pain, analgesics shall be used according to WHO guidelines. Strong opioids shall be used for severe pain. For spasmodic abdominal pain, anticholinergics like hyoscine butylbromide can be tried. Antiemetics, like haloperidol, working in the chemoreceptor triggering zone, can be tried. Besides, anticholinergics and somatostatin analogue can be used to reduce gastrointestinal resolution of intestinal obstruction. According to Cochrane review 2, there was a trend favoring the use of corticosteroid compared to control.

Malignant Intestinal Obstruction

HKSPM Newsletter 2010 Apr Issue 1 P26
The side effects were minimal, though there was no effect on survival. The number needed to treat was estimated to be 6 according the three trials that were reviewed. Selective 5-hydroxytryptamine receptor antagonists, such as granisetron 3 mg iv q24h, has also been demonstrated to be useful.

Surgical treatment is beneficial in a small number of patients. In a retrospective analysis of data on 68 operations performed on 64 patients, the mean time from original diagnosis of ovarian cancer to obstruction was 2.8 years. Surgical correction (intestinal surgery performed for relief of obstruction) was attained in 57 of 68 (84%) cases. Successful palliation (the ability to tolerate a regular or low-residue diet at least 60 days postoperatively) was achieved in 71% of cases where surgical correction was possible. Perioperative mortality rate was 6%. The median survival of the entire cohort was 8 months. However, results from literatures were heterogeneous. Cochrane review in 2000 by Feuer and Broadley showed no definite conclusion on effectiveness of surgery for intestinal obstruction.

References

Diarrhea in Acute Radiation Proctitis
Dr Chan Kwok Ying,
Palliative medical Unit, Grantham Hospital.
Correspondence: cky842@yahoo.com.hk

ABSTRACT
A case of acute radiation-induced proctitis treated with prednisolone enemas in palliative care was reported. A 51-year-old man, with history of advanced carcinoma of lung and bone secondaries, was admitted to palliative medical unit for in-patient radiotherapy to lumbar spine. During his stay, he developed profuse diarrhea due to radiation-induced proctitis. He was treated with prednisolone enema treatment with good response. DISCUSSION: Acute radiation-induced proctitis is a common adverse effect of radiotherapy to the lower spine and pelvic area. The risk factors, diagnosis and the use of Amifostine and Sulfasalazine for prevention of radiation proctitis are reviewed. Topical steroid and Butyrate enema have been found to be useful in small randomized trials. Potential useful medications included topical steroid, topical Butyrate and Sulfasalazine, but large controlled studies are warranted.

Acute radiation proctitis usually resolves after stopping the radiotherapy. However, the symptoms are sometimes bothersome and need medical treatment. The following case illustrates a good example.

Case history
Mr. Lam was a 51-year-old gentleman. The diagnosis of advanced carcinoma of lung with bony metastasis was made in 2005 and he was given genfitinib for palliative treatment. He had...
The side effects were minimal, though there was no effect on survival. The number needed to treat was estimated to be 6 according the three trials that were reviewed. Selective 5-hydroxytryptamine receptor antagonists, such as granisetron 3 mg iv q24h, has also been demonstrated to be useful 3.

Surgical treatment is beneficial in a small number of patients. In a retrospective analysis [4] of data on 68 operations performed on 64 patients, the mean time from original diagnosis of ovarian cancer to obstruction was 2.8 years. Surgical correction (intestinal surgery performed for relief of obstruction) was attained in 57 of 68 (84%) cases. Successful palliation (the ability to tolerate a regular or low-residue diet at least 60 days postoperatively) was achieved in 71% of cases where surgical correction was possible. Perioperative mortality rate was 6%. The median survival of the entire cohort was 8 months. However, results from literatures were heterogeneous. Cochrane review in 2000 by Feuer nd Broadley5 showed no definite conclusion on effectiveness of surgery for intestinal obstruction.

References

Diarrhea in Acute Radiation Proctitis
Dr Chan Kwok Ying,
Palliative medical Unit, Grantham Hospital.
Correspondence: cky842@yahoo.com.hk

ABSTRACT
A case of acute radiation-induced proctitis treated with prednisolone enemas in palliative care was reported. A 51-year-old man, with history of advanced carcinoma of lung and bone secondaries, was admitted to palliative medical unit for in-patient radiotherapy to lumbar spine. During his stay, he developed profuse diarrhea due to radiation-induced proctitis. He was treated with prednisolone enema treatment with good response. DISCUSSION: Acute radiation-induced proctitis is a common adverse effect of radiotherapy to the lower spine and pelvic area. The risk factors, diagnosis and the use of Amifostine and Sulfasalazine for prevention of radiation proctitis are reviewed. Topical steroid and Butyrate enema have been found to be useful in small randomized trials. Potential useful medications included topical steroid, topical Butyrate and Sulfasalazine, but large controlled studies are warranted.

HKSPM Newsletter 2010 Apr Issue No.1 p27-29.

Acute radiation proctitis usually resolves after stopping the radiotherapy. However, the symptoms are sometimes bothersome and need medical treatment. The following case illustrates a good example.

Case history
Mr. Lam was a 51-year-old gentleman. The diagnosis of advanced carcinoma of lung with bony metastasis was made in 2005 and he was given genfitinib for palliative treatment. He had
hypertension and suffered from stroke with left hemiplegia in 2006. Since then, he became chair-bound and was cared by his wife at home. His son was studying abroad in Australia.

He was admitted to our unit for pain control. He also received radiotherapy to lumbar spine (L5) during the hospital stay. The original plan was to give radiotherapy for 10 days. However he complained of severe diarrhea after 3 days of the treatment and the diarrhea failed to respond to conventional treatments including diphenoxylate/atropine (Lomotil) and loperamide. All the work up for infectious cause including stool culture, stool for ova, cyst, and clostridium difficile toxin were negative. He was suspected to suffer from acute post-radiation proctitis after ruling out the other causes.

In view of persistent symptoms, the radiotherapy treatment was withheld. Topical enema in the preparation of a mixture of Prednisolone 30 mg and the fleet enema was given for 2 days. The clinical response was satisfactory, with markedly decrease in bowel frequency. Although the radiotherapy was withheld, pain control could be achieved by adjusting the dose of morphine.

**Diarrhea in Acute Radiation Proctitis**

Radiation injury to the lower intestine is usually encountered following treatment of cancers of the anus, rectum, cervix, uterus, prostate, urinary bladder, and testes. Thus, the rectum and sigmoid colon are most often affected. The type of injury caused by radiation exposure can be divided into two categories: acute and chronic. Acute radiation injury occurs within six weeks of therapy. Symptoms include diarrhea, rectal urgency or tenesmus, and, uncommonly, bleeding. These symptoms usually resolve without specific therapy within two to six months. Various risk factors have been identified and listed in Table 1.

Table 1  Risk factors for developing acute radiation proctitis
- Advanced patient age
- Prior abdominal surgery leading to intraperitoneal adhesions (Adhesions fix portions of the small or large intestine in the radiated field.)
- History of pelvic inflammatory disease
- Hypertension
- Diabetes mellitus
- Thin physique
- Administration of chemotherapy
- Other risk factors (eg, collagen vascular diseases, xeroderma pigmentosum, Cockayne syndrome)

Analysis of multiple risk factors for predictive value demonstrates that multiple laparotomies, hypertension, and thin physique have the highest correlation with the development of radiation enteritis. Administration of chemotherapy with radiation therapy correlates with an increased incidence of radiation-related intestinal damage.

**Diagnosis**

In most patients, the diagnosis can be confirmed during colonoscopy or sigmoidoscopy. Mucosal features consistent with radiation injury include pallor with friability, and telangiectasias, which can be multiple, large, and serpiginous; these changes tend to be continuous.

Although mucosal biopsies are not diagnostic, they can help to exclude other causes of proctitis such as infection or inflammatory bowel disease. A histological classification system has been proposed but its role has not yet been defined.

In a sequential clinicopathologic study during pelvic radiotherapy, endoscopic pathology was maximal at 2 weeks. Biopsies obtained during treatment exhibited atrophy of the surface epithelium, acute cryptitis, crypt abscesses, crypt distortion and atrophy, and stromal inflammation. Histologic changes, particularly those in the surface epithelium, were consistently more pronounced at 2 weeks than they were at 6 weeks.

In contrast to clinical symptoms, endoscopic changes stabilize and histological changes regress from the 2nd to the 6th week of treatment. These results may have implications for the design and timing of prophylactic and therapeutic interventions to reduce radiation proctitis.

**Prevention**

In addition to modifications in the radiation technique and dose, a number of other preventive strategies have been applied in an effort to lessen the incidence and severity of radiation proctitis. Clinical trials have provided some evidence suggesting that there is a benefit associated with the use of amifostine and oral nonabsorbed salicylates (sulfasalazine and balsalazide).

1. **Amifostine**

Several controlled trials have shown a benefit for prophylactic amifostine in reducing treatment-related toxicity, without diminishing antitumor efficacy.

In a randomized trial of 100 patients with advanced inoperable rectal cancer undergoing external beam radiation: patients treated with
daily IV amifostine prior to radiation had no moderate or severe delayed radiation toxicity to normal pelvic tissue compared with 14 percent in patients treated with radiotherapy alone.\(^2\)

A reduction in both acute and late gastrointestinal toxicity was noted in a second trial in which 205 patients undergoing radiation therapy for various pelvic malignancies were randomly assigned to daily IV amifostine or no amifostine. The rates of grade 2 gastrointestinal toxicity were significantly less in the amifostine group at week 3 (22 versus 6 percent), and this difference was even more pronounced at week 7 (40 versus 0 percent).\(^3\)

2. Sulfasalazine

Nonabsorbed salicylates appear to have some protective effect against radiation-induced proctitis. This approach was evaluated in a trial in which 87 patients were randomly assigned to sulfasalazine (500mg oral twice daily) or placebo while receiving radiotherapy to the pelvis for rectal, gynaecologic, prostate, or bladder cancer. Diarrhea was significantly less in patients assigned to sulfasalazine (55 versus 86 percent), but whether this could prevent long-term radiation injury remains to be determined.\(^4\)

The Multinational Association of Supportive Care in Cancer and the International Society for Oral Oncology recommend the routine use of oral sulfasalazine (500mg orally twice daily) to help reduce the incidence and severity of radiation-induced enteropathy in patients receiving radiation therapy to the pelvis.\(^5\)

**Medical treatment for diarrhea in acute radiation proctitis**

1. **Topical steroid**

   It was found to be effective when used alone \(^6\) or in combination with oral sulfasalazine \(^7\) for the treatment of acute radiation-induced proctitis. The steroid includes hydrocortisone and prednisolone (40mg daily). However these were only small trials.

2. **Topical butyrate**

   The effect of topical butyrate has been evaluated in a randomized, crossover trial for the treatment of acute radiation-induced proctosigmoiditis. The advantage of butyrate over placebo, expressed as CI (confidence interval), odds ratio, and p value was significant for almost all the clinical, endoscopic and histological factors taken into consideration.\(^8\) However, it has shown to have no impact on the incidence and severity of late proctitis in a recent study.\(^9\)

**Summary**

Diarrhea in acute radiation proctitis can vary from mild to severe in intensity. Potential useful medications include topical steroid, topical butyrate, sulfasalazine, but large controlled studies are warranted.

**References**

3. Athanassiou H; Antonadou D; Coliarakis N; Kouveli A; Synodinou M; Paraskevaidis M; Sarris G; Georgakopoulou GR; Panousaki K; Karageorgis P; Throuvalas N. Protective effect of amifostine during fractionated radiotherapy in patients with pelvic carcinomas: results of a randomized trial. Int J Radiat Oncol Biol Phys 2003 Jul 15;56(4):1154-60.
5. Keefe DM; Schubert MM; Elting LS; Sonis ST; Epstein JB; Raber-Durlacher JE; Migliorati CA; McGuire DB; Hutchins RD; Peterson DE. Updated clinical practice guidelines for the prevention and treatment of mucositis. Cancer. 2007 Jan 18;109(5):820-831.
Introduction
Parenteral Nutrition allows the provision of nutrients via the vein, bypassing the requirement for gastrointestinal absorption. Its use in patients with advanced malignancy is always a controversial issue. Patients with malignant bowel obstruction may suffer malnutrition due to prolonged suboptimal oral intake. The administration of parenteral nutrition should be considered on an individual basis. This article would present a lady with malignant bowel obstruction who had received parenteral nutrition in our palliative medical unit, which provided her good energy level and time to settle her important life matters.

Case History
A 58 year-old lady who suffered from metastatic carcinoma of unknown primary presented in January 08 with malignant pleural effusion. Pleural tapping and biopsies failed to confirm the primary malignancy, while she received Talc-pleurodesis with good control of her pleural effusion. She had further imaging studies including PET-CT scan and screening of tumour markers. Pathologist failed to ascertain the primary of origin and she was treated as primary CA lung with carboplatin and pemetrexed (Alimta) and maintained on erlotinib (Tarceva) in the private sector. She remained relatively asymptomatic until March 09.

She developed malignant ascites in March 09 requiring repeated abdominal tapping. However she developed malignant intestinal obstruction in April 09, with CT-scan confirming small bowel distension and local segmental thickening at duodenal-jejunal junction. The surgical team performed gastro-jejunosotmy on her and retrieved samples for lymph nodes and bowel biopsies. Post-operatively, patient required 2 weeks of intensive unit care. However the biopsy samples and further PET-CT imaging still failed to confirm her primary malignancy origin.

She had recurrence of malignant intestinal obstruction in July 09 and unable to undergo further palliative surgery. Bowel decompression by Ryles tube was performed. She was started on intravenous metoclopramide and dexamethasone but her intestinal obstruction failed to response.

She further consulted private surgeon and oncologist, and agreed that her condition was not amendable to further surgical debulking or chemotherapy. Parenteral feeding as a possible option was introduced and patient insisted to proceed. Therefore, Hickman catheter was inserted and patient was started on parenteral nutrition. She was transferred to our Palliative Medical ward in July 09.

She appeared anxious upon arrival and worried about the treatment that we could prescribe, with particular concern on continuation of her TPN treatment. On further questioning, she expressed that her two major concerns are the school-bus business and the forth coming birth of her grandchild. She accepted the possible complications of parenteral nutrition including line sepsis, cholestasis and immobility during the

Parenteral Nutrition in Malignant Bowel Obstruction: An Ethical Dilemma in Palliative Care

Dr. Benjamin HW Cheng,
Palliative Medical Unit, Grantham Hospital
Correspondence: benchw@hkstar.com

ABSTRACT
Provision of parenteral nutrition in patients with advanced malignancy is always an ethical dilemma. It involves careful discussion with patients regarding the possible benefits of improve in energy level and possibly survival, together with the numerous side effects and prolonged hospital admission for TPN administration. We reported a lady with malignant bowel obstruction secondary to metastatic carcinoma of unknown origin, who had received TPN at her final 2 months which benefited her from improved energy level with her life business settled. Her improved physical condition in final stage of life also provided chance for our palliative team in fulfilling her psychological and spiritual needs.

HKSPM Newsletter 2010 Apr Issue No.1 p30-32.
Her performance status was satisfactory, and she was able to walk independently indoor and under supervision outdoor. After careful discussion, we maintained on her Nutriflex Lipid-Peri 1250ml daily, with her body weight and serum albumin being monitored regularly. Despite her slow deterioration in body weight and serum albumin level (Table 1), the initial 2 months of activity level remained satisfactory. She showed acceptance to her terminal illness and enjoyed day-centre events and home leave during weekend. She witnessed the birth of her grandson and even attended the feast held for celebration. She had her school-bus business handled to her son. She attended religious activities held by our hospital chaplain and was baptized. She was much more prepared for her death under good care of our multi-disciplinary team. TPN was withheld few days prior to her death in view of clinical deterioration and was well accepted by family members. Patient finally succumbed after 3 months of care in our unit.

**Discussion**

**TPN Usage in Terminal Illness**

Use of parenteral nutrition was first reported in infants as an alternative to oral feeding in year 1969 \(^1\). Since then its application has increased considerably to include use in patients with post-operative high-output fistulas \(^2\), necrotizing pancreatitis \(^3\), as well as inflammatory bowel disease \(^4\). Its use in patients with advanced malignancy had been reported, but clinical evidence is still lacking.

Patients suffering from advanced cancer usually have significant weight loss due to cancer cachexia. Cachexia is a complex syndrome characterized by a chronic, progressive, involuntary weight loss which is poorly or only partially responsive to standard nutritional support. It is usually attributable to two main components, namely a decreased nutrient intake, which may be due to critical involvement of the gastrointestinal tract by the tumour, or to cytokines and similar anorexia-inducing mediators; as well as metabolic alterations due to the activation of systemic pro-inflammatory processes \(^5\).

There are no randomized controlled trials evaluating the effectiveness of TPN in incurable cancer patients, because randomization between TPN and no TPN is not normally ethically acceptable in such conditions. Furthermore, it is hard to consider TPN as a palliative treatment aiming to relieve symptoms, without addressing the basic disease, because often these patients are anorexic and there is no evidence that parenteral nutrition improves this or associated asthenia.

The main rationale for giving TPN in cancer patients is the awareness that survival of healthy individuals submitted to total macronutrient starvation, hardly exceeds 2 months. Besides, in patients with malignant bowel obstruction without nutritional support the mean survival is around 48 days \(^6\). In contrast, 20-50% of advanced cancer patients selected for TPN is alive at 6 months \(^7\).

Two clinical practice guidelines were identified that met the inclusion criteria specifically on the use of parenteral nutrition in palliative care (Table 2) \(^8,9\). In general, these guidelines based on the principal on risks and benefits, recommending TPN use only in selected patients with malignant obstruction precluding oral intake who have an expected prognosis of at least a month and a Karnofsky performance status exceeding 50.

**Clinical Dilemmas**

Even if clinical guidelines exist and the success of TPN is documented in selected patients, the decision to institute TPN is fraught with dilemmas. One of these is that ongoing evaluation of nutritional status is required. This includes regular monitoring of body weight, anthropometry, as well as regular blood tests for nutritional status and liver function surveillance. It is estimated that total daily energy expenditure in cancer patients would be similar to healthy subjects, 20-25kcal/kg/day for bedridden and 25-30kcal/kg/day for ambulatory patients \(^5\).

We must always balance possible adverse events associated with TPN which includes line sepsis, fluid overload, cholestasis, reduced mobility related to the TPN set and financial constraints. The common TPN formula used in clinical practice (e.g. Structo- kabivent 1477ml, Vitrimix 1L) costs around HKD$250 to 300 per day \(^10\).

<table>
<thead>
<tr>
<th>Date</th>
<th>23/7</th>
<th>30/7</th>
<th>7/8</th>
<th>13/8</th>
<th>20/8</th>
<th>27/8</th>
<th>2/9</th>
<th>9/9</th>
<th>21/9/09</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body Weight(Kg)</td>
<td>33.0</td>
<td>31.3</td>
<td>30.7</td>
<td>30.5</td>
<td>30.6</td>
<td>30.3</td>
<td>29.7</td>
<td>29.5</td>
<td>Death</td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>32</td>
<td>30</td>
<td>-</td>
<td>-</td>
<td>28</td>
<td>-</td>
<td>23</td>
<td>27</td>
<td>26 Death</td>
</tr>
</tbody>
</table>

**Table 1 Body weight and serum albumin monitoring during TPN**

(TPN was started on 12/7/2009)
Criteria for initiation of TPN based on life expectancy imply the possibility of highly accurate survival prediction. The difficulty of accurately predicting survival is acknowledged as one of the most difficult aspects in choosing appropriate patients for nutritional support.11

Conclusion

Provision of TPN in advanced cancer patient aim at improving the functional status and possibly survival outcome by preventing and treating under-nutrition or starvation. As with all cancer treatments, in some situations there may also be psychological benefit to the patient or family in providing feeding even when there are no medical benefits.12 We must take into deep consideration of possible risks associated with TPN, and strike a balance between prolonged hospital stay for TPN administration and happy moments spent with family.

Feeding is a fundamental element in human relationships and culture, and health professionals need to approach these discussions with sensitivity for concerns about starvation and abandonment and families desire to provide love and care. From a palliative care worker point of view, TPN could never replace good psychosocial support and multidisciplinary team work approach in helping our terminally ill patients. However, it does certainly potentiate selected patients performance status and time in receiving good palliative care, as shown in the reported case.

References

10. Hospital Authority Drug Formulary Dec 2009, Hong Kong Special Administrative Region.

Table 2. Published Clinical Practice Guidelines for Use of Parenteral Nutrition in Terminally Ill Cancer Patients

<table>
<thead>
<tr>
<th>Year</th>
<th>Guidelines</th>
<th>Source Description</th>
<th>Summary of Key Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>2001</td>
<td>Palliative or terminal nutrition in adults with progressive cancer</td>
<td>French National Federation of Cancer Centers</td>
<td>Indications for enteral and parenteral nutrition May be beneficial in patients with bowel obstruction or other sources of food intolerance Not recommended in patients with prognosis &lt;3 months or Karnofsky score &lt;50% Risks need to be considered</td>
</tr>
<tr>
<td>2005</td>
<td>Parenteral nutrition in advanced cancer</td>
<td>Capital Health Home Parenteral Nutrition Program, Edmonton, Canada</td>
<td>Criteria for home parenteral nutrition when enteral nutrition is not an option Criteria include: -Potential survival benefit -Duration expected &gt;6 weeks -Karnofsky score &gt;50% and supportive home environment</td>
</tr>
</tbody>
</table>
Death rattle is a phenomenon frequently observed during the final hours of dying patients. Its occurrence is thought to cause distress on relatives and staff. Different anti-muscarinic medications have been used as the pharmacological means of controlling death rattle. Studies have looked into the meaning of death rattle and the relative efficacy of the different medications in symptoms control.

**Introduction**

Death rattle is the noise cause by the turbulent air flow through the accumulated secretions in the oropharynx and bronchial tree. This is often observed at the final stage of life when patients are no longer capable of swallowing, resulting in the pooling of secretions. Studies found the incidence of death rattle ranged from over 20% to half of all dying patients\(^2-4\). The occurrence of death rattle is recognized as a strong predictor of imminent death. Wildiers\(^2\) noted that 76% of patient died within 48 hours of onset, while Käss et al\(^3\) found the median time of death since the onset of death rattle was 16 hours only.

The salivary glands and the bronchial mucosa are the main sources of airway secretions. Two muscarinic receptors, the M2 and M3, are involved in the regulation of secretions. While vagal stimulation increases the volume of airway secretions, it has been shown that anti-muscarinic drugs effectively reduce the secretions by antagonizing acetylcholine at the muscarinic receptors.

**Impact of Death Rattle**

Death rattle is a common phenomenon among the dying patients. Studies have found the incidence of 23% to 49%\(^2-4\). Wee BL et al\(^5-6\) looked into the meaning of death rattle to relatives and found relatives interpret the sound of death rattle in a variety of ways. About half of the relatives found it distressing. Others, however, were neutral or found it a helpful sign of impending death. These authors also looked into the impact of death rattle on staff and volunteers\(^7\) and found that most expressed negative feelings about hearing the sound which may influence their decision to intervene.

**Management of Death Rattle**

Both non-pharmacological and pharmacological measures could be applied to dying patients with death rattle. These patients should be positioned on their side or in a semi-prone position with occasional gentle suctioning of oropharyngeal fluids. Communication with relatives will be helpful in addressing fears and distress caused by the rattling noise.

Anti-muscarinic medication is the mainstay of pharmacological therapy for the management of death rattle. Common drugs being used include hyoscine hydrobromide, glycopyrronium, hyoscine butylbromide and atropine.

Several studies had compared the effectiveness among these medications. Hughes et al\(^8\) did a prospective audit and found that a single dose of any of the drugs hyoscine hydrobromide, hyoscine butylbromide and glycopyrrrolate led to improvement in 35-54% of patients. Results demonstrated no overall difference in symptoms alleviation among the three drugs. Back et al\(^9\) compared hyoscine hydrobromide and glycopyrrrolate in the treatment of death rattle noting the noise scores at the start,
30 minutes, an hour and 4-hourly thereafter. They concluded that glycopyrrolate 0.2mg is less effective at reducing death rattle than hyoscine hydrobromide 0.4mg when assessed at 30min, and the use of glycopyrrolate may lead to an increased need for other sedatives or anti-emetic medications. Using the Liverpool Care Pathway, Hugel et al10 also compared these two medications. They found a significant difference in the overall response between the two groups. All patients in the glycopyrronium group had some response to the medication whereas 22% of patients in the hyoscine group had no response. More patients in the hyoscine group died with respiratory tract secretions present.

In the Cochrane review 200811, only one study12 fulfilled the inclusion review criteria. This was a randomized controlled trial examining the efficacy of scopolamine 0.5mg iv / sc given at time zero, four and eight hours. The intervention group showed a tendency to reduced death rattle than the control group in the first 10 hours but the difference was not significant.

Recently a Belgium group conducted a multicenter open-label, prospective, randomized trial comparing the effectiveness of atropine, hyoscine butylbromide and scopolamine for the treatment of death rattle13. They assigned patients randomly to one of the three groups given a sc bolus dose of the respective medication followed by a regular dose or continuous infusion of the drug. In the atropine group, a bolus of 0.5mg was followed by 3mg/24hr infusion or 0.5 mg q4H. In the scopolamine group, the bolus dose given was 0.25 mg then followed by 1.5mg/24 hr infusion or 0.25mg q4H. For the hyoscine butylbromide group, a 20mg bolus was followed by 60mg/24hr infusion or 0.5mg q4H. The rattling was scored at 30min, 60min, 4, 12, 24 hours and then, every 24 hours till death. They concluded from this study that treatment effectiveness improved steadily up to 24 hours and there was no significant difference in effectiveness among the three drugs either at 1 hour or up to 48 hours. The treatment is more effective when started at a lower baseline rattle score although this difference in efficacy as a function of intensity was no longer seen after 48 hours of treatment. They found no difference in the median and mean survival time among the 3 groups, and similar effectiveness was seen among different classes of primary tumors or among different age categories.

Conclusion

Death rattle is a frequent clinical sign at the end of life, and its occurrence is a strong predictor of imminent death. Rattling noises have been shown to cause distress to relatives and staff thus warranting interventions. Management of death rattle included both non-pharmacological and drug treatment. Where different anti-muscarinic drugs are available for the control of respiratory secretions, there is to date no evidence of significant differences in effectiveness among these medications used.

References

Respecting and preserving dignity is one of the core values in modern palliative care\(^1,2\). However, a request to die with dignity, is often a quoted reason for euthanasia\(^3\).

In a landmark qualitative study published in 2002, Chochinov et al. studied 50 terminal cancer patients using a semi-structured interview, exploring their perception of dignity\(^4\). Three major categories, including Illness Related Concerns, Dignity Conserving Repertoire and Social Dignity Inventory were identified. Under each category were different themes and subthemes, as shown in Fig. 1. These form the foundation of the Dignity Model in the Terminally Ill.

The relationship between dignity and the will to live was established in the same year in an article published in the Lancet. Chochinov et al. performed a cross-sectional study in a cohort of 213 terminally ill cancer patients. Patients were asked to rate their sense of dignity on a 7-point sense of dignity item scale. Sixteen out of 213 (7.5\%) patients indicated that loss of dignity was of great concern. Patients who indicated that their sense of dignity was fractured, were more likely to have more psychological and symptom distress, and were more likely to have loss of will to live\(^5\). It provided the empirical data to suggest that compromised dignity correlated with higher desire for death.

Based on the dignity model, Chochinov et al. established the dignity psychotherapy\(^6\). Using a standard framework of questions, the therapist allowed the client to discuss the issues that mattered most or that they would most want remembered. With the cues provided, the therapist would restructure and reorganize the clients’ thoughts. The interview would be audio-taped and the recorded dialogue was reshaped with transcript. In a pilot study with 100 patients under palliative care (50 from Australia and 50 from Canada, 3 had non-malignant condition), 91 patients felt satisfied with the intervention. Seventy-six patients out of 100 reported a heightened sense of dignity. There was significant improvement in the measurement of suffering (p=0.023) and depressive symptoms (p=0.05). There was also improvement in the sense of dignity but it was statistically insignificant (p=0.085).
Here we come to face a practical problem: Can dignity be measured? If yes, how can we measure dignity? A validated measurement becomes essential if we want to show that dignity intervention is successful. At least, we have to consider which components of dignity should be measured.

There are 22 items in the Dignity model. Chochinov et al. interviewed 211 palliative care patients and asked them to decide which items were related to their sense of dignity. All but 1 out of the 22 items were endorsed as dignity-related by over half of the subjects. The most important issues were “not being treated with respect or understanding”, and “feeling a burden to the others”. These findings established the importance of every single item in the Dignity model to help construct a measurement scale. This forms the background of Patient Dignity Inventory (PDI).

Patient Dignity Inventory
The PDI consists of 25 self-report items rated on a 5-point scale. Patient are asked to rate how much each of the specific items or issues posed a problem to their sense of dignity. The 5-point scale was rated as: (1) not a problem, (2) a slight problem, (3) a problem, (4) a major problem and (5) an overwhelming problem. (Table 1)

During the validation, the researchers administered the PDI to 253 patients receiving palliative care, 8% of whom had non-cancer advanced diseases. The mean duration of survival from the time of interview to the time of death was 78 days. The test-retest reliability was tested by asking the patient to complete PDI again 24 hours later if they agreed. The Pearson r was 0.85 for the full PDI. Cronbach’s coefficient alpha, which reflects the internal consistency, was 0.93.

During the factor analysis, five factors were identified which accounted for 58% of the overall variation. They include Symptom Distress (items 3, 5-9), Existential Distress (items 4, 11-14, 18), Dependency (items 1, 2, 20), Peace of Mind (items 15-17) and Social Support (items 21, 22, 25). The concurrent validity of different factors was tested with different psychometric

Table 1: The Patient Dignity Inventory questions
1. Not being able to carry out tasks associated with daily living (e.g. washing myself, getting dressed).
2. Not being able to attend to my bodily function independently (e.g. needing assistance with toileting-related activities).
3. Experiencing physically distressing symptoms (such as pain, shortness of breath, nausea).
4. Feeling that how I look to others have changed significantly.
5. Feeling depressed.
8. Worrying about my future.
9. Not being able to think clearly.
10. Not being able to continue with my usual routines.
11. Feeling like I am no longer who I was.
12. Not feeling worthwhile or valued.
13. Not being able to carry out important roles (e.g. spouse, parent).
14. Feeling that life no longer has meaning or purpose.
15. Feeling that I have not made a meaningful and lasting contribution during my lifetime.
16. Feeling I have ‘unfinished business’ (e.g. things left unsaid, or incomplete).
17. Concern that my spiritual life is not meaningful.
18. Feeling that I am a burden to others.
19. Feeling that I don’t have control over my life.
20. Feeling that my illness and care needs have reduced my privacy.
21. Not feeling supported by my community of friends and family.
22. Not feeling supported by my health care providers.
23. Feeling like I am no longer able to mentally ‘fight’ the challenges of my illness.
24. Not being able to accept the way things are.
25. Not being treated with respect or understanding by others.
instruments. The correlation of different factors with corresponding individual instruments were significant and obvious except in the factor Peace of Mind, which was not correlated with various measurement of psychological wellbeing except the current level of anxiety of measurement by the Edmonton Symptom Assessment Scale (ESAS) (r=0.152, p=0.021). Further analysis showed that Peace of Mind item was significantly correlated with the Functional Assessment of Chronic Illness Therapy – Spiritual Well-Being (FACIT)-Inner Peace factor (r=-0.213, p=0.002), but not with the measurement of Spiritual factor nor Meaning and Purpose factor. It was noted that the factor Existential Distress correlated well with measures of suffering, well-being, depression, anxiety, and quality of life items. This may provide hints that Peace of Mind concept and Existential Distress are distinct entities. Furthermore, during the validation, the factor Existential Distress did not correlate significantly with either the sense of dignity or the will to live.

The authors claim that the PDI has excellent face validity. It can be completed by patients both in the in-patient and out-patient settings, requiring a few minutes time. It may serve a useful tool to screen or monitor dignity related problems in the palliative care setting. The tool may be used to study the differential distribution of distress among different populations or care settings. In their pilot study, patients reported an average of 5.74 problems. However, “the impairment of dignity” was not defined, and there was no cut off values proposed to distinguish between intact or impaired dignity. The study of course has not been validated in Chinese palliative care setting.

**Upcoming research using PDI**

There are two upcoming studies to assess the effectiveness of dignity therapy using the Patient Dignity Inventory as the primary outcome measures. The first study plans to recruit 64 elderly home residents, (not necessarily suffering from a terminal illness or receiving palliative care), as the researchers regard living in elderly home as comparable to one’s end of life. The same group is also planning another randomized controlled trial aiming to recruit 40 advanced care patients referred to a hospital-based palliative care team. In both studies the participants will be allocated to either Intervention group receiving Dignity Therapy, or Control group receiving standard care. The primary outcome measures will be the participants’ sense of dignity, as measured by the Patient Dignity Inventory.

**Conclusion**

While awaiting more scientific confirmation or even trans-cultural validation of dignity therapy and the Patient Dignity Inventory, the core values of medical professionalism – kindness, humanity and respect remain universal. Not everyone of us can be the dignity psychotherapists, nonetheless, every member in palliative care team can participate in providing dignity conserving care by using A, B, C and D: ‘A’ stands for appropriate questions to be asked and actions to be taken, ‘B’ stands for the behavior during our contact with patients, clinical examination and subsequent communication, ‘C’ for compassion – we have to get in touch with patient’s own feeling in spoken and unspoken ways, and ‘D’ stands for the dialogue we use, by showing acknowledgement to personhood, as well as willingness to know the patient. Different psychotherapeutic interventions are available, however, let us not forget our therapeutic role.

**References**