Original Article

Factors Influencing Venous Pain in Patients with Cancer Receiving Gemcitabine

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Background: Gemcitabine is a chemotherapy drug used to treat several cancers. Nevertheless, pain is an adverse effect during drug administration.

Objective: To study the contributing factors relating to venous discomfort during Gemcitabine administration.

Materials and Methods: This is a retrospective study to investigate the factors including gender, age, drug, formula, dosage, time, type and volume of solution, duration, and site of administration have been retrospectively evaluated in cancer patients receiving Gemcitabine. As the occurrence of venous pain is approximately 37% of the time and each variable requires 10 times of drug administration to prove for pain distress, the calculated sample size was 372 from 72 patients. The pain discomfort was recorded by using numeric rating scale. A p of less than 0.05 was considered statistical significance.

Results: Patients receiving Gemcitabine intravenously suffered with pain at 5.1% of the time relating to the site of venipuncture at Basilic vein (p<0.005), at the fourth to the ninth cycle of drug administration (p<0.003), female patients (p<0.024), and patients younger than 65 years (p<0.032) in a successive order. Nevertheless, there were no correlations to other factors.

Discussion: The Basilic vein was a less-aching site, since it is a large superficial vein. Patients at the fourth to the ninth cycle of drug administration experienced this distress dramatically, possibly because of the drug(s) accumulating and affecting the venous framework. Female, younger than 65 years underwent this concern more than the younger. This might due to the elder member having accumulated experience of pain through their life.

Conclusion: Venous pain among subjects receiving Gemcitabine is an adverse effect during administration. However, nurses can reduce venous pain by selecting Basilic vein to administer Gemcitabine.

Keywords: Venous pain, Gemcitabine Administration, Chemotherapy

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Gemcitabine, an antimetabolite, has been used in chemotherapy to treat pancreatic cancer, non-small cell lung cancer, bladder cancer, breast cancer, ovarian cancer, cholangiocarcinoma, and cervical cancer. It can be used as single or combined regimen with Cisplatin, Carboplatin, and Paclitaxel[1,2].

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Normally, Gemcitabine is diluted with 0.9% normal saline solution [NSS] and administered intravenously in 30 minutes to reduce myelo-suppression. However, at the site of injection, adverse outcomes such as pain 1.4%, allergic reaction 1.2%, and inflammation 0.4% are inevitable[3]. At our institute, the incidence of venous pain is approximately 43 out of 117 times of drug administration (37%).

This inconsistent pain severity can be categorized at three different levels. Moreover, it yields not only physical but also psychological difficulties such as anxiety, fear, and worry during drug

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administration.

Studies revealed that combined regimens had more vascular toxicity than single regimen[3]. As a result, investigators would like to study the contributing factors relating to venous discomfort (gender, age, drug, formula, dosage, time, type and volume of solution, duration, and site of administration, etc) during Gemcitabine treatment.

Materials and Methods

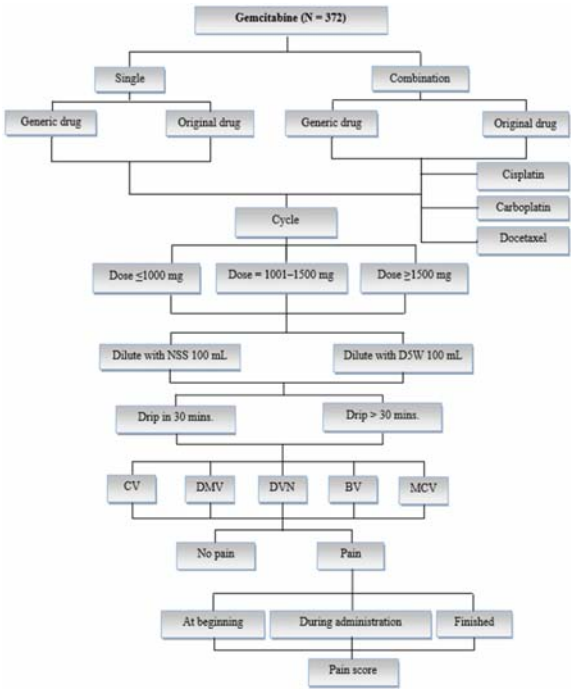
After IRB approval, the data from the Hospital Informatics System, Chulabhorn Hospital have been retrospectively evaluated between January to October 2016. Inclusion criteria were good conscious, literate, patients older than 20 years. Exclusion criteria were patients receiving chemotherapy within six hours or having history of peripheral neuropathy.

As the occurrence of venous pain is approximately 37% and each variable requires 10 times of drug administration to prove for pain distress, the calculated sample size was 372 sessions of Gemcitabine administration. Then, a purposive sampling allocated 72 patients into two groups, single and combined regimen. Each group ran Gemcitabine administration both generic and original forms, with the different dosages of less than 1,000 mg, 1,001 to 1,500 mg, and more than 1,500 mg. Either drug was diluted with normal saline or dextrose in water (D5W) solution 100 ml and transfused completely in 30 minutes or longer. In addition, the site of cannulation, such as Basilic vein [BV], Cephalic vein [CV], Dorsal metacarpal vein [DMV], Median cubital vein [MCV], or Dorsal venous network [DVN] was recorded. By this mean, the data of 372 sessions were collected and analyzed (Figure 1).

By using numeric rating scale (0 to 10), the pain discomfort was recorded at the beginning, during, and at the end of drug administration. It was classified as no (0), mild (1 to 3), and moderate to severe pain (4 to 10).

Statistical analysis was conducted by using STATA/SE version 12 (STATA Corp LP, College Station, TX, USA). Thirteen factors were expressed as percentage, mean, and standard deviation. The ordinal logistic regression with cluster was used to analyze the relationships between contributing factors and levels of venous pain. A *p*-value of less than 0.05 was considered statistical significant at 95% confidence interval.

The protocol of this research was reviewed and approved by the Human Research Ethics Committee, Chulabhorn Research Institute No. 007/2559.



CV = cephalic vein; BV = basilic vein; DMV = dorsal metacarpal vein; MCV = median cubital vein; DVN = dorsal venous network

Figure 1. Flow diagram of study protocol.

Results

Demographic characteristics showed that 72 patients with 372 visits were 31 males (43.1%) and 41 females (56.9%), aged 60.3±10.9 years (Table 1). Lung cancer was the most prevalent (56.9%). Drugs were administered in form of 285 generic (76.6%) and 87 original (23.4%) as 226 single (60.8%) or 146 combined (39.2%) regimens, with 31 (8.3%) dosages of 1,000 mg or less, 228 (61.3%) of 1,001 to 1,500 mg, and 113 (30.4%) of more than 1,500 mg.

Gemcitabine was diluted with NSS 300 (80.7%) and D5W 72 (19.3%), infused in 30 minutes in 197 (52.9%) and over 30 minutes in 175 (47.1%), and then dispensed in the first to the third cycle in 233 (62.6%) and the fourth to the ninth cycle in 139 (37.4%). The sites of venipuncture were DMV 149 (40.1%), CV130 (34.9%), BV 57 (15.3%), DVN 32 (8.6%), and MCV 4 (1.1%).

Patients complained of pain discomfort at, above, and along the venous line in 68 (48.9%), 1 (0.7%), and 78 (50.1%), respectively. This appeared at the beginning of the drug administration for 53 (38.1%), during for 82 (58.9%), and after for 4 (2.9%). However,

Table 1. Patient characteristics (n = 72)

	n	Percentage	Odds ratio	95% CI	*p*-value
Gender					
Male: female	31:41	43.1:56.9	1/1.79	“1.08 to 2.96	0.024*
Age (years)					
≤65: >65	48:24	66.7:33.3	1.70/1	1.05–2.76/-	0.032*
Type of cancer					
Lung: cholangio: other	41:8:23	56.9:11.1:32.0	1/1.66/0.96	0.73 to 3.78/ 0.55 to 1.68	0.231/0.894
Drug					
Generic: original	285:87	76.6:23.4	0.64/1	0.39 to 1.06	0.085
Regimen					
Single: combination	226:146	60.8:39.3	0.97/1	0.60 to 1.57	0.889
Dosage (mg)					
≤1,000: 1,001 to 1,500: >1,500	31:228:113	8.3:61.3:30.4	1/1.16/2.44	-/0.47 to 2.87/ 0.89 to 6.73	-/0.744/ 0.083
Solution					
NSS: D5W	300:72	80.7:19.3	1.72/1	0.31 to 9.30	0.529
Cycle					
1 to 3: 4 to 9	233:139	62.6:37.4	1/1.99	1.26 to 3.15	0.003**
Duration of infusion (min)					
30: >30	197:175	52.9:47.1	1/0.82	0.17 to 4.04	0.881
Site (vein)					
CV:DMV:DVN:BS:MCV	130:149: 32:57:4	34.9:40.1: 8.6:15.3:1.1	1/0.92/0.50/ 0.30/0.29	0.56 to 1.50/ 0.16 to 1.60/ 0.13 to 0.70/ 0.04 to 1.85	0.728/ 0.245/ 0.005**/ 0.190
Time/pain					
Start: during: after	53:82:4	38.1:58.9:2.9	-	-	-
Pain location					
At: above: along the vein	68:1:78	48.9:0.7:50.1	-	-	-
Pain score					
0: 1 to 3: 4 to 10	233:120:19	62.6:32.3:5.1	-	-	-

* $p<0.05$

NSS = normal saline; D5W = 5%, dextrose in water; CV = cephalic vein; DMV = dorsal metacarpal vein; DVN = dorsal venous network; BS = basilic vein; MCV = median cubital vein

they expressed their uneasiness as nothing in 233 (62.6%), mild pain in 120 (32.3%) and moderate to severe pain in 19 (5.1%).

Ordinal logistic regression revealed that venous pain showed significant correlation to Basilic vein ($p<0.005$), number of administration ($p<0.003$), gender ($p<0.024$) and age ($p<0.032$) (Table 1).

Discussion

During chemotherapy, patients receiving Gemcitabine intravenously suffered with pain 5.1% of the time This significantly correlated to the site of venipuncture, number of infusion, gender, and age in a successive order. Ironically, drug formula and its dosage, therapeutic regimen, duration of administration, and type and volume of solution were not significant.

The current study showed that BV was a less-aching site for Gemcitabine infusion. This might be due to the BV is a large superficial vein of the upper limb that courses visibly upwards on the medial aspect of the forearm and arm. It is generally an acceptable site for venipuncture. Canadian Cancer Society also confirmed that BV had less pain than other veins of the upper limb[4]. However, patients should be in a prone position or twist their arms during the insertion of the catheter. When a patient is supinated during venous cannulation, the vein below the elbow become awkward to access, thus, is infrequently used.

Consequently, BV became an optional location for catheter insertion[5].

Number of drug infusion appeared to be a contributing factor relating to the level of venous pain. Patients in their fourth to the ninth cycle of drug administration experienced this distress dramatically. This might due to the drug(s) slight accumulation and directly affecting venous framework[6]. In addition, Dehkordi A et al who studied the quality of life [QoL] amongst cancer patients receiving chemotherapy, confirmed that after the third to the fifth cycle, patients had a lower QoL[7].

Female patients receiving Gemcitabine had more venous pain than males. This was an unexpected phenomenon, since female normally aggregates their life experiences of pain throughout. This agreed with Bartley et al in the study of sex differences in pain: a brief review of clinical and experimental findings. He stated that female has a high risk for chronic pain and often takes more pain in terms of clinical pain. In addition, female have a higher sensitivity to pain and pain stimulator with less pain inhibitors than male[8]. In a study performed by the University of Bath on the topic of Women Feel More Pain than Men Research Shows: Science Daily, confirmed that women felt more pain than men[9]. In addition, Seong SR et al, in a study on Vascular Pain Due to Gemcitabine and According to Clinical Factors, reported that female had significantly more intravascular pain than male[10]. However, Marilia et al presented their comparison of pain threshold and duration between men and women in a study suggesting that women has a higher pain threshold than men, especially when these groups are aged between 18 and 33 years. Furthermore, in men, increasing age correlated with increased perception of pain duration [TPED] and pain threshold [LD][11].

Patients younger than 65 years underwent more pain than the elders. This was not beyond our anticipation since the elder member has accumulated experience of pain through their life. It was in accordance with Jappy et al study on Age Differences in Pain Characteristics and its Impact on Patients Receiving Chemotherapy. They found that the incidence of pain increased in patients younger than 65 years[12]. Krok et al studied on the topic-Age Differences in the Presence of Pain and Psychological Distress in Younger and Older Cancer Patients. They collected data from outpatients visiting hospital for radiation and chemotherapy treatment and stated that patients at age younger than 60 years old had more pain and stress than patient at age older than 60 years old[13].

Conclusion

During chemotherapy, patients receiving Gemcitabine intravenously suffered with pain 5.1% of the time. The Basilic vein was the less-aching site of venipuncture. Patients at the fourth to ninth cycle of drug administration experienced this distress considerably. In addition, female and all patients younger than 65 years felt more pain.

What is already known on this topic?

Generally, during chemotherapy, patients receiving Gemcitabine intravenously suffered with painful sensation. Studies claimed that administering Gemcitabine with dextrose in water helped to reduce the severity and frequency of venous pain as compared to normal saline solution. However, the combined regimens had more vascular toxicity than the single regimen.

What this study adds?

Current study revealed that patients receiving Gemcitabine intravenously suffered with pain 5.1% of the time. The Basilic vein was the less-aching site of venipuncture. Patients at the fourth to ninth cycle of drug administration experienced this distress considerably. In addition, female took more pain than male. Furthermore, patients younger than 65 years had more concern. Other contributing factors such as drug formula and its dosage, therapeutic regimen, duration of administration, and type and volume of solution did not significantly contribute to pain.

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Potential conflicts of interest

None.

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