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RAPID COMMUNICATION

Psychological intervention reduces postembolization pain during hepatic arterial chemoembolization therapy: A complementary approach to drug analgesia

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Abstract

AIM: To assess whether psychological intervention reduces postembolization pain during hepatic arterial chemoembolization therapy.

METHODS: Two hundred and sixty-two patients, who required hepatic arterial chemoembolization for hepatic malignancy and postembolization pain, were randomized into control group (n = 46, receiving medication) and intervention group (n = 216, receiving psychological intervention and medication in turn). The symptom checklist-90 (SCL-90) was used to scale the psychological symptoms of the patients before operation. Pain was scored with a 0 to 10 numeric rating scale (NRS-10) before and after analgesia as well as after psychological intervention (only in intervention group).

RESULTS: All psychological symptomatic scores measured with SCL-90 in the intervention group were higher than the normal range in Chinese ($P < 0.05$). The somatization, phobia and anxiety symptomatic scores were associated with pain numerical rating score before analgesia (r = 0.141, 0.157 and 0.192, respectively, $P < 0.05$). Patients in both groups experienced pain relief after medication, psychotherapy or psychotherapy combined with medication during the procedure ($P < 0.01$). Only some patients in the intervention group reported partial or entire pain relief (29.17% and 2.31%) after psychological intervention. The pain score after analgesia in the intervention group was significantly lower than that in the control group ($P < 0.01$).

CONCLUSION: Severe psychological distress occurs in patients with hepatic malignancy. Psychological intervention reduces pain scores significantly during hepatic arterial chemoembolization therapy and is thus, highly recommended as a complementary approach to drug analgesia.

Key words: Liver neoplasms; Radiology; Psychological intervention; Non-pharmacologica; Pain

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INTRODUCTION

Hepatic carcinoma is one of the most common malignant visceral tumors in adults worldwide. Surgical resection remains the major treatment for hepatocellular carcinoma (HCC). However, only 8%-15% of patients meet the criteria for surgical resection[1-3] and the long-term results after resection are still unsatisfactory[4]. The liver is also the most frequent site of metastatic disease from extrahepatic primary tumors[5]. Resection of metastases can prolong the survival time of a small percentage of selected patients[6]. Transarterial chemoembolization (TACE), as a palliative therapy, is recommended for the treatment of unresectable hepatic neoplasms (primary and metastatic)[7,8]. The current routine technique of TACE is to inject iodized oil mixed with a single or a combination of chemotherapeutic agents into the neo-vasculature of hepatic neoplasms. The therapeutic goal is ischemic and cytotoxic insults to the tumor by occluding the feeding and collateral arteries of tumors. Right upper quadrant pain appears to be the most common complaint, followed by fidget, anxiety and noncompliance. Analgesia induced by drugs, such as intraarterial lidocaine and intravenous narcotic

analgesics, is required to alleviate the pain[9,10]. However, these medications have side effects and a few patients are not sensitive to sedative and analgesic medications. It is, therefore, necessary to develop non-pharmacologic approaches to improving the patient experience with painful procedures.

Non-pharmacologic practices, such as guided imagery, music therapy, hypnosis, and distraction, can effectively improve patient experiences during painful medical procedures, such as endoscopy[11]. There are few studies analyzing the effect of psychological intervention on pain suffered by hepatic cancer patients undergoing hepatic arterial chemoembolization therapy.

The aim of this investigation was to assess whether psychological intervention reduces postembolization pain during hepatic arterial chemoembolization therapy.

MATERIALS AND METHODS

Subjects

Between April 2002 and March 2006, 262 patients requiring hepatic arterial chemoembolization for hepatic malignancy (primary or metastatic) and postembolization pain agreed to participate in the study. The group comprised 186 men and 76 women with their age ranged from 13 to 76 years (mean age, 51.96 years). The diagnosis of hepatic tumor was confirmed by pathologic and histologic examination or elevated serum tumor markers. Patient exclusion criteria were as follows: (1) history of interventional diagnosis and/or therapy, (2) bellyache before embolization, (3) treatment with anxiolytic or narcotic analgesics 72 h prior to the therapy, (4) presence of encephalopathy or other significant alterations of mental status or cognitive impairment or visual and auditory deficits, (5) considerable cardiopulmonary morbidity.

Methods

Patients were randomized into control group (n = 46, receiving medication) and intervention group (n = 216, receiving psychological intervention and medication in turn). Their baseline characteristics, including demographic information (i.e., age and gender) and tumor type, were collected from the medical records.

The Chinese version of symptom checklist-90 (SCL-90), a psychiatric self-report inventory, was used to scale the psychological symptoms of the patients before operation. All patients were guided to answer 90 items with the uniform advices, and the 90 items in the questionnaire were scored on a five-point scale to reflect the psychological symptom patterns of patients. The items referred to the assessment of index for somatization dimensions, obsessive-compulsive tendencies, depression, anxiety, phobia, interpersonal sensitivity, hostility, paranoid ideations and psychotic states.

During the procedure, patients in the control group received medication when they experienced pain, whereas psychological intervention and drug analgesia were performed in turn on patients who were assigned to the intervention group for the postembolization pain. Patients in the control group and those with painful experience after psychotherapy in the intervention group received medications according to the digital subtraction angiograms and symptoms, e.g. antispasmodics for arterial spasm, narcotic analgesics for pain without characteristic signs and symptoms. The doses of medications were determined by the operator who performing the procedure according to the condition of patients. Psychological intervention was performed by two registered nurses with 7- and 10-year professional experience, respectively. Psychotherapy included encouragement, verbal suggestion, relaxation training, distraction with verbal communication on interest of the patients, therapeutic touch on face of the patients, guided imagery and intra-arterial placebo (0.5 mL of 0.9% sodium chloride injection). The pain was scored using a 0 to 10 numeric rating scale (NRS-10)[12] (0 = "no pain at all", 1-3 = "mild pain", 4-6 = "moderate pain", 7-9 = "severe pain", 10 = "unbearable pain") before and after analgesia, as well as after psychological intervention (only in intervention group).

Table 1 Baseline characteristics of patients

Characteristics	Control group (n = 46)	Intervention group (n = 216)	Significance	
Age (yr)	54.11 ± 10.85	51.50 ± 11.54	t = 1.41	P = 0.16
Gender				
Male	37	149		
Female	9	67	χ^2 = 2.42	P = 0.12
Tumor type				
Primary	27	135		
Metastatic	19	81	χ^2 = 0.23	P = 0.63

P > 0.05 for each comparison.

Statistical analysis

The data were analyzed with the Statistical Package for Social Sciences (SPSS 11.0 for Windows). The measurement data were expressed as mean ± SD and the enumeration data as proportions. Statistical tests used in bivariate analysis included χ^2 test and Student t test. The relationship between mental status and postembolization pain was evaluated with the Pearson correlation coefficient. $P < 0.05$ was considered statistically significant.

RESULTS

There were slight differences in baseline characteristics between the control and intervention groups and none of these differences was statistically significant (Table 1). No significant difference was found in psychological symptoms before the procedure between the two groups (Table 2). The psychological symptom scores in the intervention group were higher than the normal range in Chinese and the differences were statistically significant ($P < 0.05$) (Table 3).

Pearson correlation coefficients showed that the somatization dimensions and phobia were positively correlated with pain numerical rating score before analgesia in intervention group ($P < 0.05$). In addition, the anxiety level was also positively correlated with the pain numerical rating score before analgesia ($P < 0.01$) (Table 4).

Table 2 Psychological symptoms of patients measured with SCL-90 before the procedure (mean ± SD)

Psychological symptoms	Control group (n = 46)	Intervention group (n = 216)	Significance	
			t (or t')	P value
Somatization	1.55 ± 0.46	1.58 ± 0.44	0.42	0.68
Obsessive-compulsive tendencies	1.53 ±0.67	1.68 ± 0.61	1.49	0.14
Sensitivity	1.65 ± 0.57	1.58 ± 0.55	0.78	0.44
Depression	1.72 ± 0.50	1.64 ± 0.48	1.02	0.31
Anxiety	1.47 ± 0.40	1.51 ± 0.39	0.63	0.53
Hostility	1.41 ± 0.57	1.50 ± 0.60	0.93	0.35
Phobia	1.46 ± 0.38	1.40 ± 0.33	1.09	0.28
Paranoia	1.50 ± 0.49	1.42 ± 0.48	1.02	0.31
Psychosis	1.46 ± 0.30	1.41 ± 0.37	0.98	0.33

P > 0.05 for each comparison.

Table 3 Differences in psychological symptoms measured with SCL-90 in patients of intervention group and normal Chinese (mean ± SD) (Jin H *et al*, 1986)

Psychological symptoms	Intervention group (n = 216)	Norm (n = 7273)	Significance	
			t (or t')	P value
Somatization	1.58 ± 0.44	1.40 ± 0.40	5.94	< 0.01
Obsessive-compulsive tendencies	1.68 ± 0.61	1.49 ± 0.54	4.53	< 0.01
Sensitivity	1.58 ± 0.55	1.45 ± 0.52	3.61	< 0.01
Depression	1.64 ± 0.48	1.42 ± 0.49	6.51	< 0.01
Anxiety	1.51 ± 0.39	1.31 ± 0.42	6.91	< 0.01
Hostility	1.50 ± 0.60	1.37 ± 0.50	3.15	< 0.01
Phobia	1.40 ± 0.33	1.25 ± 0.40	6.54	< 0.01
Paranoia	1.42 ± 0.48	1.35 ± 0.49	2.07	< 0.05
Psychosis	1.41 ± 0.37	1.22 ± 0.37	7.44	< 0.01

Patients in both groups experienced pain relief after medication, psychotherapy or combined analgesia during the procedure. The pain scores after analgesic therapy were lower than those before analgesic therapy and the differences were statistically significant (P < 0.01) (Table 5).

Only some patients in the intervention group reported partial or entire pain relief (29.17% and 2.31%, respectively) after psychological intervention (Table 6).

The pain numerical rating scores for the control and intervention groups before analgesia showed no statistical difference, whereas the pain score after analgesia for the intervention group (psychological intervention and medication) was significantly lower than that for the control group (medication) (P < 0.01), indicating that the pain control was better in the intervention group than in the control group during the embolization procedure (Table 7).

Table 4 Correlation between psychological symptom scores (SCL-90) and pain numeric rating scores (NRS-10) before analgesia in intervention group (n = 216)

Psychological symptoms	Numerical rating score	
	Correlation coefficient (r)	P value
Somatization	0.141	< 0.05
Obsessive-compulsive tendencies	0.106	> 0.05
Sensitivity	0.097	> 0.05
Depression	0.031	> 0.05
Anxiety	0.192	< 0.01
Hostility	0.083	> 0.05
Phobia	0.157	< 0.05
Paranoia	0.124	> 0.05
Psychosis	0.08	> 0.05

Table 5 Pain score measured with numeric rating scale (NRS-10) during the procedure (mean ± SD)

	Numerical rating score	Significance[1]	
		t'	P value
Control group (n = 46)			
Pre-medication	4.35 ± 3.82		
Post-medication	1.64 ± 1.53	4.47	< 0.01
Intervention group (n = 216)			
Pre-psychotherapy	3.69 ± 2.46		
Post-psychotherapy	2.45 ± 1.96	5.79	< 0.01
Post-medication	0.29 ± 0.21	20.24	< 0.01

[1]Compared with pre-therapy NRS.

Table 6 Pain control with psychological intervention in intervention group (n = 216)

	n	%
Entire relief[1]	5	2.31
Partial relief[2]	63	29.17
Not relief	148	68.52

[1]Pain numerical rating scores (PNRS ⩽ 1) after psychotherapy; [2]PNRS ⩾ 3 before psychotherapy.

Table 7 Pain numerical rating scores (NRS-10) before and after analgesia: Comparison between control group and intervention group (mean ± SD)

	Control group (n = 46)	Intervention group (n = 216)	Significance	
			t'	P value
Pre-therapy	4.35 ± 3.82	3.69 ± 2.46	1.12	> 0.05
Post-therapy	1.64 ± 1.53	0.29 ± 0.21	7.3	< 0.01

DISCUSSION

TACE is an accepted palliative treatment modality for patients with primary HCC or hepatic metastases. If the tumor is unresectable, the patient is a poor surgical candidate. The clinical yield and survival rate in patients undergoing TACE have been proved[7,8,13]. More studies on TACE or combined methods, such as TACE combined with radiofrequency ablation, radiotherapy or percutaneous ethanol injection, have been reported recently[14-17]. In patients undergoing TACE, postembolization pain appears to be the most common complaint[2]. The pain usually occurs after embolization and peaks within 12-24 h. A large dose of opioid analgesics is often required in most patients when the pain is too severe to endure[2].

The etiology of pain after TACE is not well understood, but several theories have been postulated, including distention of the liver capsule, tumor necrosis, acute

ischemia of the liver parenchyma, and gallbladder ischemia secondary to inadvertent embolization of the cystic artery[2,18]. Infusion of iodized oil mixed with chemotherapeutic agents, in particular, results in acute, sharp right hypo-chondrium pain, followed by a deeper visceral pain, most likely due to swelling of the liver and stretching of the capsule that contains the nerve fibers[2]. It is believed that administration of narcotic analgesics can effectively control the pain during the procedure[9,10,19]. In our study, forty-six patients in the control group experienced a significant decrease in abdominal pain after drug analgesia ($P < 0.01$). However, the pain of most patients was not completely relieved after medication therapy.

In addition to physical suffering, psychiatric syndrome is increasingly recognized as a major component of distress in cancer patients[20-26]. Several factors, including the grief about current and anticipated losses, fear of death, concerns about loved ones and the effect of certain chemotherapeutic drugs on mood, *etc*[20-23], contribute to psychological distress[24]. Minagawa *et al*[27] and Godding *et al*[28] showed that about 30%-60% cancer patients have psychiatric disorders. Our study demonstrated that the SCL-90 factor scores for the intervention group were higher than those for the normal ($P < 0.05$), indicating that the psychological status is abnormal in patients with severe psychiatric disorders and hepatic carcinoma.

Psychological distress can result in systemic responses. Rorarius *et al*[29] performed a case-control study to evaluate the stress response and the sensitivity of clinical and biochemical stress markers in patients undergoing laparoscopically assisted vaginal or abdominal hysterectomy and showed that the most sensitive symptoms and markers of the systemic response are pain scores. Passik *et al*[25] surveyed 1109 cancer patients treated by 12 oncologists with Zung Self-Rating Depression Scale (ZSDS) and numerical rating scale, and found that the untreated psychological distress in cancer patients is associated with amplified pain. In our study, somatization, phobia and anxiety symptoms measured with SCL-90 were correlated with the postembolization pain ($P < 0.05$), which is consistent with the reported data[25].

Pariser *et al*[30] examined the effects of a telephone intervention in adults with arthritis and suggested that minimal intervention may produce positive changes in arthritis self-efficacy (ASE), depression, and pain in some adults. Other psychotherapies, e.g. hypnotic suggestion, relaxation training[31], distraction therapy[32], therapeutic touch[33,34], and imagery[35,36], are used in the treatment of disease-related pain. Our results reveal that psychological intervention decreased the pain score significantly ($P < 0.01$). However, only five patients (2.31%) reported entire pain control and most (68.52%) patients showed a slightly alleviated pain. Drug analgesia was still required by most patients in the intervention group during the procedure.

Several studies reported that psychological intervention during an invasive procedure, e.g. listening to music during endoscopy, could improve tolerance and compliance[37], alleviate pain[32] and decrease the dose of sedative drugs[38,39]. In our study, pain was well controlled after psychotherapy combined with medication, demonstrating that the pain control is better in the intervention group than in the control group ($P < 0.01$). The satisfaction of patients was increased accordingly.

In conclusion, patients with hepatic malignancy have severe psychological distress and psychological symptoms (i.e., somatization, phobia and anxiety) associated with the postembolization pain. Psychological intervention reduces pain scores significantly during hepatic arterial chemoembolization therapy and is highly recommended as a complementary approach to drug analgesia.

COMMENTS

Background

Postembolization pain is the most common complaint of patients during and after transarterial chemoembolization (TACE) for unresectable hepatic neoplasms. Drug analgesia is often required to decrease pain. However, these medications have side effects and a few patients are not sensitive to sedative and analgesic medications.

Research frontiers

Non-pharmacologic practices, such as guided imagery, music therapy, hypnosis, and distraction, can effectively improve patient experiences during painful medical procedures, such as endoscopy.

Innovations and breakthroughs

Psychological intervention can reduce pain significantly during hepatic arterial chemoembolization therapy.

Applications

Psychological intervention should be considered during hepatic arterial chemoembolization therapy.

Peer review

This is an interesting report on a complementary approach to drug analgesia during TAE for hepatic carcinoma.

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