ORIGINAL

Influence of an artificial pleural effusion technique on cardio-pulmonary function and autonomic activity

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Abstract :

Objective :

Percutaneous treatment of hepatocellular carcinoma (HCC) located directly under the diaphragm is problematic because ultrasonic imaging is difficult, and the lung may be injured during the procedure. It has been reported that an infusion of 5% glucose solution into the thoracic cavity enables percutaneous treatment in such cases. However, the safety aspects of this have not been investigated. In this study, variations in heart rate and changes in circulatory and respiratory dynamics were examined during the infusion of artificial pleural effusion directly under the diaphragm in patients with HCC.

Method :

The subjects were 13 patients with an HCC directly under the diaphragm. About 500 ml of a 5% glucose solution was infused into the thoracic cavity, and mean blood pressure, heart rate, and oxygen saturation were measured. Holter electrocardiography was simultaneously recorded to evaluate autonomic nerve function. To analyze variations in heart rate, the low-frequency waves (LF : 0.04-0.15 Hz), high-frequency waves (HF : 0.15-0.40 Hz, an index of parasympathetic nerve activity), and the LF/HF ratio (index of sympathetic nerve activity) were examined. The above parameters were measured before, during (when infusion of the half the planned volume was complete), and after infusion were compared.

Results :

No significant changes in the mean blood pressure or heart rate were found. Oxygen saturation was significantly decreased during and after the infusion. The HF value was slightly higher after infusion and the LF value was significantly increased during infusion. The LF/HF ratio was significantly increased during infusion, and this increase persisted after infusion.

Conclusions :

The infusion of artificial pleural effusion had no effect on circulatory dynamics, but transiently affected respiratory functions. It was also revealed that infusion stimulated the parasympathetic nerves. J. Med. Invest. 54 : 48-53, February, 2007

Received for publication October 30, 2006 ; accepted December 4, 2006.

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INTRODUCTION

Various non-surgical treatments of hepatocellular carcinoma (HCC) have recently been proposed. Such treatments include ethanol injection therapy (PEIT), microwave coagulation therapy (PMCT),

and radiofrequency ablation (RFA) (1, 2). The application of these treatments is difficult when the lesion cannot be imaged by ultrasonography because ultrasonic guiding is needed. The ultrasonic imaging of lesions that are located directly under the diaphragm is particularly difficult because the penetration of ultrasonic waves is reduced by air in the lung (3, 4). Moreover, the presence of the lung in the puncture pathway increases the risk of lung injury, making percutaneous treatment difficult in many cases (5. 6). Ohmoto and Yamakado reported that an infusion of 300-400 ml of physiological saline into the abdominal cavity of patients with an HCC located directly under the diaphragm separated the liver from the lung and improved the ultrasonic imaging of the lesion (7). It has also been reported that an infusion of a 5% glucose solution into the thoracic cavity (artificial pleural effusion technique) for the same purpose increased the efficacy and safety of the percutaneous treatment of lesions located directly under the diaphragm (8, 9). The technique was reported to be safe, but its influence on respiratory function and circulatory dynamics were not investigated. Moreover, an infusion of 400-500 ml of an artificial pleural effusion affects respiratory function, such as decreasing oxygen saturation, in clinical cases, suggesting that RFA after infusion may affect circulatory functions or the autonomic nervous system, such as causing an increase in blood pressure due to the severe pain involved. Studies of changes in respiratory function, circulatory dynamics, and the autonomic nervous system induced by the infusion of artificial pleural effusion could provide important information that would permit RFA for an HCC located directly under the diaphragm to be performed safely. In this study, we investigated heart beat variation and changes in circulatory and respiratory dynamics during the infusion of an artificial pleural effusion in patients with an HCC located directly under the diaphragm.

METHODS

Patients

The subjects were 13 patients (10 males and 3 females) with an HCC located directly under the diaphragm. The background liver disease was HCV in 11 patients, HBV in 1, and alcoholic liver disease in 1, and the Child-Pugh classification was Grade A in 11 and B in 2. All patients were diagnosed with HCC by abdominal dynamic CT, and underwent percutaneous RFA after an infusion of the artificial pleural effusion. Imformed consent to the study was obtained from all patients before the start of the treatment.

Artificial pleural effusion technique

A local anesthetic was administered along the puncture pathway from the skin surface to the thoracic cavity, followed by the insertion of a 14-G needle with ultrasonic guiding. 300 to 500 ml of 5% glucose solution was then infused into the thoracic cavity through this needle.

Measurement items

1) Holter electrocardiography

Holter electrocardiography (ECG) (SM-28 or SM-50, Fukuda Denshi Co., Ltd., Tokyo, Japan) was recorded using CM5 and NASA leads. ECG changes before and after the infusion were recorded on a compact memory card (Secure Digital Memory Card). The records were reproduced and analyzed using an ECG analysis work station (DMW-9000H ; Fukuda Denshi Co., Ltd., Tokyo, Japan).

2) Blood pressure

Blood pressure was measured at 3 minute intervals, starting before the initiation of infusion using an automatic hemomanometer (Olympus Co., Ltd., Tokyo, Japan).

3) Oxygen saturation

Oxygen saturation was continuously measured starting before the initiation of infusion using a percutaneous oxygen saturation measurement instrument (Olympus Co., Ltd., Tokyo, Japan).

The above parameters were measured before, during (when half of the planned infusion volume was complete), and after infusion were compared.

Analysis of heart beat variation

In the analysis of heart beat variation, autonomic nerve function was analyzed based on R-R intervals on Holter ECG (10-13). The R-R interval data were transferred to a compact memory card (Secure Digital Memory Card), and subjected to Fast Fourier Transform (FFT) using software (MenCalc/Win GMS Co., Ltd., Tokyo, Japan) designed for computers (Windows 2000) and the Holter ECG. Extrasystoles were excluded from the R-R interval data analysis so as to exclude their influence. Heart

beat variation was analyzed in R-R intervals of 256 heart beats.

In the analysis of heart beat variation, low-frequency waves (LF : 0.04-0.15 Hz), high-frequency waves (HF : 0.15-0.40 Hz), and LF/HF ratios were measured. LF components were measured to evaluate sympathetic nerve function containing parasympathetic nerve function. HF components were measured to evaluate respiration-related parasympathetic nerve function (14). LF/HF was measured to evaluate sympathetic nerve function (15). These parameters, measured before, during (when half of the planned volume was complete), and after infusion were compared.

Statistical analysis

All measured values are presented as the means± SD. Statistical analyses were performed using the StatView 5.0 software program (SAS Institute Inc., Cary, North Carolina, USA). Between-group comparisons were performed using the Wilcoxon signed-ranks test, and $p<0.05$ was regarded as being significant.

RESULTS

Patients

Detailed information on the patients is shown in Table 1. The mean infused volume of artificial pleural effusion was 415 ml (300-500 ml). No complications (hemothorax, pneumothorax, dyspnea, and others) were caused by the artificial pleural effusion technique. The infused pleural effusion disappeared after an average of 1.6 days following infusion in the case of Child-Pugh Grade A patients, but 3 and 4 days after infusion were required in the 2 Child-Pugh Grade B patients.

Mean blood pressure

No significant changes were noted in mean blood pressure before infusion (114.8±9.7mmHg), when half of the planned volume of artificial pleural effusion was complete (116.7±10.4mmHg), or after complete infusion (117.0±9.8mmHg) (Figure 1A).

Heart rate

No significant changes were noted in heart rate before infusion (77.5±13.3bpm), when half of the planned volume was complete (76.8±13.9bpm), or after complete infusion (75.4±13.3bpm) (Figure 1B).

Oxygen saturation

Oxygen saturation was significantly lower during the period when half the planned volume was complete than before infusion (95.4±1.9% vs. 97.0± 1.8%, P=0.02), and lower after complete infusion than before infusion (95.4±1.8%, P=0.01) (Figure 1C). Oxygen saturation was improved within 2 days after infusion in all patients, but the time required for the improvement was slightly longer in the case of 2 Child-Pugh Grade B patients.

Analysis of heart beat variation

No significant changes were noted in the HF value before infusion (28.6±30.3ms^2), when half of the planned volume was complete (30.0±30.3ms^2), or after complete infusion (35.6±27.6ms^2) (Figure 2A).

Table 1 Patients characteristics

case	age (y.o)	size (mm)	segment	sex	Child-Pugh classification	artifical pleural effusion (ml)	The time to disappearance of the artificial pleural effusion (day)
1	55	45	S3	male	B	400	3
2	75	26	S8	female	A	300	1
3	78	25	S8	male	A	450	2
4	78	25	S7	male	A	350	1
5	82	30	S8	male	A	350	3
6	71	55	S4	female	B	500	4
7	75	20	S4	male	A	500	2
8	69	20	S7	male	A	500	1
9	52	25	S8	male	A	400	1
10	73	30	S7	female	A	500	2
11	38	180	S7	male	A	300	1
12	66	55	S2	male	A	350	1
13	76	20	S7	male	A	500	1

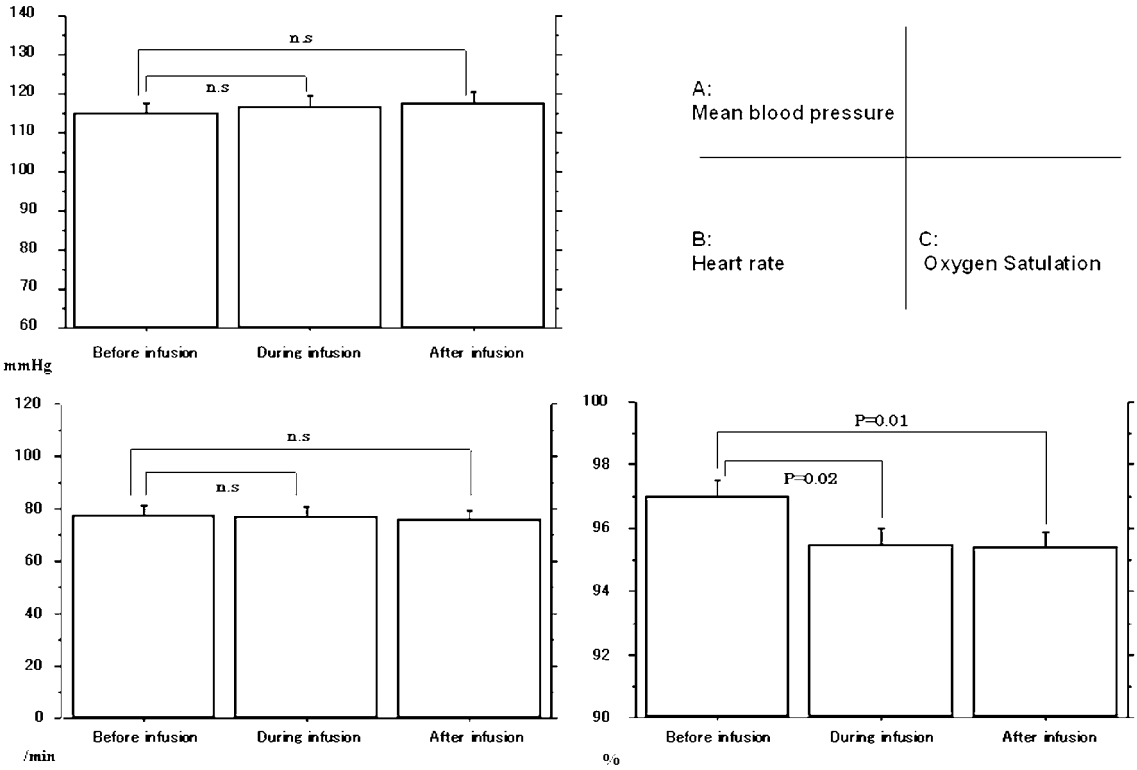

Figure 1 : Influence on circulatory and respiratory functions
A : No significant changes were noted in mean blood pressure between before infusion, during infusion, or after infusion.
B : No significant changes were noted in heart rate between before infusion, during infusion, or after infusion.
C : Oxygen saturation was significantly lower during infusion than before infusion and lower after infusion than before infusion.

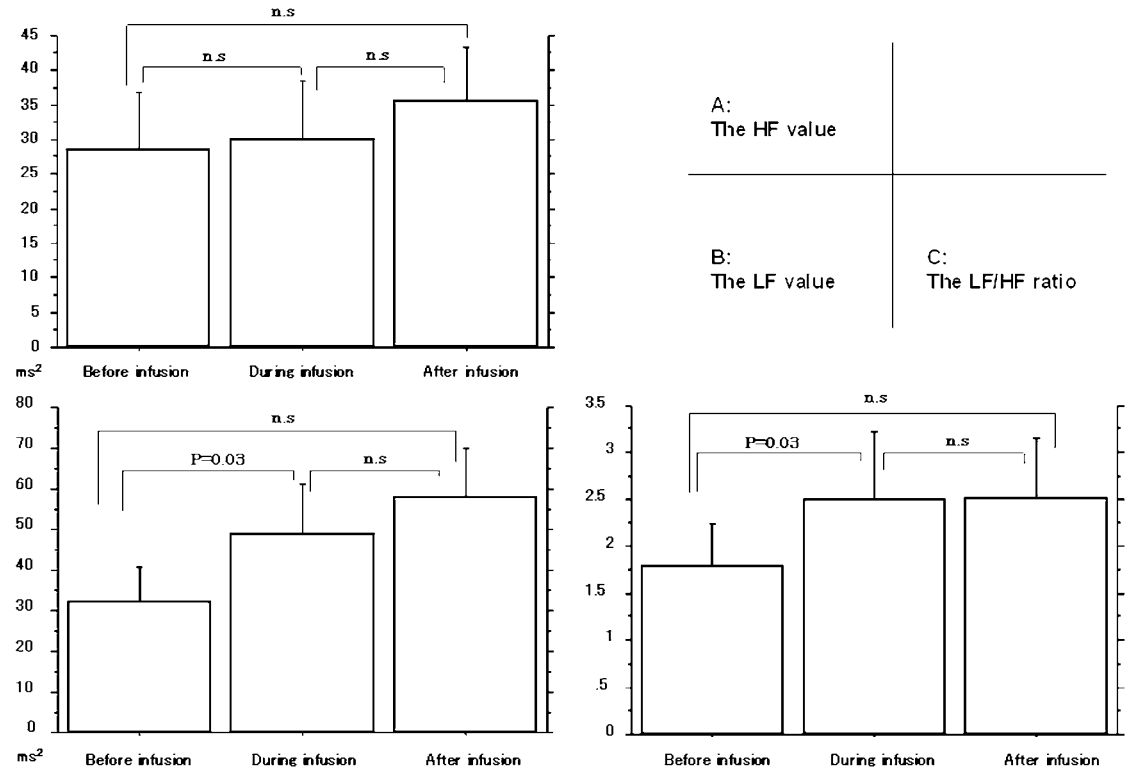

Figure 2 : Influence on the autonomic nerve system
A : No significant changes were noted in HF between before infusion, during infusion, or after infusion.
B : The LF value was significantly higher during infusion than before infusion, while no significant change were found between before infusion and after infusion.
C : The LF/HF ratio was significantly higher during infusion than before infusion and the increase persisted following infusion.

The LF value was significantly higher during the period when half the planned volume was complete than before infusion (48.7±44.5ms^2 vs. 32.1±31.8ms^2, P=0.03), while no significant change was found between before infusion and after complete infusion (75.4±13.4ms^2) (Figure 2B).

The LF/HF ratio was significantly higher after half of the planned volume was infused than before infusion (2.50±2.6ms^2 vs. 1.78±13.4ms^2, P=0.03) and the increase persisted following complete infusion (2.51±2.3ms^2, P=0.25) (Figure 2C).

DISCUSSION

The infusion of an artificial pleural effusion has recently been performed in many facilities. In addition, the advancement of non-surgical treatments of HCC has enabled percutaneous treatment without the need for laparotomy (16, 17). The efficacy of artificial pleural effusion has been reported by Shimada *et al.* and others (8).

The artificial pleural effusion technique is generally thought to have no influence on the safety and general condition of patients (9), but these items have not been systematically evaluated.

The infusion of artificial pleural effusion had no effect on heart rate or blood pressure. It was expected that filling the thoracic cavity with the pleural effusion solution would compress the lung and reduces the volume of blood trapped in the lung, thus affecting the circulatory dynamics. However, the possibility of such a major influence on circulatory dynamics may be low when the volume of pleural effusion infused is only about 500 ml.

Oxygen saturation was significantly decreased by infusion, suggesting that filling the thoracic cavity with pleural effusion causes transient atelectasis and reduces oxygenation. However, non of the patients reported any respiratory distress, and decreased oxygen saturation was improved by the nasal administration of oxygen. The time required to eliminate the pleural effusion tended to be longer in patients with decreased liver reserve capacity, which may have been due to a hypoalbuminemia-induced decrease in colloidal osmotic pressure.

On comprehensive analysis of HF and LF, infusion of the artificial pleural effusion had no effect on the parasympathetic nerves with regard to an influence on the autonomic nervous system, but the sympathetic nerves were stimulated.

LF/HF is considered to be an index of sympathetic nerve function. On comparing of LF/HF between before and after infusion, the ratio was significantly increased, indicating that sympathetic nerve function was enhanced. The pleural effusion may have induced stress, and made the sympathetic nerves dominant. However, the increased LF/HF may have reflected cardiac parasympathetic nerve activity in some patients because LF/HF is inversely proportional to the size of the HF component.

The HF component is generally considered to represent parasympathetic nerve function. HF was not affected by infusion of the artificial pleural effusion. Although HF receptors (Pulmonary Strech Receptors) are thought to be present in the thoracic cavity (18), stimulation by about 500 ml of pleural effusion may not have changed the HF value, and, thus, would have a small influence on the parasympathetic nerves.

Regarding the analysis of heart beat variation, the LF component is assumed to represent sympathetic nerve function which contains the parasympathetic nerve function. LF was significantly increased during infusion, showing that infusion of the artificial pleural effusion activated sympathetic nerves containing parasympathetic nerves.

Overall, the infusion of artificial pleural effusion appeared to increase the stimulation of sympathetic nerves. Since paroxysmal arrhythmia may occur under such conditions, ECG monitoring is important during an infusion such as used herein.

In conclusion, infusion of an artificial pleural effusion had no effect on circulatory dynamics, but transiently affected respiratory function. Since arrhythmia may occur due to the stimulation of sympathetic nerves, ECG monitoring during infusion is essential when an artificial pleural effusion is used.

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