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Original Research Article

Safety and efficacy of cell-free concentrated ascites reinfusion therapy in gastric cancer patients with refractory ascites

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Abstract

Patients of gastrointestinal carcinoma with the refractory ascites are often chemotherapy-resistant cancer patients, and these patients are good indication of the cell-free and concentrated ascites reinfusion therapy (CART). CART is predicted to enhance symptoms related to refractory ascites of patients with gastrointestinal carcinoma. The aim of this study is to evaluate the safety and efficacy of the CART system performed on the gastric cancer patients with massive refractory ascites. Descriptive cross sectional study. October 2019 to March 2020. Khost Shiekhzayed University Afghanistan. In this retrospective observational study, we evaluated 5 CART processes performed 5 patients with the gastric cancer. We evaluated the effectiveness and adverse events during CART procedures. The amounts of collected and concentrated ascites were 2415.0 ± 1851.7 ml (mean ± SD), and concentration ratio was 11.4 ± 4.5 times. the quantity of collected protein in ascites was 3.5± 1.2 g/dl, and concentration ratio of protein was 5.1 ± 1.8 times. Serum protein level was no significant different between before and fortnight after CART. No patients received an albumin (23% albumin preparation Alb) transfusion within fortnight before the primary CART. Thus, CART allowed for the reduction doses of Alb to be administered. CART has been reported to cause two adverse reactions as elevation of blood heat and reduce in vital sign. In our study, decreased vital sign wasn't observed altogether patients, and blood heat significantly rose after CART, but there have been no patients quite 38 degrees. In patients with refractory ascites of the gastric cancer patients in whom complete cure can't be expected, CART improves their QOL and, in terms of medical economy, allows for the reduction doses of Alb. CART are often effectively applied as a palliative procedure for refractory ascites of the gastric cancer patients.

Keywords: Cell-free concentrated ascites reinfusion therapy, Gastric cancer, Palliative procedure, Refractory ascites.

INTRODUCTION

The cancer often shows various symptoms, and one among the representative symptoms is ascites, and ascites produces organ dysfunction like a stomachache, abdominal distention dyspnea dysphagia and as a result as for ascites patients become anorexia (Gotlieb et al., 1998). Moreover, especially ascites markedly impairs patient quality of life (QOL) by causing abdominal distention. Thus, ascites results in deteriorate patient's QOL (Hanafusa et al., 2014). Although originally, the cell-free and Concentrated Ascites Reinfusion Therapy (CART) was used for refractory ascites caused by the end stage of chronic liver diseases within the decompensated stage but involves be used for the carcinomatous ascites in present. The representative

article on the CART procedures was published in 1977 by Inoue et al. (Maeda et al., 2015). The conventional CART system was approved by the social insurance Scheme in 1981 in Japan, and has been used as a treatment for refractory ascites. By the way, CART is an ascites processing system. With this technique, ascites is collected from patients filtered concentrated and infused to patients. At any facility equipped with this technique, CART are often easily performed for the treatment of refractory ascites (Maeda et al., 2014; Maeda et al., 2012).

CART comprises three processes, first step: paracentesis, second step: removal of cell components from ascites by filtration and concentrating ascetic fluid and last step: reinfusion of fluid obtained through this process (Katou et al., 1991). This report describes “the effectiveness and adverse events of CART for gastric patients with refractory ascites” at our hospital (Borzio et al., 1995). Biologically clean ascites were obtained by paracentesis under local anaesthesia. Drainage was continued until flow stopped spontaneously or was interrupted at the physicians’ discretion (Zaak et al., 2001). We confirmed that endotoxins weren't detected within the collected ascites, because it is understood that CART is unable to eliminate endotoxin with filtration (Takamatsu et al., 2014).

MATERIALS AND METHODS

We collected data for patient age gender ascites volume, ascites cytology and number of procedures. We evaluated laboratory data (serumprotein;Pro, albumin;Alb, sodium;Na, potassium;K, chloride;Cl, hemoglobin;Hb, hematocrit;Ht, platelet;Plt and creatinine;Cr) and calculated estimated glomerular filtration rate (eGFR) in before CART and two week later. We also collected volume, protein and albumin concentrations and cell counts in ascites of pre and post-CART. We defined the fever 38 degrees or more as during this study. All data were collected from medical records to perform this retrospective study to clarify the security and clinical problems associated with CART.

RESULTS

In this retrospective observational study, we evaluated 5 CART processes performed 5 patients with the gastric cancer. We evaluated the effectiveness and adverse events during CART procedures. The amounts of collected and concentrated ascites were 2415.0 ± 1851.7 ml (mean ± SD), and concentration ratio was 11.4 ± 4.5 times. the quantity of collected protein in ascites was 3.5± 1.2 g/dl, and concentration ratio of protein was 5.1 ± 1.8 times. Serum protein level was no significant different between before and fortnight after CART. No patients received an albumin (23% albumin preparation Alb) transfusion within fortnight before the primary CART. Thus, CART allowed for the reduction doses of Alb to be administered. CART has been reported to cause two adverse reactions as elevation of blood heat and reduce in vital sign. In our study, decreased vital sign wasn't observed altogether patients, and blood heat significantly rose after CART, but there have been no patients quite 38 degrees. (Table 1 and Table 2)

By the way, the rise in temperature was found after CART, but required all no treatment in the 36 degrees level. Also, the significant change of the blood pressure and heart rate were not found during CART.

DISCUSSION

Results of ours study show that CART is a relatively safe and effective method for the refractory ascites of gastric cancer patients. And consistent with our study, CART has the several advantages. First, the technique of CART is straightforward and convenient. Second, protein loss would be unlikely. Third, there is little influence on patient’s circulatory system and renal function. Fourth, CART allowed for the reduction of the specified doses of the albumin preparations to be administered. Last, there's little risk of infection including hepatitis as compared with use of FFP (Okamoto et al., 2013).

On the opposite hand, previous reports have shown that the adverse effect of CART. In short, CART has been reported to cause two adverse reactions as elevation of blood heat and reduce in blood pressure. In our study, decreased vital sign wasn't observed in all patients. The circulatory dynamics were stable without hypotension (Orimi et al., 2011; Gotlieb et al., 1998).

And there have been not the patients with fever 37 degrees or more during CART. Regarding elevation in blood heat caused by CART, there have been previous several reports. Borzio et al. reported that 12%of their patients as pyrexia by CART (Inoue et al., 1977). Another study reported that 43% of the patients was observed pyrexia by CART (Inoue et al., 1977). According to KANSAI CART STUDY GROUP, it had been a report that ascites processing rate was associated with elevation of body temperature. Consistent with this report, the correlation that approximately 1°C increased at processing rate of 3000 ml/hr=50 ml/min was obtained. Endotoxin was considered as a candidate of the causes of this fever, but, consistent with the report of the Okamoto et al. that measured endotoxin during CART, the endotoxin wasn't actually detected in ascites at which point in time of the whole CART either (Takamatsu et al., 2014). Therefore it's hard to think about endotoxin as a explanation for the fever by the CART. In our hospital, the CART performed at processing rate of 3000~6000ml/hr=50~100 ml/min, but no patient had fever. Also, as for the Kao et al., polymorphonuclear leukocyte or

Table 1. Details of CART procedure.

	Original ascites	Processed ascites	Concentration ratio (times)	P-value
Collected ascites volume (mL)	2415.0 ± 1851.7 (range 500-4753)	267.0 ± 243.8 (91-560)	11.3± 4.3 (6.7-18.2)	0.038
Amount of protein in ascites (g/dL)	3.5 ± 1.4 (2.5-5.9)	14.6 ± 6.7 2(3.2-17.6)	5.2 ± 2.1 (1.7-6.8)	0.015
Amount of albumin in ascites (g/dL)	1.9 ± 0.4 (1.6-2.3)	6.5 ± 3.2 (2.8-12.4)	5.6 ± 2.3 (1.7-7.6)	0.0002

Values are mean ± standard deviation (SD). P-value by paired t-test. P-value of <0.05 were considered statistically significant. CART: Cell-Free and Concentrated Ascites Reinfusion Therapy.

Table 2. Comparison of CART pre and post ascites, blood and physiological examination (3 patients and 5 times CART).

	Pre-CART	Post-CART	P-value
Ascites			
TP (g/dL)	3.5 ± 1.2	12.6 ± 6.7	0.013
Alb (g/dL)	1.6 ± 0.2	7.6 ± 2.2	0.0001
Cell count	2445.2 ± 4351.5	0	
Volume (ml)	2415.0 ± 1851.7	274.0 ± 234.7	0.034
Blood			
TP (g/dL)	6.6 ± 1.0	6.6 ± 1.9	NS
Alb (g/dL)	2.4 ± 0.6	2.9 ± 0.3	NS
Na (mEq/L)	141.8 ± 4.92415.0 ± 1851.7	141.3 ± 0.7	NS
K (mEq/L)	3.0 ± 0.7	5.0 ± 0.8	NS
Cl (mEq/L)	105.2 ± 2.0	107.0 ± 2.7	NS
Cr (mg/dL)	1.0 ± 0.3	1.2 ± 0.1	NS
eGFR	62.7 ± 17.9	54.3 ± 16.2	NS
Hb (g/dl)	9.1 ± 2.1	10.4 ± 1.2	0.007
Ht (%)	29.2 ± 5.4	29.8 ± 3.5	0.005
Plt (10^4/μl)	24.6 ± 10.1	19.4 ± 10.0	NS
Physiology			
Body temperature (°C)	37.3 ± 0.4	36.7 ± 0.1	0.044
SBP (mmhg)	100.8 ± 22.4	122.0 ± 15.3	NS
DBP (mmHg)	72.8 ± 6.9	71.0 ± 12.6	NS
HR (beats/min)	81.4 ± 10.5	71.2 ± 10.2	NS

Values are mean ± standard deviation (SD). P-value by paired t-test. P-value of <0.05 were considered statistically significant. CART: Cell-Free and Concentrated Ascites therapy. TP: total protein, Alb: alubumin, Na: sodium, K: potassium, Cl: chloride, Cr: creatinie, eGFR: estimated glomerular filtration rate, Hb: hemoglobin Ht: hematocrit, Plt: platelet, SBP: systolic blood pressure, DBP: diastolic blood pressure and HR: heart rate.

lymphocytes during ascites attached to a filter device, and when ascites was filtered, shear stress had blood cells, and therefore the activation of blood cells occurred, and inflammatory cytokine like IL-6 was released from activated blood cells to concentrated ascites. They assumed that it was a cause of the fever. Another study reported that IL-6 didn't increase by physical stimulation in ascites that took out outside a body subsequently (Gotlieb et al., 1998). Therefore inflammatory cytokine represented by IL-6 is less likely to because of the fever by the CART also as endotoxin. Thus far the explanation for the fever within the CART is unclear. However, consistent with our study, we expect that we don't got to make a clinical problem about the fever at the CART (Gotlieb et al., 1998). As a result, there wasn't the main problem by the CART, we were ready to continue cancer chemotherapy. In contrast, although the decrease of Hb and Ht were found during an observation period, we considered about this for bone marrow suppression caused by chemotherapy (Orimi et al., 2011).

In our study, we didn't use the albumin preparations for albumin supplement during CART. With the CART procedure the specified doses of the albumin preparations to be administered might be reduced. To infuse one 25% albumin preparation and FFP the expense is approximately JPY 7000 (USD 60), and 17000 (USD 150) respectively. Cost of blood product was curtailed by CART.

CONCLUSION

Our study had a limitation. This study was a retrospective observational study performed at a single center with very small number of patients. To conduct one CART procedure, the estimated expense was JPY 90 500 (USD 820; JPY 62 400 for material costs and JPY 28 100 for technical costs). CART is an expensive and time-consuming method. Therefore, it is important to produce suitable CART method and determine appropriate patient's indication of CART.

In patients with refractory ascites of gastric cancer patients in who complete cure cannot be expected, CART improves their QOL and in terms of medical economy allows for the reduction in the required doses of albumin preparations to be administered. CART can be effectively applied as a palliative procedure for refractory ascites.

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