

Effect of Humanistic Nursing Care on Relieving Generalized Pain and Negative Emotions in Patients with Advanced Liver Cancer Complicated with Respiratory Failure

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To investigate the effect of humanistic nursing care on relieving generalized pain and negative emotions in patients with advanced liver cancer complicated with respiratory failure. 80 patients with advanced liver cancer complicated with respiratory failure who were admitted to the oncology department of our hospital (November 2018–November 2019) were chosen as the study subjects and split into group X (n=40) and group Y (n=40), according to method of coin tossing. Among them, group Y received clinical routine nursing care, while group X received humanistic nursing care based on the nursing care in group Y; after that, the effect of these two nursing care models on generalized pain and negative emotions in patients was compared. No obvious difference in sex ratio, age, smoking history, drinking history, Child-Pugh classification of liver function, tumor morphotype and place of residence was found between the two groups ($P < 0.05$). With no obvious differences in HAMA and HAMD scores between the two groups before nursing care ($P > 0.05$), HAMA and HAMD scores in group X after nursing care were obviously lower compared with group Y ($P < 0.001$). The VAS scores of the patients in both groups after nursing care were obviously lower ($P < 0.001$), VAS scores in group X after nursing care were obviously lower compared with group Y ($P < 0.001$). With no significant differences in quality of life and PSQI scores between the two groups before nursing care ($P > 0.05$), quality of life and PSQI scores in group X after nursing care were obviously better compared with group Y ($P < 0.001$). The scores of optimism, self-reliance and tenacity of the patients in both groups after nursing care were obviously higher ($P < 0.05$), and scores of optimism, self-reliance and tenacity of the patients in group X were obviously higher compared with group Y ($P < 0.05$). The total nursing satisfaction in group X was obviously higher compared with group Y ($P < 0.05$). Humanistic nursing care can effectively relieve generalized pain and improve negative emotions as well as life quality in patients with advanced liver cancer complicated with respiratory failure, with significant therapeutic effect, which is worthy of application and popularization in clinical nursing.

Keywords: Humanistic nursing care; advanced liver cancer; respiratory failure; generalized pain; negative emotions

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Liver cancer is a highly prevalent tumor disease in hepatobiliary surgery with high mortality rate, and due to its insidious onset, the majority of patients may have entered middle and advanced stages when diagnosed^{1,2}. At present, surgery is the main treatment for liver cancer, but

patients' fear of cancer and prognosis brings a series of negative emotions, seriously affecting their quality of sleep, with unfavorable effect on clinical treatment. Relevant studies have found that³, with the progress of liver cancer in middle and advanced stages, multiple tissues and organs have been greatly

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affected. For example, respiratory failure is a common complication of liver cancer characterized by pulmonary ventilation dysfunction or air exchange dysfunction caused by various causes, which finally results in hypoxia and a series of physiological and metabolic disorders. In addition, cancer pain is the other main clinical manifestation in patients with liver cancer in advanced stage, in which intense physical pain will not only exacerbate patients' suffering, but also induce multiple clinical complications, greatly affecting the quality of life⁴⁻⁶. Humanistic nursing caring refers to the all-round implementation of clinical nursing care for patients, so as to make patients maintain positive attitudes during clinical treatment and improve prognosis⁷. Based on this, in our study, in order to further investigate the effect of humanistic nursing care on relieving generalized pain and negative emotions in patients with advanced liver cancer complicated with respiratory failure, 80 patients were chosen as the study subjects, and reported as below.

MATERIALS AND METHODS

General Information

80 patients with advanced liver cancer complicated with respiratory failure admitted to the oncology department of our hospital (November 2018-November 2019) were chosen as the study subjects and split into group X (n=40) and group Y (n=40), according to method of coin tossing.

Inclusion Criteria

① Patients met the diagnostic criteria for advanced liver cancer and they also had respiratory failure. ② Patients had the expected survival of more than or equal to 3 months. ③ Patients had clear consciousness and had no communication barriers. ④ This study got approval of the Hospital Ethics Committee, and the patients and their families were informed of the purpose and process and signed the informed consent.

Exclusion Criteria

① Patients had other malignant tumors. ② Patients died during the nursing care. ③ Patients had mental and other cognitive disorders or refused to cooperate with the study.

Methods

Group Y received clinical routine nursing care, including various physical examinations, medication guidance and supervision, clinical health education, dietary interventions, etc.⁸.

Based on the treatment in group Y, group X received the humanistic nursing care, and specific implementation steps were as follows. ① Establis

hment of humanistic nursing care teams. After humanistic nursing care teams were established, the nurses with more than 5-year experience in clinical practise were appointed as the team leaders, who had to shoulder the responsibility of arranging tasks according to the working ability of each nurse and the needs of patients and making tour supervision.

② Medication guidance. Medical staff should proactively inform patients of medication methods, the mechanism of the drugs as well as potential adverse reactions after medication, so that they can have correct understanding of the drugs. Besides, daily supervision by nursing staff should be carried out for patients' regular, quantitative medication.

③ Establishment of a good nurse-patient relationship. On the daily tour, medical staff should actively ask about patients' conditions with gentle and slow tone to obtain patients' trust, and encouraged patients to take positive attitudes towards life to enhance their confidence in treatment.

④ Environmental nursing support. Medical staff should keep wards tidy and in preference temperature and humidity, and after getting permission, they could play soothing music to help patients relax, thus providing quiet and comfortable treatment environment for patients.

⑤ Pain management. A body pain curve table made by our department was used to help medical staff record and grasp the times and severity of patients' daily pain and remind patients to take medication on time. Plus, for patients with severer pain, medical staff should notify attending doctors promptly for treatment.

⑥ Health education. After mastering patients' perception of their own diseases, medical staff should explain the progression of disease, specific treatment, etc. to patients and distribute cancer-related knowledge brochures to enrich patients' knowledge of liver cancer. ⑦ Social support. Medical staff should communicate with accompanying family members to inform them of patients' clinical conditions and their psychological states and encourage family members to communicate with the patients, so as to help the patients feel more love and support from their families and evoke their inner desire for a good life.

Evaluation Indexes

Degree of depression of the patients in both groups was evaluated before and after nursing care, according to the *Hamilton Depression Scale*⁹ (HAMD), which consisted of 17 scoring items. The score (< 8 points) represented normal condition, the score (8-20 points) represented potential depression, the score (21-35 points) represented depression and the score (> 35 points) represented severe depression.

Degree of anxiety of the patients in both groups was evaluated before and after nursing care,

according to the *Hamilton Anxiety Scale*¹⁰ (HAMA), which consisted of 14 scoring items. The score (< 7 points) represented normal condition, the score (7-14 points) represented potential anxiety, the score (15-21 points) represented anxiety and the score (> 21 points) represented severe anxiety.

Degree of body pain of the patients in both groups was evaluated before and after nursing care, according to the *Visual Analog Scale*¹¹ (VAS), with the total score of 10 points, and higher scores indicated severer body pain in patients.

Quality of life was evaluated before and after nursing care, according to the *Quality of Life Scale for Cancer Patients*¹², which consisted of 15 scoring items, with first 10 items scoring 5 points for each one, last 5 items scoring 10 points for each one, and higher scores represented better life quality.

Quality of sleep quality of the patients in both groups was evaluated before and after nursing care, according to the *Pittsburgh Sleep Quality Index Scale*¹³ (PSQI), with the total score of 21 points, and higher scores indicated worse quality of sleep.

Psychological resilience of the patients in both groups was evaluated before and after nursing care, according to the *Psychological Resilience Scale*¹⁴ in Chinese version, which consisted of optimism, self-reliance and tenacity, with each scoring of 20, 32 and 42 points, respectively, and higher scores indicated greater psychological resilience.

Clinical nursing satisfaction of the patients in both groups was evaluated by the *Clinical Satisfaction Questionnaire of Patients with Advanced Liver Cancer* made by our department, with the total score of 100 points. The score (≥ 85 points) represented very satisfied, the score (84-65 points) represented satisfied and the score (≤ 64 points) represented unsatisfied. Total satisfaction rate = very satisfaction rate + satisfaction rate.

Statistical Treatment

All the data were processed for statistical analysis by SPSS21.0 software, and GraphPad Prism 7 (GraphPad Software, San Diego, USA) was used to draw the pictures of the data. Measurement data were expressed by ($\bar{x} \pm s$) and tested by t-test. Enumeration data were expressed as [n (%)] and tested by χ^2 test. The differences had statistical significance when $P < 0.05$.

RESULTS

Comparison Of Clinical Information

No obvious difference in sex ratio, age, smoking history, drinking history, Child-Pugh classification of liver function, tumor morphotype and place of residence was found between the two groups ($P < 0.05$; Table 1).

Table 1.
Comparison of clinical information

Types	Group X (n=40)	Group Y (n=40)	χ^2/t	P
Gender			0.053	0.818
Male	25 (62.50%)	24 (60.00%)		
Female	15 (37.50%)	16 (40.00%)		
Average age (years old)	53.68 \pm 3.42	53.65 \pm 3.45		
BMI (kg/m ²)	21.36 \pm 0.59	21.38 \pm 0.61		
Smoking history			0.228	0.633
No	12 (30.00%)	14 (35.00%)		
Yes	28 (70.00%)	26 (65.00%)		
Drinking history			0.313	0.576
No	9 (22.50%)	7 (17.50%)		
Yes	31 (77.50%)	33 (82.50%)		
Child-Pugh classification of liver function			0.251	0.617
Level B	12 (30.00%)	10 (25.00%)		
Level C	28 (70.00%)	30 (75.00%)		
tumor morphotype				
Massive type	9 (22.50%)	11 (27.50%)	0.268	0.606
Nodular type	14 (35.00%)	13 (32.50%)	0.056	0.813
Diffuse type	17 (42.50%)	16 (40.00%)	0.052	0.820
Place of residence			0.474	0.491
Urban area	14 (35.00%)	17 (42.50%)		
Rural area	26 (65.00%)	23 (57.50%)		

Comparison Of The Hama And Hamd Scores

With no obvious differences in the HAMA and HAMD scores between the two groups before

nursing care ($P > 0.05$), HAMA and HAMD scores in group X after nursing care were obviously lower compared with group Y ($P < 0.05$; Table 2).

Table 2.

Comparison of the HAMA and HAMD scores ($\bar{x} \pm s$, points)

Group	n	HAMA score		HAMD score	
		Before nursing care	After nursing care	Before nursing care	After nursing care
Group X	40	17.62 \pm 2.14	7.23 \pm 1.52	21.24 \pm 2.16	9.23 \pm 1.24
Group Y	40	17.59 \pm 2.15	13.43 \pm 1.58	21.26 \pm 2.18	16.52 \pm 1.83
t		0.063	17.885	0.041	20.857
P		0.950	0.000	0.967	0.000

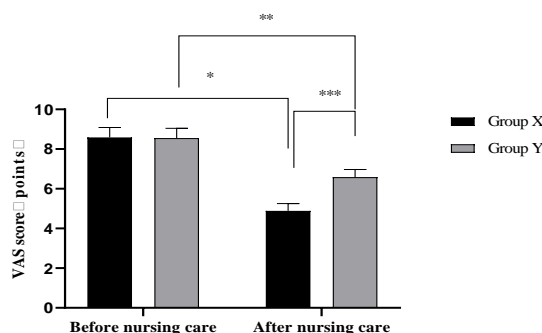
Comparison Of The VAS Scores

VAS scores in both groups after nursing care were obviously lower ($P < 0.05$), and VAS scores in

group X after nursing care were obviously lower compared with group Y ($P < 0.05$; Figure 1).

Figure 1.

Comparison of the VAS scores ($\bar{x} \pm s$)



Note: The abscissa indicated before and after nursing care, while the ordinate indicated VAS score, points.

In group X, VAS scores before and after nursing care were (8.23 \pm 0.71) points and (4.63 \pm 0.52) points, respectively, while in group Y, VAS scores before and after nursing care were (8.21 \pm 0.69) points and (6.32 \pm 0.54) points, respectively.

* indicated an obvious difference in VAS scores of group X before and after nursing care ($t = 25.872$, $P = 0.000$).

** indicated an obvious difference in VAS scores of group Y before and after nursing care ($t = 13.643$, $P = 0.000$).

*** indicated an obvious difference in VAS scores between the two groups before and after nursing care ($t = 14.258$, $P = 0.000$).

Comparison Of The Quality Of Life And Psqi Scores

With no obvious differences in the quality of life and PSQI scores between the two groups before

nursing care ($P > 0.05$), quality of life and PSQI scores in group X after nursing care were obviously better compared with group Y ($P < 0.05$; Table 3).

Table 3.

Comparison of the quality of life and PSQI scores ($\bar{x} \pm s$, points)

Group	n	Quality of life score		PSQI score	
		Before nursing care	After nursing care	Before nursing care	After nursing care
Group X	40	34.56 \pm 5.64	62.31 \pm 3.58	16.04 \pm 2.35	4.58 \pm 1.04
Group Y	40	34.59 \pm 5.67	42.26 \pm 3.42	16.07 \pm 2.33	9.18 \pm 1.03

t	0.024	25.612	0.057	19.876
P	0.981	0.000	0.954	0.000

Comparison Of The Psychological Resilience Scores

The sores of optimism, self-reliance and tenacity of the patients in both groups after nursing care

were obviously higher ($P < 0.05$), and the sores of optimism, self-reliance and tenacity of the patients in group X were obviously higher compared with group Y ($P < 0.05$; Table 4).

Table 4.
Comparison of the psychological resilience scores ($\bar{x} \pm s$, points)

Group	n	Time	Optimism	Self-reliance	Tenacity
Group X	40	Before nursing care	9.78 \pm 1.25	21.17 \pm 4.32	28.94 \pm 5.41
		After nursing care	13.26 \pm 2.26	27.13 \pm 3.53	35.29 \pm 4.39
Group Y	40	Before nursing care	9.82 \pm 1.28	21.19 \pm 4.36	28.91 \pm 5.45
		After nursing care	11.85 \pm 2.17*	24.15 \pm 3.49*	31.85 \pm 4.41*

Note: The sores of optimism, self-reliance and tenacity of the patients in both groups after nursing care were obviously higher than those before nursing care. * indicated the comparison of the scores of optimism, self-reliance and tenacity after nursing care between the two groups, $P < 0.05$.

Comparison Of The Clinical Nursing Satisfaction

Clinical nursing satisfaction in group X was

obviously higher compared with group Y ($P < 0.05$), as shown in Table 5.

Table 5.
Comparison of the clinical nursing satisfaction [n (%)]

Group	n	Very satisfied	Satisfied	Unsatisfied	Total satisfaction
Group X	40	18 (45.00%)	19 (47.50%)	3 (7.50%)	92.50% (37/40)
Group Y	40	13 (32.50%)	17 (42.50%)	10 (25.00%)	75.00% (30/40)
χ^2					4.501
P					0.034

DISCUSSION

As advanced liver cancer is mainly characterized by the difficult treatment, poor clinical prognosis, rapid progression and high mortality, the patients often suffer from negative emotions after diagnosis and lose confidence in treatment, with heavy psychological burdens, resulting in poor treatment outcomes¹⁵. Due to the insidious onset of liver cancer in early stage, most patients have entered the middle and advanced stages when diagnosed, missing the optimal treatment period. Clinical studies have confirmed¹⁶ that there is a close association between the onset of liver cancer and hepatitis B, as hepatitis can damage hepatocytes, inhibit the regeneration of hepatocytes and increase the sensitivity of other pathogenic cancer cells. At present, radiotherapy, chemotherapy, interventional therapy, etc. are the main treatment methods for advanced liver cancer, which can effectively prolong patients' survival and improve their quality of life. Respiratory failure, a common complication in patients with advanced liver cancer, is mainly manifes

ted by dyspnea, hypoxia, and some symptoms in blood circulation system, digestive system as well as nervous system, increasing the difficulty of clinical treatment^{17,18}.

Liver pains combined with the suffering from radiotherapy and chemotherapy will exacerbate negative emotions, increase psychological burdens or even lead to suicide in patients; therefore, an effective clinical nursing care model that can alleviate generalized pain and improve negative emotions in patients with advanced liver cancer complicated with respiratory failure should be adopted as soon as possible. Studies have revealed that patients with advanced liver cancer not only need effective medical technology for treatment, but also need appropriate humanistic nursing care to relieve their negative emotions and enhance the confidence in treatment. The humanistic nursing care pays much attention to the role and value of the person, provides patients with all-round clinical nursing care and emotional support and shows much care about the progress of patients' diseases, thus greatly relieving body pain, enhancing the

confidence in treatment and improving prognosis¹⁹⁻²¹. The study confirmed that VAS scores of the patients with advanced liver cancer complicated with respiratory failure after humanistic nursing care were obviously lower compared with group Y ($P < 0.001$), indicating that application of body pain curve table for the clinical nursing care in patients helps medical staff precisely grasp patients' physical conditions and implement corresponding treatment methods, which can effectively reduce the times and severity of daily pain.

Studies at home and abroad have demonstrated that most patients with advanced cancer have severe sleep disorders caused by multiple factors, such as clinical treatment, body pain, and psychological burdens; therefore, focusing on the sleep disorders of cancer patients, improving the quality of sleep and ensuring adequate sleep are also the key contents of clinical nursing care²². Our study found that the quality of sleep scores of the patients in group X after humanistic nursing care were obviously higher compared with group Y ($P < 0.001$), which is consistent with results of Singh et al²³ who have stated that after the implementation of humanistic nursing care for patients with breast cancer, the PSQI scores of the patients after nursing care were (4.43 ± 1.43) points, which were obviously lower than (16.28 ± 1.82) points before nursing care, illustrating that humanistic nursing care model can alleviate negative emotions and improve sleep quality of patients with advanced liver cancer complicated with respiratory failure.

In conclusion, humanistic nursing care can effectively relieve generalized pain and improve negative emotions as well as life quality of patients with advanced liver cancer complicated with respiratory failure, with significant therapeutic effect, which is worthy of application and popularization in clinical nursing.

REFERENCES

1. Nierop, P. M. H., Verseveld, M., Galjart, B., et al. The liver-first approach for locally advanced rectal cancer and synchronous liver metastases[J]. *European Journal of Surgical Oncology: The Journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology*, 2019, 45(4): 591-596. DOI: 10.1016/j.ejso.2018.12.007.
2. Christian Toso, Glenda Meeberg, Axel Andres, et al. Downstaging prior to liver transplantation for hepatocellular carcinoma: advisable but at the price of an increased risk of cancer recurrence - a retrospective study[J]. *Transplant International*, 2019, 32(2): 163-172.
3. Sasaki, Akinori, Nakamura, Yoshiaki, Mishima, Saori, et al. Predictive factors for hyperprogressive disease during nivolumab as anti-PD1 treatment in patients with advanced gastric cancer[J]. *Gastric cancer: official journal of the International Gastric Cancer Association and the Japanese Gastric Cancer Association*, 2019, 22(4): 793-802. DOI: 10.1007/s10120-018-00922-8.
4. Darko Castven, Diana Becker, Carolin Czauderna, et al. Application of patient - derived liver cancer cells for phenotypic characterization and therapeutic target identification[J]. *International Journal of Cancer*, 2019, 144(11): 2782-2794. DOI: 10.1002/ijc.32026.
5. Zhampeissov, Nurlan, Manap, Erlan, Rustemova, Kulsara, et al. High-intensity focused ultrasound ablation: a non-surgical approach to treat advanced and complicated liver alveococcosis[J]. *Journal of medical ultrasonics: official journal of the Japan Society of Ultrasonics in Medicine*, 2019, 46(2): 251-255.
6. Pang, Junfeng, Jin, Xiongjie, Cho, Wonkyoung, et al. The Molecular Chaperone Heat Shock Protein 70 Controls Liver Cancer Initiation and Progression by Regulating Adaptive DNA Damage and Mitogen-Activated Protein Kinase/Extracellular Signal-Regulated Kinase Signaling Pathways[J]. *Molecular and Cellular Biology*, 2019, 39(9). doi: 10.1128/MCB.00391-18.
7. Kuo, LiCheng, Ballangrud, Ase M., Ho, Alice Y., et al. A VMAT planning technique for locally advanced breast cancer patients with expander or implant reconstructions requiring comprehensive postmastectomy radiation therapy[J]. *Medical dosimetry: official journal of the American Association of Medical Dosimetrists*, 2019, 44(2): 150-154. DOI: 10.1016/j.meddos.2018.04.006.
8. Ni, Xiang, Zhang, Xiaoyan, Duan, Xingchen, et al. Near-Infrared Afterglow Luminescent Aggregation-Induced Emission Dots with Ultrahigh Tumor-to-Liver Signal Ratio for Promoted Image-Guided Cancer Surgery[J]. *Nano letters*, 2019, 19(1): 318-330. DOI: 10.1021/acs.nanolett.8b03936.
9. Ord, Helen L., Griksaitis, Michael J.. Fifteen-minute consultation: Using point of care ultrasound to assess children with respiratory failure[J]. *Archives of disease in childhood. Education and practice edition*, 2019, 104(1): 2-10. DOI: 10.1136/archdischild-2017-313795.
10. Wadwekar Vaibhav, Pillai Rajit Remanan, Sesh S, et al. Pregnancy - associated respiratory failure in muscle specific kinase muscle specific kinase congenital myasthenic syndrome[J]. *Muscle and Nerve*, 2019, 59(4): E24-E26. doi: 10.1002/mus.26410.
11. Vaibhav Wadwekar, Rajit Remanan Pillai, S Sesh, et al. Pregnancy - associated respiratory failure in muscle specific kinase congenital myasthenic syndrome[J]. *Muscle & Nerve*, 2019, 59(4): E24-E26.
12. Sood, Ravi F., Lipira, Angelo B., Neligan, Peter C., et al. Respiratory Failure following Abdominal Wall Reconstruction: An Analysis of the Nationwide Inpatient Sample[J]. *Plastic and reconstructive surgery*, 2019, 143(1): 165E-171E. doi: 2706

- 10.1097/PRS.0000000000005115.
13. Huang, Hsin-Hui, Chen, Su-Jung, Chao, Tze-Fan, et al. Influenza vaccination and risk of respiratory failure in patients with chronic obstructive pulmonary disease: A nationwide population-based case-cohort study[J]. *Journal of microbiology, immunology, and infection: Wei mian yu gan ran za zhi*, 2019, 52(1):22-29. doi: 10.1016/j.jmii.2017.08.014.
14. Borders, James C., Fink, Daniel, Levitt, Joseph E., et al. Relationship Between Laryngeal Sensation, Length of Intubation, and Aspiration in Patients with Acute Respiratory Failure[J]. *Dysphagia*, 2019, 34(4):521-528.
15. Menaker, Jay, Rabinowitz, Ronald P., Tabatabai, Ali, et al. Veno-Venous Extracorporeal Membrane Oxygenation for Respiratory Failure: How Long Is Too Long? [J]. *ASAIO journal*, 2019, 65(2):192-196.
16. Bauer, Philippe R., Chevret, Sylvie, Yadav, Hemang, et al. Diagnosis and outcome of acute respiratory failure in immunocompromised patients after bronchoscopy[J]. *The European respiratory journal* :, 2019, 54(1).
17. Patrick B. Murphy, Eui - Sik Suh, Nicholas Hart. Non - invasive ventilation for obese patients with chronic respiratory failure: Are two pressures always better than one? [J]. *Respirology*, 2019, 24(10):952-961.
18. Athena F. Zuppa, Daniela J. Conrado, Nicole R. Zane, et al. Midazolam Dose Optimization in Critically Ill Pediatric Patients With Acute Respiratory Failure: A Population Pharmacokinetic-Pharmacogenomic Study[J]. *Critical care medicine*, 2019, 47(4):e301-e309.
19. Azoulay, Elie, Mokart, Djamel, Kouatchet, Achille, et al. Acute respiratory failure in immunocompromised adults[J]. *The lancet. Respiratory medicine*., 2019, 7(2):173-186.
20. Ozawa, Mio. The impact of the guideline for pain management in Japanese neonatal intensive care units: A 5-year follow-up[J]. *Child: care, health and development*, 2019, 45(6):867-870.
21. Jie Qiu, Li Zhao, Yang Yang, et al. Effects of fentanyl for pain control and neuroprotection in very preterm newborns on mechanical ventilation[J]. *The Journal of Maternal-Fetal & Neonatal Medicine*, 2019, 32(22):3734-3740.
22. Gabi Koller, Andreas Schwarzer, Kathrin Halfter, et al. Pain management in opioid maintenance treatment[J]. *Expert Opinion on Pharmacotherapy*, 2019, 20(16):1993-2005.
23. Singh, Ashima, Yan, Ke, Brandow, Amanda M., et al. Longitudinal Trend in Emergency Department Reliance for Pain Among Sickle Cell Disease Patients in Wisconsin[J]. *Journal of pediatric hematology/oncology: Official journal of the American Society of Pediatric Hematology/Oncology*, 2019, 41(7):E438-E442.