Pakistan J. Zool., vol. 54(6), pp 2997-3000, 2022 **DOI**: https://dx.doi.org/10.17582/journal.pjz/20201117141155

Short Communication

Effect of Dexamethasone Combined with Ganglioside on Acute Carbon Monoxide Poisoning and its Influence on Cognitive Function

Huajun Lin, Wei Qu and Zhuxian Yu*

Emergency Department, Weihai Central Hospital, Wendeng, 264400, China

ABSTRACT

This study aims to investigate the efficacy of dexamethasone (Dex) with ganglioside in the treatment of patients with acute carbon monoxide poisoning (ACMP) and its effect on patients' cognitive function. A total of 64 patients with ACMP treated in our hospital from January 2019 to March 2020 were selected as the research object, and these 64 patients were divided into an experimental group and a control group by random number table method. Patients in the experimental group were treated with Dex and ganglioside, and the control group was treated with conventional methods. The clinical treatment effects, connective tissue growth factor (CTGF), TGF-β1 levels in serum and cognitive function were compared between the two groups. The total effective rate of treatment in the combination group was 93.75%, which was significantly higher than 62.50% in the control group (P<0.05); after treatment, the serum CTGF and TGF-β1 levels in both groups were higher than before treatment. The serum CTGF and TGF in the combination group -The level of β1 was higher than that of the conventional group, and the difference was statistically significant (both P <0.05). After treatment, the Mini–Mental State Examination (MMSE) scores of the patients in both groups were improved, and the cognitive ability of the patients in the experimental group was better than that in the control group (P<0.05). It seems Dex experimental with ganglioside is effective in the treatment of ACMP and can significantly improve the cognitive function of patients.

Article Information
Received 17 November 2020
Revised 01 March 2021
Accepted 06 April 2021
Available online 03 March 2022 (early access)
Published 23 September 2022

Authors' Contribution
HL and ZY collected the samples. HL and WQ analysed the data. WQ and ZY conducted the experiments and analysed the results. All authors discussed the results and wrote the manuscript.

Key words
Carbon monoxide poisoning, Dexamethasone, Ganglioside, Cognitive function.

Common in the clinic, acute carbon monoxide (CO) poisoning (ACMP) is caused by work factors and life factors. In China, the work factor that causes CO poisoning (CMP) is often the explosion of coal mine gas in mineral operations; in cold winter in the north, leakage of firewood heating appliances and gas pipe appliances is the main reason for CMP in the living environment (Xiang *et al*., 2017). The main clinical symptoms of ACMP include weakness in the extremities, dizziness, nausea, *etc*. The poisoned person will suffer from severe coma and shock (Liao *et al*., 2018). The mechanism of ACMP is that CO enters the body and binds to hemoglobin in the blood, which greatly destroys the combination of oxygen and hemoglobin, resulting in ischemia and hypoxia, and ultimately causing disturbance of sugar metabolism in the poisoned person. The increased lactic acid or even acidosis seriously affects the health of poisoned people (Ning *et al*., 2020). ACMP has extremely high mortality and disability rate. In clinical practice, delayed encephalopathy is a common neurological complication in patients with ACMP, with an incidence of 10-40% (Kitamoto *et al*., 2016). ACMP patients with delayed encephalopathy often display mental retardation, slow response, incontinence, and even coma (Mizuno *et al*., 2014).

Dexamethasone (Dex) therapy early in the course of CO poisoning might help to avoid delayed encephalopathy and lower serum myelin basic protein MBP levels (Li *et al*., 2015). Therefore, timely and effective rehabilitation intervention carries great significance for the treatment of ACMP.

Ganglioside is sphingolipids containing sialic acid, which can greatly enhance the regeneration and development of cerebral nerves, showing good efficacy in treating ACMP (Kitamoto *et al*., 2016). Dex can not only reduce inflammation, alleviate poisoning, eliminate allergies and treat rheumatic diseases, but also promote blood circulation in the brain and slow down the deformation and necrosis of brain cells (Li *et al*., 2020). In recent years, our hospital has used ganglioside in combination with Dex to treat ACMP patients, with good

* Corresponding author: yzx13563153677@163.com
0030-9923/2022/0006-2997 $ 9.00/0

results received.

Connective tissue growth factor (CTGF) is a well-known factor that is studied in inhalation poisonings as well as paraquat (PQ) poisoning, in which lung damage is connected to increased CTGF (Yang *et al*., 2015). Also, some researchers have suggested biological roles of the platelet-derived transforming growth factor (TGF)-β1 in response to CMP and related pathologic fibrosis due to oxidative stress (Ahamed *et al*., 2017). So we choose these biological factors as the variables of interest in our study.

Materials and methods

A total of 64 patients with ACMP who were treated in our hospital from January 2019 to March 2020 were selected as the research subjects. They were randomly divided into control group (n=32) and experimental group (n=32). Where, the control group had male-female ratio of 21/11, average age of 46.02±11.85 years, and average poisoning time of 4.28±1.12 h; the experimental group had male-female ratio of 19/13, average age of 46.45±9.56 years, and average poisoning time of 3.97±2.03 h. There was no significant difference between basic data of the two groups, such as average age, sex ratio, poisoning time, and poisoning degree, *etc*. (P>0.05).

Inclusion criteria: (1) aged 18-60 (minors and the elderly have relatively weak physiological function, choosing young adults aged 18-60 can reduce the impact of personal constitution on the treatment effect); (2) all patients had severe CMP; (3) all patients were poisoned for 2-8 h; (4) All enrolled patients understood the content of this study and signed an informed consent; (5) This study was approved by in-hospital ethics committee. Exclusion criteria: patients with (1) mild to moderate CMP; (2) neurological diseases such as cerebral infarction and cerebral hemorrhage; (3) heart, liver, lung, kidney and other tissue and organ dysfunction.

The control group received conventional treatment after admission, and the experimental group was given intravenous infusion of ganglioside 100 mg/d once a day on the basis of conventional treatment. At the same time, intravenous infusion of Dex (Chengdu Tiantaishan Pharmaceutical Co., Ltd., National Medicine Permission Number H51020723) was given, 10 mg/time, once daily. The efficacy of the two groups was observed after 2 weeks of treatment.

Treatment effect, adverse drug reactions (blood routine, blood sugar, liver and kidney function), serum connective tissue growth factor (CTGF) and TGF-β1 levels and cognitive function were compared between the two groups. Judgment criteria for treatment effect (Ning *et al*., 2020): (1) Cured: After treatment, the patient's clinical symptoms are all eliminated, the EEG examination result is completely normal, and there is no adverse effect on future daily life. (2) Markedly effective: After treatment, the patient's clinical symptoms have been significantly improved, the EEG examination result is basically normal. The patient will have certain self-living ability, but his life will be affected to some extent. (3) Effective: After treatment, the patient's clinical symptoms are improved, but the EEG examination shows obvious abnormalities, and the patient's daily work and life will be affected. (4) Ineffective: After treatment, the patient has no changes or the condition deteriorates. The Simple Intelligent Mental State Examination Scale (MMSE) is used to judge the patient's cognitive function. MMSE includes speaking ability, direction ability, arithmetic ability, memory and attention (Deng, 2017). Where, 0-9 points indicate severe dementia; 10-19 points indicate moderate dementia; 20-23 points indicate mild dementia; 24-27 points indicate mild cognitive impairment; 28-30 points indicate recovery to normal state. In short, better body function comes with a higher score.

SPSS 19.0 was used to analyze the relevant data. Where, the measurement data was expressed as ($x \pm s$) and tested by t test; the count data was expressed as rate (%), and tested by χ^2 test. $P < 0.05$ indicates statistically significant difference.

Results

Comparison of efficacy of the two groups showed that the total effective rate of the experimental group was 93.75% after treatment, which was significantly higher than 62.50% of the control group (P<0.05), specifically shown in Table I.

Comparison of the occurrence of adverse reactions in the two groups showed that there were no obvious adverse reactions in the two groups, and no significant changes and differences were shown in liver function, renal function, blood glucose level and hematuria routine before and after treatment in the two groups.

Comparison of serum CTGF and TGF-β1 levels in the two groups showed that before treatment, there was no significant difference in serum CTGF and TGF-β1 levels between the two groups (P>0.05). After treatment, the serum CTGF and TGF-β1 levels were significantly increased in both groups, which was significantly higher in the experimental group than in the control group (P <0.05), specifically shown in Table I.

Comparison of MMSE scores of the two groups showed that before treatment, there was no significant difference in the MMSE scores of the two groups (P>0.05); after treatment, MMSE scores of both groups were higher, and the experimental group had significantly higher MMSE score than the control group (P<0.05), specifically shown in Table I.

Table I.- Comparison of study variables between the two groups (n (%)/Mean±SD).

Group	Control group (n=32)	Experimental group (n=32)
Efficacy		
Cured	3(9.38)	6(18.75)
Markedly effective	6(18.75)	8(25.00)
Effective	12(37.50)	16(50.00)
Ineffective	12(37.50)	2(6.25)
Total effective rate (%)	62.5	93.75
CTGF(μg/L)		
Before treatment	19.94±2.03	21.07±1.89
After treatment	33.86±3.37[a]	40.23±4.21[ab]
TGF-β1(ng/L)		
Before treatment	19.63±1.59	19.72±1.18
After treatment	46.23±4.63[a]	57.75±6.25[ab]
MMSE scores		
Before treatment	12.98±2.24	13.64±3.25
After treatment	29.13±2.54[a]	22.51±2.04[a]

CTGF, connective tissue growth factor; TGF-β1, transforming growth factor β1; [a], significant difference after treatment, with statistical analysis significance (P <0.05); [b], significant difference compared with the control group, with statistical analysis significance (P<0.05); NS, not significant.

Discussion

Carbon monoxide (CO) bonds to hemoglobin in the body to form carboxyhemoglobin. Since CO can better bond to hemoglobin than oxygen, after the CO enters the body, the oxygen carrying capacity of hemoglobin drops greatly, which is very likely to cause cerebral circulatory disturbance in the patients, eventually leading to hypoxia and causing related diseases such as thrombosis, focal ischemic necrosis of cerebral cortex and cerebral basal surface (Tan and Wang, 2012). Some patients with severe ACMP have symptoms such as incontinence and mental retardation, which is clinically known as delayed encephalopathy (Bi *et al*., 2017).

At present, related studies show that the cause of acute CO delayed encephalopathy (ACMPDE) is that the human brain's blood vessels have few anastomotic branches and relatively strong metabolism, thus prone to damage. After the human body inhales CO, the small blood vessels in the brain will be paralyzed and expand, and due to insufficient oxygen, it will consume Adenosine triphosphate (ATP) in the blood, which will hinder the normal transport of sodium ion to a certain extent, so that sodium ions accumulate in the cells, which in turn causes edema in the brain cells and leads to swelling of the vascular endothelial cells, eventually inducing obstacles in the circulation of cerebral blood vessels (Jeong *et al*., 2015). In addition, the accumulation of acidic metabolites in the brain changes the permeability of cerebral blood vessels, producing interstitial edema of the brain cells. Cerebrovascular circulatory disturbance can induce thrombosis, ischemic necrosis and extensive demyelinating lesions (Zou *et al*., 2015). Some studies believe that the occurrence mechanisms of delayed encephalopathy in ACMP include ischemic hypoxia mechanism, cytotoxic injury mechanism, reperfusion injury and free radical mechanism, excitatory amino acid and apoptosis mechanism, immunologic dysfunction and neurotransmitter interference mechanism *etc*. (Wu *et al*., 2016; Xiang *et al*., 2017; Wen *et al*., 2019; Pang *et al*., 2016; Kudo *et al*., 2014; Zhao *et al*., 2018). In short, no matter what causes ACMP, the main treatment purpose is to repair nerve cells of the poisoned patients.

Ganglioside can penetrate the blood-brain barrier to increase the activity of related enzymes on the brain nerve cell membranes, thus playing a certain role in promoting the transport of sodium ions, which in turn relieves cell edema. Ganglioside can also promote the growth and recovery of cellular nerves, which in turn repairs damage to the nervous system, thus protecting nerve cells from neurotoxin damage caused by excitatory amino acids. It has been widely used to repair damage to the central nervous system (Fang *et al*., 2011). Dex is a glucocorticoid that can eliminate inflammation, relieve pain and suppress vomiting. Related research proves that Dex can improve immune function of the body and play an anti-inflammatory role, so it can be used to treat ACMPDE (Luo *et al*., 2020). Dex can eliminate brain edema to a certain extent, expand the cerebral blood vessels to promote blood transport in the brain, which reduces the probability of degeneration and death of brain cells to a certain extent, so Dex can alleviate CO damage to nerve cells of the poisoned person. Related animal experiments have proved that ganglioside can enter the nerve cell membrane across the blood-brain barrier, which can increase the activity of Na^+-K^+-ATPase and Ca^{2+}-ATPase on it, promote ion balance on cell membrane, thereby alleviating cell edema and slows the occurrence of cerebral perfusion, cerebral ischemia, cerebral hypoxia, etc. to a certain extent (Ki *et al*., 2020). At the same time, ganglioside can accelerate the metabolism of animal body, slow down the body's lipid peroxidation, neutralize the toxicity of neurotoxic substances such as glutamic acid and arachidonic acid, and remove free radicals. These functions can improve the structure and function stability of nerve cell membranes. Related studies have shown that ganglioside can shorten the consciousness recovery time of DEACMP, and can increase the content of nitric oxide, lipid peroxides and

superoxide dismutase in patients' plasma, thereby reducing the occurrence probability of delayed encephalopathy (Ning *et al*., 2020). In this study, the total effective rate of the experimental group was 93.75% after treatment, which was significantly higher than 62.50% of the control group (P<0.05). After treatment, the serum CTGF and TGF-β1 levels were significantly increased in both groups, which was significantly higher in the experimental group than in the control group (P <0.05). After treatment, MMSE scores of both groups were higher, and the experimental group had significantly higher MMSE score than the control group (P<0.05). This result is similar to that of Qin Haiyan (Wang *et al*., 2010).

Conclusion

To conclude, Dex experimental with ganglioside has a significant effect in treating ACMP, not only lowering incidence of adverse reactions, but also enhancing patients' cognitive ability, which can be popularized and applied clinically.

Statement of conflict of interest

The authors have declared no conflict of interests.

References

Ahamed, J. and Laurence, J., 2017. *Antioxid. Redox Signal*., **27**: 977-988. https://doi.org/10.1089/ars.2017.7064

Bi, M.J., Sun, X.N., Zou, Y., Ding, X.Y., Liu, B., Zhang, Y.H., Guo, D.D. and Li, Q., 2017. *Front. Pharmacol*., **8**: 64. https://doi.org/10.3389/fphar.2017.00064

Deng, Y.L., 2017. *J. Acute Dis*., **6**: 18. https://doi.org/10.12980/jad.6.2017JADWEB-2016-0060

Fang, P., Xu, Y.X. and Lei, X., 2011. *Modern Prevent. Med*., **3**: 44-47.

Jeong, K.Y., Suh, G.J., Kwon, W.Y., Kim, K.S., Jung, Y.S. and Kye, Y.C., 2015. *J. Trauma Acute Care Surg*., **79**: 247-255. https://doi.org/10.1097/TA.0000000000000761

Ki, S., Myoung, I., Cheong, S., Lim, S., Cho, K., Kim, M.H., Han, Y., Oh, M., Park, Y. and Kim, K., 2020. *Anesthesia Pain Med*., **15**: 441. https://doi.org/10.17085/apm.20057

Kitamoto, T., Tsuda, M., Kato, M., Saito, F., Kamijo, Y. and Kinoshita, T., 2016. *Acute Med. Surg*., **3**: 315-319. https://doi.org/10.1002/ams2.197

Kudo, K., Otsuka, K., Yagi, J., Sanjo, K., Koizumi, N., Koeda, A., Umetsu, M.Y., Yoshioka, Y., Mizugai, A. and Mita, T., 2014. *BMC Emerg. Med*., **14**: 1-7. https://doi.org/10.1186/1471-227X-14-3

Li, N., Gao, X., Wang, W., Wang, P. and Zhu, B., 2020. *Cardiovasc. Diagn. Ther*., **10**: 1785. https://doi.org/10.21037/cdt-20-591

Li, Q., Song, J.J., Zhang, H.Y., Fu, K., Lan, H.B. and Deng, Y., 2015. *Biotech. Histochem*., **90**: 561-567. https://doi.org/10.3109/10520295.2015.1019565

Liao, S.C., Mao, Y.C., Hung, Y.M., Lee, C.H. and Yang, C.C., 2018. *BioMed Res. Int*., **2018**: 2543018. https://doi.org/10.1155/2018/2543018

Luo, Y., Liao, Z., Shu, J., Zhang, J. and Yu, X., 2020. *Pak. J. Pharm. Sci*., **33**: 489-494.

Mizuno, Y., Sakurai, Y., Sugimoto, I., Ichinose, K., Ishihara, S., Sanjo, N., Mizusawa, H. and Mannen, T., 2014. *Intern. Med*., **53**: 1441-1445. https://doi.org/10.2169/internalmedicine.53.2132

Ning, K., Zhou, Y.-Y., Zhang, N., Sun, X.J., Liu, W.W. and Han, C.H., 2020. *Med. Gas Res*., **10**: 30. https://doi.org/10.4103/2045-9912.279981

Pang, L., Zhang, N., Dong, N., Wang, D.W., Xu, D.H., Zhang, P. and Meng, X.W., 2016. *Inflammation*, **39**: 561-568. https://doi.org/10.1007/s10753-015-0280-4

Tan, Q. and Wang, X.B., 2012. *J. clin. Med. Pract*., **2012**: 13.

Wang, Y.G., Wei, G.Q. and Chen, J., 2010. *Med. J. natl. Defend. Forc. N. China*, **3**: 26-30.

Wen, J., Zhang, X. and Li, C., 2019. *J. Coll. Phys. Surg. Pak*., **29**: 119-122. https://doi.org/10.29271/jcpsp.2019.02.119

Wu, L., Zhang, H., Xing, Y., Gao, Y., Li, Y., Ren, X., Li, J., Nie, B., Zhu, L. and Shang, H., 2016. *Medicine*, **95**: e2875. https://doi.org/10.1097/MD.0000000000002875

Xiang, W.P., Xue, H. and Wang, B.J., 2017. *Asia Pacific J. clin. Trials: Nerv. Syst. Dis*., **2**: 15. https://doi.org/10.4103/2542-3932.198961

Yang, Z., Sun, Z., Liu, H., Ren, Y., Shao, D., Zhang, W., Lin, J., Wolfram, J., Wang, F., Nie, S., 2015. *Mol. Med. Rep*., **12**: 1091-1097. https://doi.org/10.3892/mmr.2015.3537

Yang, F., Yang, F., Wang, G., Kong, T., Wang, H. and Zhang, C., 2020. *Aquaculture*, **515**: 734542. https://doi.org/10.1016/j.aquaculture.2019.734542

Zhao, N., Liang, P., Zhuo, X., Su, C., Zong, X., Guo, B., Han, D., Yan, X., Hu, S. and Zhang, Q., 2018. *Basic clin. Pharmacol. Toxicol*., **122**: 470-480. https://doi.org/10.1111/bcpt.12940

Zou, J.F., Guo, Q., Shao, H., Li, B., Du, Y., Liu, M., Liu, F., Dai, L., Lin, H.J. and Su, S.B., 2015. *PLoS One*, **10**: e0119126. https://doi.org/10.1371/journal.pone.0119126