American Journal of Emergency Medicine 37 (2019) 1611–1617

Contents lists available at ScienceDirect

American Journal of Emergency Medicine

journal homepage: www.elsevier.com/locate/ajem

Original Contribution

Efficacy and outcomes of lipid resuscitation on organophosphate poisoning patients: A systematic review and meta-analysis

Shiyuan Yu [a,1], Shanshan Yu [a,1], Lili Zhang [a,1], Yanxia Gao [b], Joseph Walline [c], Xin Lu [a], Yong Ma [a], Huadong Zhu [a], Xuezhong Yu [a,*], Yi Li [a,*]

[a] *Department of Emergency Medicine, Peking Union Medical College Hospital, Peking Union Medical College and Chinese Academy of Medical Sciences, Beijing, China*
[b] *Department of Emergency Medicine, The First Affiliated hospital of Zhengzhou University, Zhengzhou, China*
[c] *Accident and Emergency Medicine Academic Unit, 2/F, Main Clinical Block and Trauma Centre, Prince of Wales Hospital, The Chinese University of Hong Kong, Shatin, Hong Kong, China*

A R T I C L E I N F O

Article history:
Received 26 July 2018
Received in revised form 13 November 2018
Accepted 17 November 2018

Keywords:
Organophosphate poisoning
Lipid emulsion resuscitation
Meta-analysis

A B S T R A C T

Objective: Organophosphate (OP) pesticides are still widely available in developing countries, leading to numerous accidental or suicidal poisonings every year. Lipid emulsion treatments are commonly used in resuscitating OP poisoning patients but few studies regarding their use have been reported. Our meta-analysis aimed to analyze the efficacy and outcomes of lipid resuscitation on OP poisoning patients.
Methods: A systematic search for associated studies was conducted in Pubmed, EMBASE, MEDLINE, the Cochrane Library and the Chinese National Knowledge Infrastructure. Collected data was pooled using Revman v5.3. Outcomes included prognosis (cured vs. mortality rates), hepatic function (serum ALT, AST, Total Bilirubin (TBIL) level), serum acetylcholinesterase (AchE) level and respiratory function (rate of respiratory muscular paralysis).
Results: Seven randomized controlled studies consisting of 630 patients meeting inclusion criteria were identified. Lipid emulsion helped to improve the cure rate [OR = 2.54, 95% CI (1.33, 4.86), $p = 0.005$] and lower the mortality rate [OR = 0.31, 95% CI (0.13, 0.74), $p = 0.009$]. Serum ALT, AST and TBIL in patients undergoing lipid resuscitation were lower than those in the control groups [ALT, SMD = −1.52, 95% CI (−2.64, 0.40), $p = 0.008$; AST, SMD = −1.66, 95% CI (−3.15, 0.16), $p = 0.03$; TBIL, SMD = −1.26, 95% CI (−2.32, 0.20), $p = 0.02$]. Serum AchE level were increased in patients treated with lipid emulsion [SMD = 2.15, 95% CI (1.60, 2.71), $p < 0.00001$]. Rate of respiratory muscular paralysis was lower in patients undergoing lipid resuscitation than those in the control groups [OR = 0.19, 95% CI (0.05, 0.71), $p = 0.01$].
Conclusion: Based on our meta-analysis of included RCT reports, lipid resuscitation seems likely to help improve prognosis and liver function of OP poisoning patients. However, larger multi-center RCTs are still recommended.

1. Introduction

Insecticide poisoning is a leading cause of death in developing countries [1]. Organophosphate (OP) is widely used in multiple insecticides and is also a major cause of accidental or suicidal poisonings [2]. OP poisoning makes up almost half of all intoxication cases and causes >80% of all poisoning deaths in China [3]. There are more than ten kinds of OP insecticides sold worldwide with slight variations in their ingredients. OP pesticides are classified into hydrosoluable (such as ethylpyrophosphate, methamidophos, omethoate and dipterex) or liposoluable (such as alkron, rogor, malathion, methyl parathion, dichlorvos, diethion, chlorpyrifos), meaning that different kinds of OP poisoning may be more amenable to different types of treatment [4].

Nevertheless, antidotes and current supportive management against severe OP poisoning may not be enough to sustain patients admitted for shock or circulatory failure.

Lipid emulsion is a commonly used intravenous nutrient solution. Lipid emulsion has gradually been applied beyond its original indication for nutritional supplementation. Lipid resuscitation for drug intoxication is recommended by the American College of Medical Toxicology in cases of hemodynamic collapse, such as cardiac arrest, shock, or others (e.g. intractable seizures) after standard resuscitation measures have failed [5]. Many medical centers have reported using intravenous lipid emulsion treatments for severe drug intoxications with calcium channel blockers and antipsychotic drugs. Meanwhile, a few medical centers have reported administering lipid emulsions to treat OP patients, especially in those with unstable vital signs and/or presenting with an inadequate response to standard therapies [3]. However, clinical evidence for the efficacy of lipid emulsion on OP patients is rather

* Corresponding authors at: Emergency Department of Peking Union Medical College Hospital, Beijing 100730, China.
E-mail addresses: billiyi@126.com (Y. Li), yxz@pumch.cn (X. Yu).
[1] These authors contribute equally to this research.

https://doi.org/10.1016/j.ajem.2018.11.022
0735-6757/

limited especially high quality RCTs or in English-language studies. Also, there has not yet been a meta-analysis of the available studies exploring the efficacy of lipid emulsion on OP poisoning patients. Our meta-analysis aims to review all currently published articles on the efficacy of lipid emulsions toward OP poisoning and illustrate the efficacy and outcomes of lipid resuscitation on OP poisoning patients.

2. Methods

2.1. Study selection

Pubmed, EMBASE, Cochrane library, MEDLINE, Chinese National Knowledge Infrastructure (CNKI), Chinese Biomedical literature (CBM) and the Chinese Medical Current Contents (CMCC) were all screened by our search team. English search terms included organophosphorus, organophosphate poisoning (MeSH term), organophosphorus poisoning, OP, OP poisoning, lipid, lipid emulsion, lipid resuscitation and lipid therapy. Chinese search term included words meaning lipid and poisoning, including 'you ji lin', 'zhi fang ru' and 'zhong du'. All reference lists from the main reports were cross-checked by two members of our team.

2.2. Inclusion and exclusion criteria

Articles were included if they met all of the following criteria:

1) Randomized controlled study (RCT)
2) Study population consisted of accidental or suicidal OP poisoning patients, regardless of the severity.
3) Study population consisted of patients who potentially received lipid resuscitation once they presented to the emergency department.
4) One or more of the following were reported: cure rate, mortality rate, hepatic function and rate of respiratory muscular failure.

Articles were excluded if any of the following were present:

1) Studies not published in Chinese or English
2) Study data unavailable
3) Studies involving primarily special populations (e.g. AIDS or tuberculosis patients).

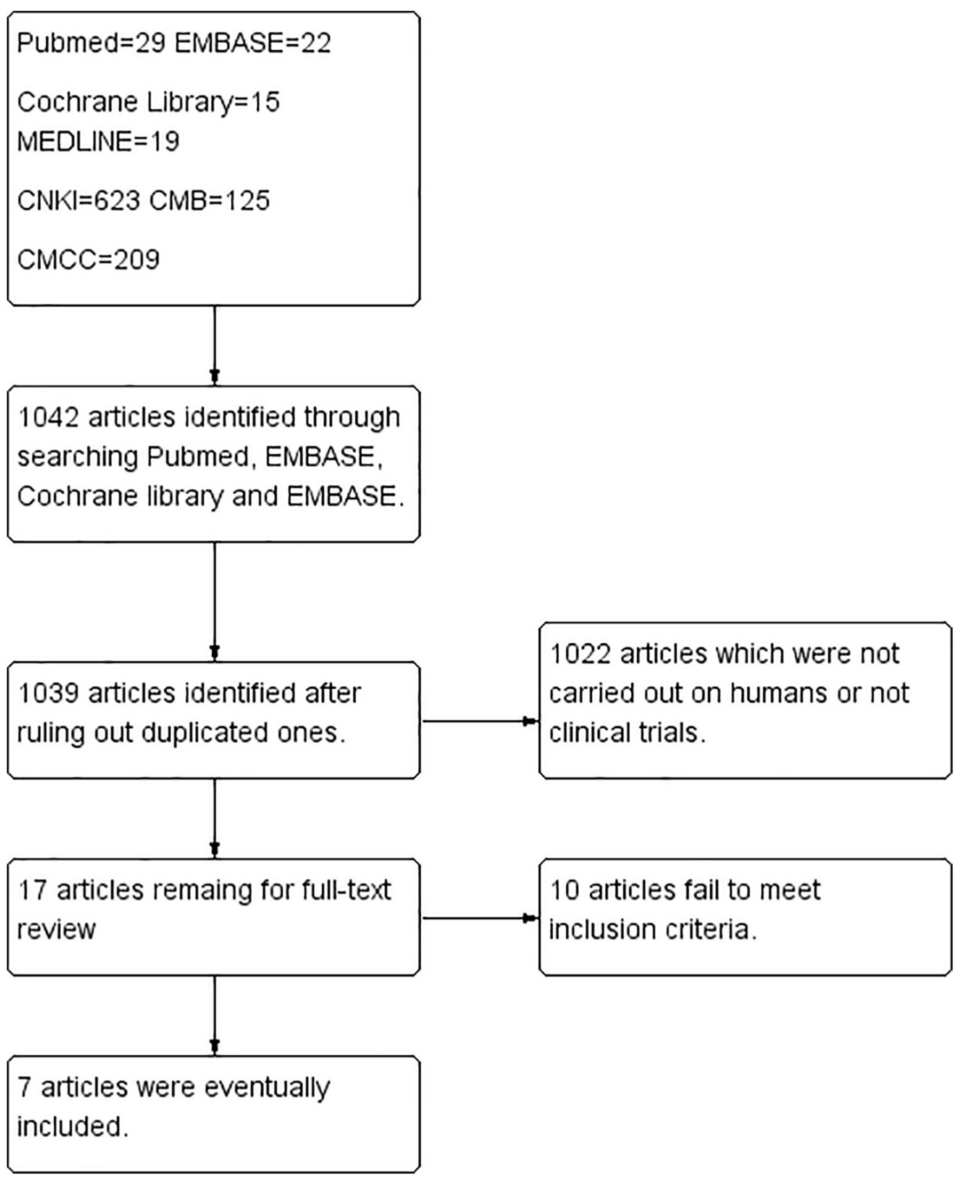


Fig. 1. Flow diagram.

Table 1
Included articles.

Research	Journal	Database	Type	Toxicant[a]	N	Male	Age		Lipid emulsion administration
							Drug	Control	
Wang Liwen 2012	Journal of Heze Medical College 菏泽医学专科学校学报 (in Chinese)	CNKI	RCT	Not reported	247	N/A	N/A	N/A	10% lipid emulsion 500 mL iv drip qd for 5 days
Ding Minjun 2013	CNKI 中国知网学位论文 (in Chinese)	CNKI	RCT	Dichlorvos, rogor, malathion, diethion, chlorpyrifos	34	15	41.15 ± 14.62	40.38 ± 16.62	20% lipid emulsion 250 mL iv drip qd until AchE normalized
Huang Weibin 2015	Journal of Clinical Emergency 临床急诊杂志 (in Chinese)	CNKI	RCT	Methamidophos, dichlorvos, malathion, methyl parathion	58	N/A	N/A	N/A	30% lipid emulsion 250 mL iv drip qd for 7 days
Guo Jinping 2015	Internal Medicine 内科 (in Chinese)	CNKI	RCT	Not reported	115	51	35.1 ± 9.4	35.3 ± 9.2	20% lipid emulsion 250 mL iv drip qd for 5 days
Qin Pu 2016	Journal of Clinical Emergency 临床急诊杂志 (in Chinese)	CNKI	RCT	Dichlorvos, rogor, omethoate, methamidophos, alkron	36	17	43.9	45.3	20% lipid emulsion 250 mL iv drip qd for 6 days
Zheng Langning 2016	China Pharmaceuticals 中国药业 (in Chinese)	CNKI	RCT	Not reported	92	50	52.42 ± 10.29	52.36 ± 10.58	20% lipid emulsion 250 mL iv drip qd for 3 days
Wu Mingzheng 2016	Modern Diagnosis and Treatment 现代诊断与治疗 (in Chinese)	CNKI	RCT	Not reported	48	22	35.8 ± 7.5	36.2 ± 8.4	30% lipid emulsion 250 mL iv drip qd for 7 days

Toxicant dissolved in both lipid solution and water, dichlorvos, diethion, methamidophos, omethoate.
[a] Toxicant dissolved in lipid solution, alkron, rogor, malathion, methyl parathion, chlorpyrifos.

2.3. Quality assessment

Two reviewers (SY and XL) independently conducted the study selection and reviewed the included studies using the Cochrane Collaboration's tool [6]. The following seven items were evaluated, random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting and other sources of bias. The results were classified as low risk of bias, high risk of bias and unclear risk of bias.

2.4. Statistical analysis

The baseline characteristics and available data of each article were evaluated and extracted separately by two researchers using Microsoft Excel 2013. The main outcomes were cure rate (all symptoms/syndromes disappeared and vital signs returned to normal), mortality rate, hepatic function (serum ALT, AST, TBIL levels) and serum AchE level on the fifth day after OP poisoning and the rate of respiratory muscular failure (progressive dyspnea after cholinergic crisis). The estimated odds ratio (OR), 95% confidence intervals (95% CI) and standardized mean difference (SMD) of the available data were pooled using Review Manager v5.3. A p-value < 0.05 was defined as statistically significant. I^2 was used to estimate the heterogeneity level of the included studies. $I^2 > 50\%$ was defined as high heterogeneity among studies and a randomized model was conducted to pool the data, while a fixed model was conducted if the I^2 score was no >50%. Reporting bias was evaluated by using a funnel plot.

3. Results

3.1. Included studies

Our meta-analysis included 1042 potentially eligible articles, including 29 articles from Pubmed, 22 articles from EMBASE, 15 articles from Cochrane library, 19 from MEDLINE, 623 from CNKI, 125 from CBM and 209 from CMCC. Seven articles all from the CNKI database were eventually identified after abstract and full-text screening, which included a total of 630 patients [3,7-12]. The screening process is shown in Fig. 1. All of the included studies were RCTs and all articles were published in Chinese. Details of the included articles are shown in Table 1.

3.2. Baseline characteristics of included articles

Seven RCTs recruited a total of 630 OP patients, all of whom ingested OP. 312 of the patients underwent lipid resuscitation since the first day of OP poisoning, while 318 patients were enrolled as controls. Main characteristics of the patients are shown in Table 2. Baseline characteristics show no significant difference between patients divided into the lipid emulsion group or control group.

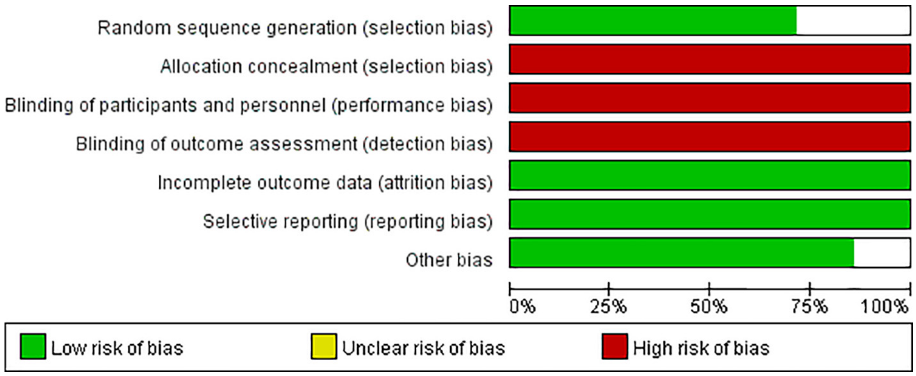
3.3. Risk of bias

The methodological quality of selected trials was assessed using the Cochrane Collaboration's tool. All of the studies included suggested randomization, but only five studies reported the method of random sequence generation while all of the studies failed to report details about allocation concealment. There was a high risk of bias regarding participants, personnel and outcome assessment. The reasons for dropout between groups were similar in the included studies. The risk of selective reporting bias is low. Six studies had low risk of other bias while one failed to report baseline similarity. Therefore, all studies were

Table 2
Baseline characteristics.

Characteristics	Experimental		Control		p value
	Mean	SD	Mean	SD	
N	312		318		–
Male (n)	14.8	8.93	16.2	9.12	0.108
Age	41.67	7.04	41.91	7.06	0.543
Ingestion amount (mL)	98.2	70.50	99.8	73.82	0.610
Presentation Ache (U/L)	616.9	520.64	618.3	510.18	0.881
Presentation ALT (U/L)	226.4	140.28	230.2	144.40	0.246
Presentation AST (U/L)	275.5	180.05	272.3	176.30	0.274
Presentation TBIL (U/L)	59.7	7.96	59.1	6.39	0.605

Table 3
Risk of bias



judged to be of a relatively poor methodological quality (Tables 3 and 4).

3.4. Cure rate and mortality rate

Four studies included data on cure rates, consisting of 220 patients. A fixed model was conducted because of low heterogeneity among studies ($I^2 = 0\%$). Pooled statistics demonstrated the cure rate was significantly higher after lipid resuscitation on OP patients compared to patients in the control group [OR = 2.54, 95% CI (1.33, 4.86), $p = 0.005$]. Forest plot is shown in Fig. 2.

Four studies included eligible data on mortality rates, consisting of 301 patients. A fixed model was conducted because of low heterogeneity among studies ($I^2 = 37\%$). Pooled statistics demonstrated mortality rate was significantly lower after lipid resuscitation in OP poisoning patients compared to those in the control group [OR = 0.31, 95% CI (0.13, 0,74), $p = 0.009$]. Forest plot is shown in Fig. 3.

Table 4
Risk of bias summary

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Ding minjun 2013	+	−	−	−	+	+	+
Guo jinping 2015		−	−	−	+	+	+
Huang weibin 2015	+	−	−	−	+	+	+
Qin pu 2016	+	−	−	−	+	+	+
Wang liwen 2012		−	−	−	+	+	
Wu mingzheng 2013	+	−	−	−	+	+	+
Zheng langning 2016	+	−	−	−	+	+	+

3.5. Hepatic function

Hepatic function was evaluated through serum ALT, AST and TBIL levels on the fifth after OP poisoning.

Three studies included eligible data on serum ALT levels consisting of 255 patients. A randomized model was conducted because of high heterogeneity among studies ($I^2 = 93\%$). Pooled statistics demonstrated serum ALT levels on the fifth day after OP poisoning were significantly lower after lipid resuscitation on OP patients than OP patients in the control group [SMD = −1.52, 95% CI (−2.64, −0.40), $p = 0.008$]. Forest plot is shown in Fig. 4.

Three studies included eligible data on serum AST level, consisting of 255 patients. A randomized model was conducted because of high heterogeneity among studies ($I^2 = 96\%$). Pooled statistics demonstrated serum AST levels on the fifth day after OP poisoning were significantly lower after lipid resuscitation on OP patients than OP patients in the control group [SMD = −1.66, 95% CI (−3.15, −0.16), $p = 0.03$]. Forest plot is shown in Fig. 5.

Three studies include eligible data on serum TBIL levels, consisting of 255 patients. A randomized model was conducted because of high heterogeneity among studies ($I^2 = 93\%$). Pooled statistics demonstrated serum TBIL levels on the fifth day after OP poisoning were significantly lower after lipid resuscitation on OP patients than OP patients in the control group [SMD = −1.26, 95% CI (−2.32, −0.20), $p = 0.02$]. Forest plot is shown in Fig. 6.

3.6. Cholinesterase function

Only two studies included eligible data on activated cholinesterase levels, consisting of 82 patients. A fixed model was conducted because of low heterogeneity among studies ($I^2 = 0\%$). Pooled statistics demonstrated activated cholinesterase level on the fifth day after OP poisoning was significantly higher after lipid resuscitation on OP patients than OP patients in the control group [SMD = 2.15, 95% CI (1.60, 2.71), $p < 0.00001$]. Forest plot is shown in Fig. 7.

3.7. Respiratory muscle function

Only two studies included eligible data on the rate of respiratory muscle failure, consisting of 305 patients. A fixed model was conducted because of low heterogeneity among studies ($I^2 = 0\%$). Pooled statistics demonstrated that the rate of respiratory muscle failure in OP poisoning patients was significantly lower after lipid resuscitation on OP patients than OP patients in the control group [OR = 0.19, 95% CI (0.05, 0.71), $p = 0.01$]. Forest plot is shown in Fig. 8.

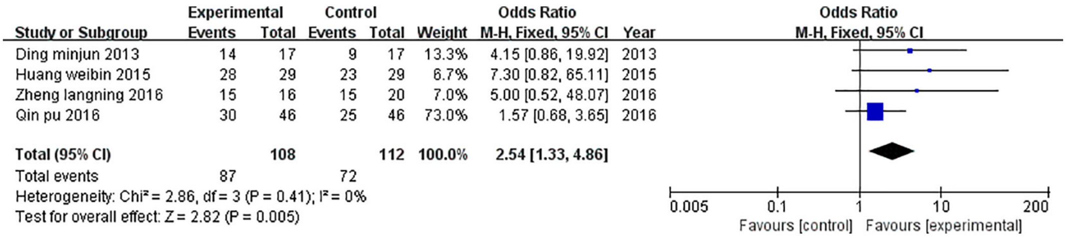


Fig. 2. Cured rate between LR and control group on OP patients.

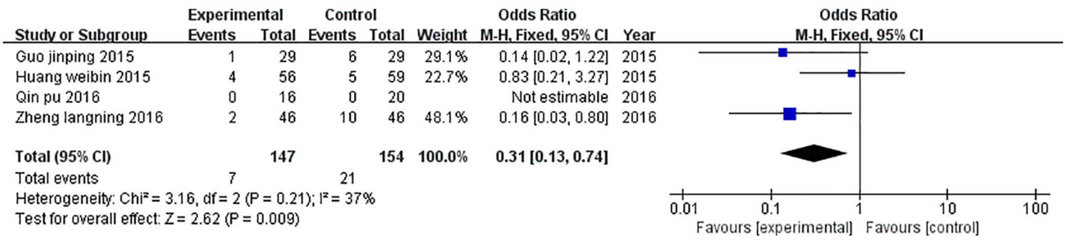


Fig. 3. Mortality rate between LR and control group on OP patients.

4. Discussion

OP poisoning is still a leading cause of death among accidental or suicidal poisonings worldwide. China has reported a majority of OP patients worldwide [9,13]. In recent years, lipid emulsion therapy has been actively applied to OP poisoning cases in China. However, except for a handful of case reports, retrospective analyses and a few low-quality RCTs, higher level evidence for the use of lipid emulsion therapy for resuscitating OP poisoning patients is rather limited. Our meta-analysis, which is the first one in this area, combined seven studies with a combined total of 630 OP poisoning patients. The results of this meta-analysis demonstrate that starting lipid emulsion therapy when an OP patient presents to the emergency department is likely to improve the overall prognosis and certain organ performance (e.g. liver and respiratory muscle function).

Current treatment targeting OP poisoning is made up of two aspects. The first is to administer symptom relieving agents such as atropine and the second is to reactivate the function of cholinesterase (AchE) [14]. However, the dose of atropine administration is case-dependent, and can lead to over/underdosing of atropine [15].

Currently, OP challenged rats have demonstrated the positive effect of lipid emulsion therapy on resuscitating respiratory and pancreatic function. Dunn carried out research on 18 OP poisoning (parathion) rats undergoing tracheostomy, recording their airflow, respiratory rate, tidal volume, mean arterial pressure, and pulse rate [16]. They found that lipid resuscitation was able to prolong the time to apnea. Tuzcu carried out a research on 50 OP poisoning (malathion) rat models [17]. They recorded serum levels of glucose, insulin and oxidants as an observational index for the pancreas and concluded that lipid resuscitation helped to prevent pancreatic beta cell injury, oxidative stress and hyperglycemia. A meta-analysis on animal models also supported use of lipid resuscitation on liposoluable drug intoxication [18].

In a case study, an OP patient presenting with muscarinic symptoms and hemodynamic collapse insensitive to vasoactive agents was administered lipid emulsion starting on the first day of poisoning [19]. With a combined treatment with atropine and lipid emulsion, the AchE level and liver function returned to normal by the 12th day after poisoning. The effect of lipid emulsion therapy has also reported in adolescents. Yesilbas also reported a child suffering from OP poisoning, who was treated with atropine and lipid emulsion therapy and subsequently recovered [20].

Similarly, our included 7 articles all reported positive outcomes toward LR therapy in OP poisoning patients, who underwent standard atropine combined with pyridine aldoxime methiodide (PAM) therapy. But the baseline hemodynamic state of the recruited patients was not strictly restrained to those presenting hemodynamic collapse and insensitivity to vasoactive agents, which may expand the use of LR therapy beyond its previous ACMT indications.

However, the mechanism of lipid emulsion therapy on OP poisoning is not completely understood and is still a matter under investigation.

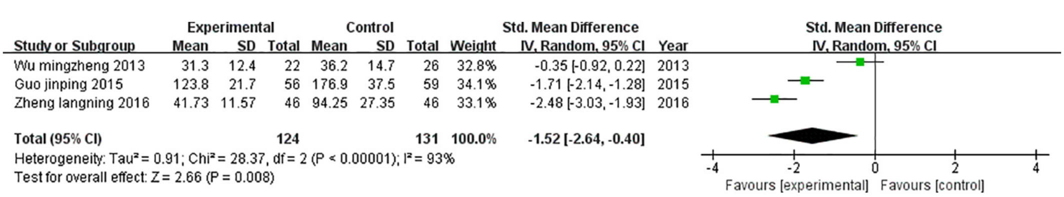


Fig. 4. The 5th day ALT level between LR and control group on OP patients.

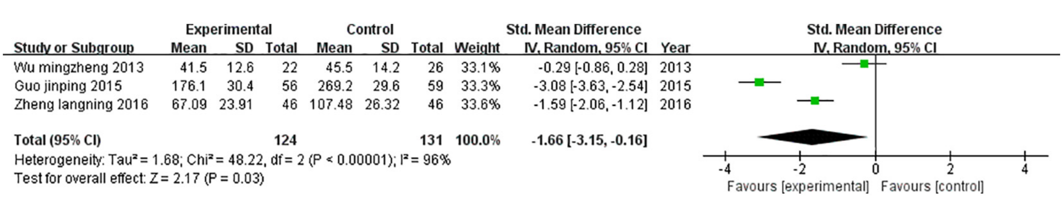


Fig. 5. The 5th day AST level between LR and control group on OP patients.

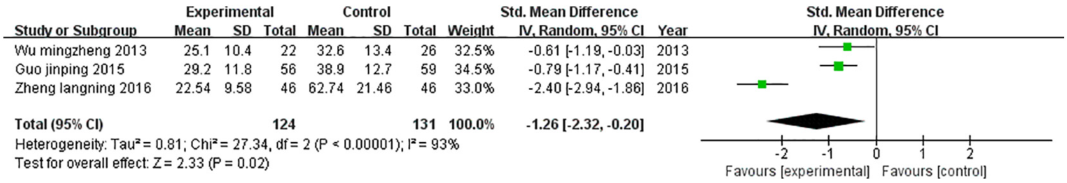


Fig. 6. The 5th day TBIL level between LR and control group on OP patients.

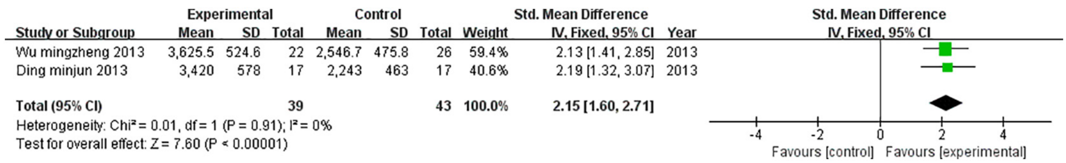


Fig. 7. The 5th day AchE level between LR and control group on OP patients.

OP pesticide damages body tissue due to its toxic characteristics and lipid emulsion may help sequester these fat-soluble OP molecules and slow down their absorption into organs [21]. Besides the direct toxic effect of OP on end-organs, immune system reaction is another cause of tissue damage in OP patients. The release of inflammatory factors such as IL-1 and TNF-alpha, as well as the activation of the overall immune system, may also contribute to worse end-organ damage [22,23]. A lipid emulsion may help to take away OP molecules and reduce the inflammatory factors released after OP poisoning, thus improving hepatic and respiratory function [11]. Also, the initial injection of lipid emulsion may reduce the amount of atropine needed, helping to avoid severe adverse effect of anti-muscarinic receptor effects [12]. However, the exact mechanism of lipid emulsion on OP patients still needs further elucidation.

Our meta-analysis had some limitations. First, all the identified RCTs included were carried out in a single country (China), mainly due to OP being one of the most common means for suicide in the country. The methodological quality of these included studies was relatively low, especially considering the procedures of allocation concealment and blinding. Four out of the seven included studies carried out their research only on severe OP poisoning patients, but baseline characteristics such as circulatory and respiratory function were not restricted to those patients insensitive to basic therapy in each study, leading to potential different reactions to lipid emulsion therapy. The type of OP pesticides consumed, especially the soluble characteristics in lipid was not listed in each study. The dose of lipid emulsion administered and the time from exposure to treatment also varied depending on the medical centers involved.

Lipid resuscitation is likely to cause several severe adverse drug effects. Nevertheless, the main complications such as acute pancreatitis and lipid embolism resulting from lipid resuscitation were not discussed in the included studies, so we were unable to comment on the safety of lipid emulsion therapy. Finally, the relatively small number of patients and patient characteristics contributed to the high heterogeneity in our study, limiting our final recommendation for lipid emulsion therapy in OP poisoning patients.

Despite of these limits, our research synthesis of the most current studies of lipid resuscitation on OP patients is still helpful is giving an overall state of lipid emulsion therapy for OP poisoning patients. Our research suggests that the initial administration of lipid emulsion improves overall survival and leads to better liver and neuromuscular function. Nevertheless, our current results are based on relatively low quality evidence and future multi-center studies utilizing larger sample sizes are still needed to figure out the best procedures for lipid emulsion administration and a better understanding of potential complications for OP poisoning patients.

5. Conclusion

Lipid emulsion may help improve the overall prognosis for OP poisoning patients, including improved liver function, acetylcholinesterase levels and respiratory muscle function. However, the best protocols for lipid emulsion administration as well as a better understanding of potential complications resulting from lipid resuscitation are not yet fully understood. Larger high quality multi-center RCTs are needed in the future to better elucidate these issues.

Abbreviations

OP	organophosphate
ALT	alanine aminotransferase
AST	aspartate aminotransferase
TBIL	total bilirubin
AchE	acetylcholinesterase
OR	odd ratio
RCT	randomized controlled trial
CNKI	Chinese National Knowledge Infrastructure
CBM	Chinese Biomedical literature
CMCC	Chinese Medical Current Contents
CI	convinced interval
SMD	standard mean difference
LR	lipid resuscitation

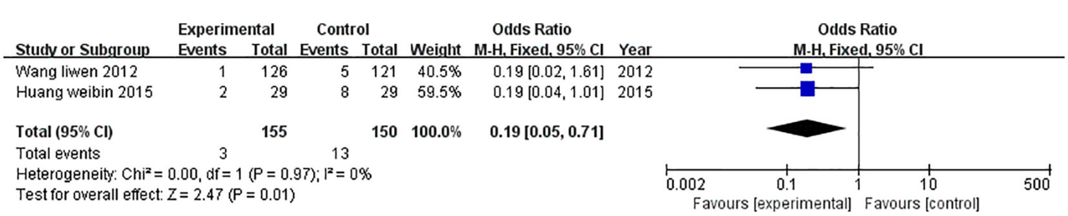


Fig. 8. Rate of respiratory muscular paralysis between LR and control group on OP patients.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and supporting materials section

Data sharing not applicable to this article as no new datasets were generated or analyzed during the current study.

Competing interest

On behalf of all authors, the corresponding author states that there are no conflicts of interest for this study.

Authors' contributions

Shiyuan Yu, Shanshan Yu, Lili Zhang, Xin Lu, Yanxia Gao and Yong Ma identified the included articles and performed the statistical analysis. Shiyuan Yu was a major contributor in writing the manuscript. Yi Li, Yanxia Gao, Huadong Zhu, Joseph Walline and Xuezhong Yu read and modified the manuscript. All authors approved the final manuscript.

Acknowledgements

This project was sponsored by grants from the National Natural Science Foundation of China (No: 81550034 and No: 81701893).

References

[1] Chowdhary S, Bhattacharyya R, Banerjee D. Acute organophosphorus poisoning. Clin Chim Acta 2014;431:66–76.
[2] Malarvannan G, et al. Organophosphorus flame retardants in the European eel in Flanders, Belgium: occurrence, fate and human health risk. Environ Res 2015;140.
[3] Guo Jinping, et al. Analysis of therapeutic effect of lipid emulsion for liver function damage in acute severe organophosphorus pesticide poisoning. J Clin Emerg 2015; 05.
[4] Zilker T. Acute intoxication in adults - what you should know. Dtsch Med Wochenschr 2014;139(1–2).
[5] ACMT position statement: interim guidance for the use of lipid resuscitation therapy, J Med Toxicol 2011;7(1).
[6] JPT Higgins, Green S. Cochrane handbook for systematic reviews of interventions. Version 5.1.0. Cochrane Collaboration; 2009.
[7] Qin Pu, et al. Fat emulsion used for lung injury of acute organophosphorus pesticide poisoning. China Pharm 2016;24.
[8] Zheng Langning, Wu Xinbao. Clinical observation of lipid emulsion treating acute severe organophosphorus poisoning. Mod Diagn Treat 2016;17.
[9] Chen Anbao, Wu Mingzheng. Clinical study on therapy effect of lipid emulsion in patients with acute moderate and severe organophosphorus pesticide poisoning. Available from: http://www.cnki.net/; 2016.
[10] Huang Weibin, Chen Weiying, Liao Xinyuan. Outcomes of lipid emulsion combined with blood perfusion on severe organophosphorus poisoning. Intern Med 2015;05.
[11] Ding Minjun, Tang Jianguo. Clinical study of intravenous lipid emulsion in treatment of severe organophosphorus pesticide poisoning. J Clin Emerg 2013;11.
[12] Wang Liwen. Fat emulsion to prevent acute organophosphorus pesticide poisoning causing peripheral type of breathing machine paralysis of clinical research. J Heze Med Coll 2012;03.
[13] Pei YV, Xiao F. Emergency medicine in China: present and future. Modern diagnosis and treatment 2014;12.
[14] Zhou Y, et al. Intravenous lipid emulsions combine extracorporeal blood purification: a novel therapeutic strategy for severe organophosphate poisoning. Med Hypotheses 2010;74(2).
[15] Soltaninejad K, Abdollahi M. Current opinion on the science of organophosphate pesticides and toxic stress: a systematic review. Med Sci Monit 2009;15(3).
[16] Dunn C, Bird SB, Gaspari R. Intralipid fat emulsion decreases respiratory failure in a rat model of parathion exposure. Acad Emerg Med 2012;19(5).
[17] Tuzcu K, et al. Oral intralipid emulsion use: a novel therapeutic approach to pancreatic beta-cell injury caused by malathion toxicity in rats. Drug Chem Toxicol 2014;37 (3).
[18] Fettiplace MR, McCabe DJ. Lipid emulsion improves survival in animal models of local anesthetic toxicity: a meta-analysis. Clin Toxicol (Phila) 2017;55(7).
[19] Han SK, et al. Use of a lipid emulsion in a patient with refractory hypotension caused by glyphosate-surfactant herbicide. Clin Toxicol 2010;48(6).
[20] Yesilbas O, et al. Acute severe organophosphate poisoning in a child who was successfully treated with therapeutic plasma exchange, high-volume hemodiafiltration, and lipid infusion. J Clin Apher 2016;31(5).
[21] Basarslan SK, et al. Is intralipid fat emulsion a promising therapeutic strategy on neurotoxicity induced by malathion in rats? Eur Rev Med Pharmacol Sci 2014;18 (4).
[22] Abdollahi M, Karami-Mohajeri S. A comprehensive review on experimental and clinical findings in intermediate syndrome caused by organophosphate poisoning. Toxicol Appl Pharmacol 2012;258(3).
[23] Glynn P. A mechanism for organophosphate-induced delayed neuropathy. Toxicol Lett 2006;162(1).