RESEARCH COMMUNICATION

Endostar Combined with Chemotherapy versus Chemotherapy alone for Advanced NSCLCs: A Meta-analysis

Wei Ge*, De-dong Cao, Hui-min Wang, Fang-fang Jie, Yong-fa Zheng, Yu Chen

Abstract

Background: Use of recombinant human endostatin combined with conventional cytotoxic therapy to treat tumors has been growing because of evidence of increased efficacy. However, whether antiangiogenic therapy combined with chemotherapy really benefits patients with advanced non-small cell lung cancers (NSCLCs) remains unclear. Objectives: This study was conducted to evaluate the clinical efficacy and safety of rh-endostatin (Endostar) combined with chemotherapy in the treatment of NSCLC patients. Methods: We selected data from the Cochrane Library, EMBASE, Medline, SCI,CBM, CNKI, to obtain all clinical controlled trials, including the addition of endostar to chemotherapy in advanced NSCLC patients. Twenty-two trials with 1884 patients were included according to the inclusion criteria. All were randomized controlled trials, and four trials were adequate in reporting randomization. Seventeen trials did not mention the blinding methods. Results: Meta-analysis indicated that the NPE arm (Vinorelbine+ cisplatin+Endostar) had a different response rate compared with NP(Vinorelbine+ cisplatin) arm (OR 2.22, 95%CI 1.62 to 3.03). The incidences of severe leukopenia (OR0.94, 95%CI 0.66 to 1.32) and severe thrombocytopenia (OR 1.00, 95%CI 0.64 to 1.57) and nausea and vomiting (OR 0.85, 95%CI 0.61 to 1.20) were similar in the two arms. There were significant differences between the comparisons of TCE (Paclitaxel + carboplatin + Endostar) versus TC (OR 2.49, 95%CI 1.30 to 4.74) and GPE (Gemcitabine + cisplatin + Endostar) versus GP (OR 2.02, 95%CI 1.11 to 3.68) and TPE (Paclitaxel + cisplatin + Endostar) versus TP (OR 2.22, 95%CI 1.32 to 3.75). Conclusions: Our results suggested that in the treatment of advanced NSCLC, endostar in combination with platinum-based chemotherapy could improve the response rate without obviously increasing side effects.

Keywords: Non-small cell lung cancer - rh-Endostatin - chemotherapy - efficacy - safety - systematic review

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Introduction

Because of the high incidence and poor prognosis, lung cancer remains to be one of the main diseases threatening human health. Non-small cell lung cancer (NSCLC) accounts for more than 80% of all lung cancers (Pignon et al. 2008). For early stage NSCLC, surgical resection is the preferred treatment. However, nearly 70% of the patients was diagnosed as advanced NSCLC when they doctored (locally advanced or metastatic lesions appear) (Azim et al., 2009).Because of the biological characteristics of relatively large lesions and easily transferred to the upper clavicle, ipsilateral or contralateral mediastinum, the treatment benefits of advanced NSCLC are not good and get more chances to occur complications. Chemotherapy or chemoradiotherapy with platinum-based treatments are usually used, but its effects often limited.

Tumor antiangiogenic is one of the current most interested researches, and the recombinant human endothelial inhibitor (Endostar, rh-Endostatin) is one of the numerous antiangiogenic agents. In 1997, O'Reilly discovered Endostatin was a kind of endogenous anti-angiogenic substance by interacting with endothelium cells, especially the microvascular endothelial cells, to prevent the immigration of endothelium cells and induce apoptosis (O'Reilly et al., 1997), and they also have the functions in inhibiting the vascular endothelial growth factor and metalloproteinases, binding with heparin sulfate-like protein and zinc, affecting gene expression such as HIF-1α (Folkman, 2006). In recent years, the researches about recombinant human endostatin combined with conventional cytotoxic therapy to treat tumors have been growing, and showed that combination therapy was more effective than conventional therapies (Te Velde et al., 2002; Huang et al., 2010). However, whether antiangiogenic therapy combined with chemotherapy really benefits patients with advanced NSCLC and how about the security remains unclear now. Thus, we investigated the major electronic databases worldwide, and selected the researches which could meet the requirements of randomized controlled trials and made a systematic analysis to provide an evidence-based basis of efficacy and safety for the advanced NSCLC when recombinant human endostatin combined with chemotherapy.

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In this study, the deadline for trial publication eligible was December 30, 2011. And we used Cochrane systematic reviews software RevMan 5.0 to analysis, to resolve the following problems: The clinical efficacy and safety of Endostar combined with conventional chemotherapy in advanced NSCLC treatment,and the side effects of endostar combined with conventional chemotherapy in advanced NSCLC treatment.

Materials and Methods

Samples

The patients were diagnosed by cytology or pathology as non-small cell lung cancer, and determined by imaging or other clinical examination to be the stage III, IV NSCLC without age and gender restrictions. Before treatment, blood, urine, liver and kidney function, etc., revealed no obvious abnormalities.

Experimental design

The selected articles are quasi-randomized controlled trials and randomized controlled trials using endostar combined with conventional chemotherapy, designed with parallel comparison, and the total sample should be more than 40.

Interventions

Endostar combined with chemotherapy A versus chemotherapy A; Endostar replaced one or more chemotherapy drugs of the regimen A versus the regimen A; Endostar combined with chemotherapy A versus chemotherapy B; Endostar combined with chemotherapy A and radiotherapy versus chemotherapy A and radiotherapy.

Treatment efficacy

The treatment efficacy was evaluated by the follows: Overall survival, median time of progression, median survival time, and effective (CR + PR), quality of life, adverse events (according to the WHO toxicity criteria).

Excluded criteria

The excluded criteria were as follows: Metastatic non-small cell lung cancer with other tumor diseases at the same time; Serious medical illness or infections; Opt-in research does not match the inclusion criteria.

Search strategy

The key words included: non small cell lung cancer; non small cell lung; carcinoma; lung alveolus cell carcinoma; lung adenocarcinoma; NSCLC; drug therapy; antiangiogenic; antiangiogenesis; adjuvant therapy; combination therapy; endostatin; rh-endostatin; chemotherapy. The Chinese key words: chemotherapy;Endostar; endostatin; Antiangiogenesis therapy; targeted drug; tumor vessel; lung cancer;lung tumor; non small cell lung cancer.

Document type

The document types included systematic reviews, meta-analyses, major clinical studies, randomized controlled trials (RCT) and practice guidelines.

Computer retrieval

The computer retrieval included: No language restrictions were applied.

Manual retrieval

We searched the data in the college library: “lung cancer”; “cancer”; “Chinese journal of lung cancer”; “Chinese Journal of Oncology”; “Chinese Journal of Clinical Oncology”, “Journal of Practical Oncology”. The time was ranged between 1995 and 2011.

Other retrievals

Google search was used to find relative data and contacting authors through E-mail on the internet to obtain original data.

Trial abstraction

Two investigators selected data from each article independently using one standardized data extraction forms. When there were some controversies, they would go to help each other, and reached consensus on all items. Data integrity was also considerated.

Methodological quality assessment

The Cochrane Handbook 5.0 for Systematic Reviews of Interventions was used to evaluate the methodological quality, and was mainly as the following: random methods, depending on whether randomized methods were used rationally, the studies could be divided into three categories (correct and sufficient, insufficient, unclear); hidden groups, the studies could be divided into four categories (correct and adequate, inadequate, unclear, unused); blind, according to whether blind method was used reasonable, researches could be divided into single-blind, double-blind and three blind; management, whether there was the entire following-up, report the number of lost, whether the number of lost was less than 10%, whether intentional analysis was applied.

Study qualities could be recognized as three levels: A, B, CA: mild bias, completely fulfill with the above quality standards, the possibility of bias was minimum; B: moderate bias, satisfy partly one or more standards, the possibility of the bias was moderate; C: high bias, didn’t meet any one of the standards, the chance of bias occurs was the highest.

Data extraction

The extracted data from each trial contained: general data: title, author, published year, study sources; Study characteristics: study designs, study and follow-up time, interventions, measurement indicators, lost number and management; Outcome pointer: response rate, survival rate, symptom improvement and adverse effects.

Statistical analysis

The RevMan5.0 software provided by Cochrane collaboration network was used to undertake Meta-analysis. We use relative risk (RR) or odds ratio (OR) and 95%CI (confidence intervals) to express the count data;

Table 1. Quality Analysis was Included in this Study

Cases	Randomized methods	Allocation hidden	Blind	Lost	Quality of studies
Yang Lin et al.	unclear	insufficient	Unclear	2 cases	C
Wang Jingwan et al.	sufficient	insufficient	Clear	7 cases	B
Huang Chun et al.	clear	sufficient	clear	7 cases	B
Cheng Shaojun et al.	clear	insufficient	unclear	Not reported	B
Huang Guosheng	unclear	insufficient	unclear	Not reported	C
Fan Qingling et al.	unclear	insufficient	unclear	Not reported	C
Cai Li et al.	unclear	insufficient	unclear	Not reported	C
Xie Yanru et al.	clear	insufficient	unclear	Not reported	B
Liu Jin et al.	unclear	insufficient	unclear	Not reported	B
Ma Baojia et al.	unclear	insufficient	unclear	Not reported	C
Zhang Te et al.	unclear	insufficient	unclear	Not reported	C
Tang Zhi et al.	unclear	insufficient	unclear	Not reported	C
Han Lichun et al.	unclear	insufficient	unclear	Not reported	C
Jin Jun	unclear	insufficient	unclear	Not reported	C
Liu jing et al.	unclear	insufficient	unclear	Not reported	C
WenFeng et al.	unclear	insufficient	unclear	none	C
LiaoHongyin et al.	unclear	insufficient	unclear	none	B
LouYuanjie et al.	unclear	insufficient	unclear	2 cases	C
JiangFengshou	sufficient	insufficient	none	none	B
DiJianshi et al.	unclear	insufficient	unclear	Not reported	C
HanBaohui et al.	clear	sufficient	clear	4 cases	A
ZhaoXin et al.	clear	sufficient	clear	2 cases	A

Table 2. Basic Informations Included in the Clinical Study

Cases	Regions	Time(year)	Grade	Samples	Experimental group (cases)	Control group(cases)	Standard methods Quality of life
Yang Lin et al.	Multi-center	2002-2003	III-IV	87	54	33	ECGO
Wang Jingwan et al.	Multi-center	2003-2004	III-IV	486	322	164	ECGO
Huang Chun et al.	TianJin	2005	III-IV	74	50	24	no
Cheng Shaojun et al.	GuangXi	2005-2007	IV	50	24	26	ECGO
Huang Guosheng	HeNan	2006-2007	III-IV	40	20	20	karnofsky
Fan Qingling et al.	ShanDong	2006-2007	III-IV	40	20	20	karnofsky
Cai Li et al.	HeiLongjiang	2006-2007	III-IV	71	39	32	karnofsky
Xie Yanru et al.	ZheJiang	2006-2008	III-IV	48	22	26	karnofsky
Liu Jin et al.	Jilin	2007-2008	III-IV	62	31	31	karnofsky
Ma Baojia et al.	SiChuan	2007-2008	III	46	23	23	ECGO
Zhang Te et al.	Zhejiang	2007-2008	III-IV	104	48	56	karnofsky
Tang Zhi et al.	GuangDong	2007-2008	III-IV	53	27	26	karnofsky
Han Lichun et al.	JiLin	2007-2009	III-IV	68	37	31	no
Jin Jun	HuNan	2008	III	40	15	25	no
Liu jing et al.	HeNan	2008-2009	III-IV	60	30	30	karnofsky
WenFeng et al.	BeiJing	2007-2010	III, IV	84	43	41	Karnofsky
LiaoHongyin et al.	GuangDong	2006-2008	III, IV	85	30	55	none
LouYuanjie et al.	HeNan	2008-2009	III, IV	69	38	31	Karnofsky
JiangFengshou	AnHui	2008-2010	IV	67	32	35	Karnofsky
DiJianshi et al.	ShanDong	2010	III, IV	53	26	27	ECOG
HanBaohui et al.	Multi-center	2007-2008	III, IV	122	61	61	ECOG
ZhaoXin et al.	Sichuan	2010	III, IV	69	33	36	ECOG

Continuous data, using WMD(weight mean difference) and 95%CI to express. To investigate the statistical difference between studies, the standard chi-squared test was implemented (significantly differences between trials indicated by $p<0.1$).The results were generated using the fixed effect model. When there was statistical significance, a random-effect model would be performed. All p-values were two-sided. All CIs had two-sided probability coverage of 95%.

Results

After abstracts were reviewed, 41 articles were discarded and Chinese RCTs were primarily included. After full-text review, 22 were finally included, and 6 trials were discarded for the following reasons: the numbers of sample were not qualified (Li et al., 2008; Liu et al., 2009; Xiao et al., 2009). Inventions did not fulfill the need (Mu et al., 2009; Zhu et al., 2009), and the reality of trial could not be identified (Wang et al., 2008).

Basic information

Twenty-two trials were included in clinical RCTs depending on the recommend standards in Cochrane Handbook 5.0 for systematic review. All the qualities were not satisfied and had different degree bias. The results are shown in Table1.

For this meta-analysis there were 1294 males and

Table 3. Inventions and Endpoint Included in the Trials

Cases	Inventions		Cases		Endpoints
	Experimental group	Control group	Experimental group	Control group	
Yang Lin et al.	NPE	NP	54	33	RR, symptoms, adverse reactions
Wang Jingwan et al.	NPE	NP+placebo	322	164	RR, symptoms, adverse reactions
Huang Chun et al.	NPE	NP	50	24	RR, survival rate, adverse reactions
Cheng Shaojun et al.	NOE	NO	24	26	RR, adverse reactions
Huang Guosheng	NPE	NP	20	20	RR, survival rate, symptoms, adverse reactions
Fan Qingling et al.	NPE	NP	20	20	RR,adverse reactions
Cai Li et al.	NPE	NP	39	32	RR, survival rate, symptoms, adverse reactions
Xie Yanru et al.	GPE	GP	22	26	RR, survival rate, symptoms, adverse reactions
Liu Jin et al.	NPE+RT	NP+RT	31	31	RR, survival rate, adverse reactions
Ma Baojia et al.	NPE+RT	NP+RT	23	23	RR, survival rate, symptoms, adverse reactions
Zhang Te et al.	GPE	T	48	56	RR, symptoms, adverse reactions
Tang Zhi et al.	TCE	TC	27	26	RR, adverse reactions
Han Lichun et al.	TPE	TP	37	31	RR, adverse reactions
Jin Jun	NPE	NP	15	25	RR, survival rate, adverse reactions
Liu jing et al.	TE	T	30	30	RR, adverse reactions
WenFeng et al.	NPE	NP	43	41	RR, Survival rate, Adverse reactions
LiaoHongyin et al	GPE	GP	30	55	RR, Survival rate, Adverse reactions
LouYuanjie et al.	TPE	TP	38	31	RR, Survival rate, Adverse reactions
JiangFengshou	TPE	TP	32	35	RR, Survival rate, SI, Adverse reactions
DiJianshi et al.	TPE	TP	26	27	RR, Adverse reactions
HanBaohui et al.	TCE	TC	61	61	RR, Survival rate, SI, Adverse reactions
ZhaoXin et al.	GPE	GP	33	36	RR, Survival rate, Adverse reactions

RT, radiotherapy

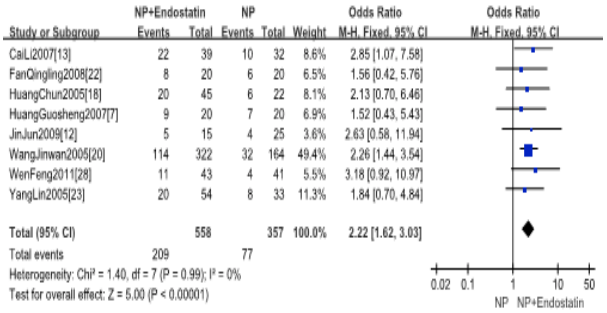

Figure 1. Meta-analysis of the RR (CR+PR) Between NP plus Endostar and NP Alone

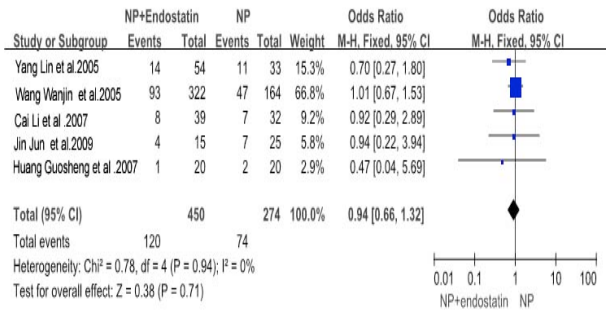

Figure 2. Meta-analysis of the Severe Leucopenia Between NPE and NP

590 females. Phrase III patients were 845, and phrase IV patients were 1039. The results are shown in Table 2. Intravenous ways and platinum-based treatments were applied in these studies. 8 RCTs (Huang, 2005; 2007; Wang et al., 2005; Fan et al., 2008; Yang et al., 2008; Cai et al., 2009; Jin et al., 2009; Wen et al., 2011) were compared NPE (Vinorelbine + oxaliplatin + Endostar) scheme with NP (Vinorelbine + oxaliplatin) scheme, and 2 trials (Ma et al.,2005; Liu et al., 2009) used NPE + radiotherapy scheme and NP + radiotherapy to have a comparison, and there was only one trial in the following comparisons (Chen et al., 2008; Liu et al., 2009; Zhang et al., 2009). NOE (Vinorelbine + oxaliplatin + Endostar) versus NO (Vinorelbine + oxaliplatin); GPE (Gemcitabine + cisplatin + Endostar) versus T (Paclitaxel); TE (Paclitaxel + Endostar) versus T (Paclitaxel). More details were shown in Table 3.

RR (PR+CR) was reported in all studies, and 14 trials were also reported adverse response (Ma et al., 2005; Wang et al., 2005; Huang, 2007; Fan et al., 2008; Yang et al., 2008; Chen et al., 2008; Cai et al., 2009; Han et al., 2009; Jin et al., 2009; Liu et al., 2009a; 2009b; Tang et al., 2009; Xie et al., 2009; Zhang et al., 2009; Wen et al., 2011; Liao et al., 2009; Lou et al., 2010; Di et al., 2011; Han et al., 2011; Jiang et al., 2011; Zhao et al., 2011). A study reported 1-year progression-free survival rate and survival rate (Ma et al.,2005), 7 studies reported a median time of progression (Wang et al., 2005; Huang, 2005; Chen et al., 2008; Yang et al., 2008; Xie et al. 2009; Jin et al., 2009; Liu et al., 2009), 3 studies reported physical improvements under the Karnofsky standard (Huang, 2007; Xie et al., 2009; Zhang et al., 2009).

Statistical analysis results Eight RCTs (Huang, 2005; 2007; Wang et al., 2005; Fan et al., 2008; Yang et al., 2008; Cai et al., 2009; Jin et al., 2009; Wen et al., 2011) reported response rate after treatment. Combined results of these studies revealed that there was a significant difference in the response rate between NPE scheme and NP scheme (OR=2.22, 95%CI 1.62 to 3.03) (Figure 1). Five RCTs (Wang et al., 2005; Huang, 2007; Yang et al., 2008; Cai et al., 2009; Jin et al., 2009) reported severe leucopenia (III, IV levels of WHO standard) after treatment and the combined results revealed that there was no significant difference in the happening of severe leucopenia between

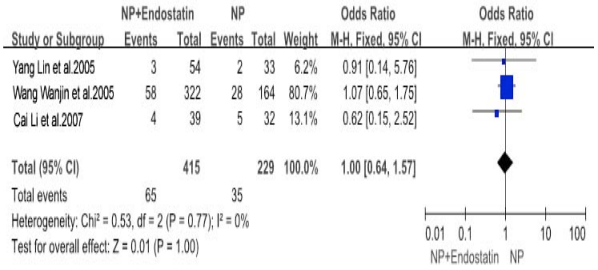

Figure 3. Meta-analysis of Severe Thrombocytopenia Between NPE Treatment and NP Treatment

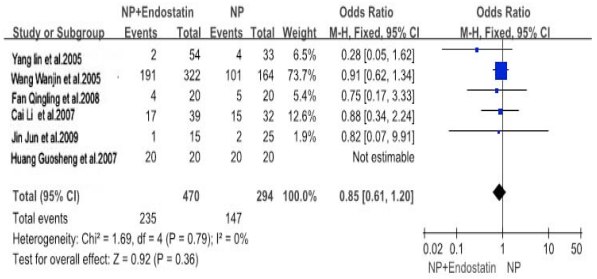

Figure 4. Meta-analysis of Nausea and Vomiting Between NPE and NP Scheme

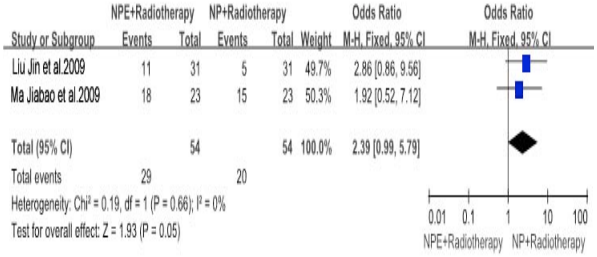

Figure 5. Meta-analysis of the RR Between NPE+RT and NP+RT

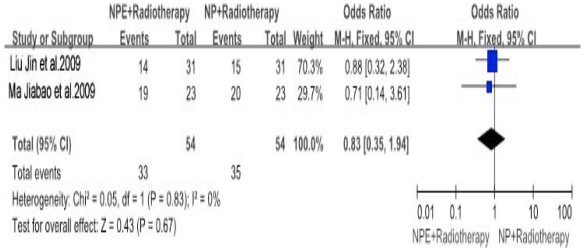

Figure 6. Meta-analysis of the Leucopenia Between NPE+RT and NP+RT

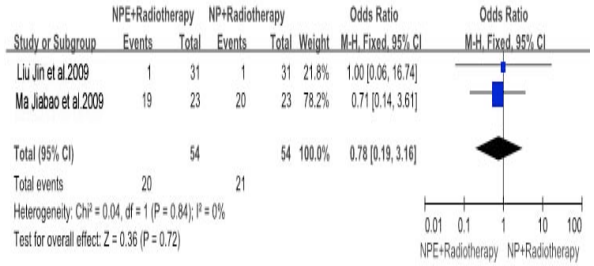

Figure 7. Meta-analysis of Thrombocytopenia after Treatment Between NPE+RT and NP+RT

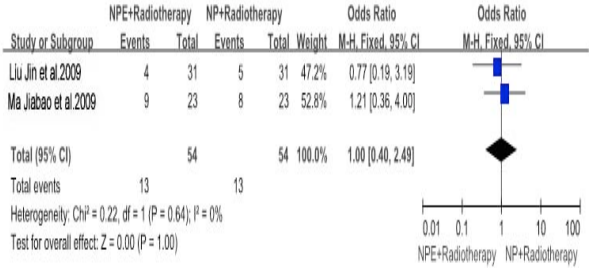

Figure 8. Meta-analysis of Radioactive Esophagitis After Treatment Between NPE+RT and NP+RT

NPE scheme and NP scheme (OR=0.94, 95%CI (0.66, 1.32) (Figure 2).

Only four RCTs (Wang et al., 2005; Huang, 2007; Yang et al., 2008; Cai et al., 2009) reported severe thrombocytopenia after treatment and the combined results of these trials revealed that the difference of the happening of severe thrombocytopenia between NPE and NP treatment was no significant (OR=1.00, 95%CI, 0.64,1.57)(Figure 3) .

Three RCTs (Wang et al., 2005; Yang et al., 2008; Cai et al., 2009) reported TTP and they were 6.3 months and 3.6 months, 146.68 days and 91.12 days, 6.3 months and 3.6 months(p=0.0000), 151 days and 100days(p=0.000). Six RCTs (Wang et al., 2005; Huang, 2007; Fan et al., 2008; Yang et al., 2008; Cai et al., 2009; Jin et al., 2009) reported the cases of nausea and vomiting after treatment, and the combined results suggested that the difference of nausea and vomiting in NPE and NP was not so significant (OR=0.85, 95%CI(0.61,1.20)(Figure 4).

Two RCTs reported response rate after treatment (Ma et al., 2005; Liu et al., 2009). Combined results of these studies revealed that there was no significant difference in the response rate between NPE + radiotherapy scheme and NP + radiotherapy scheme (OR=2.39, 95%CI(0.99,5.79) (Figure 5) .

Two RCTs (Ma et al., 2005; Liu et al., 2009) reported leucopenia after treatment, and the combined results revealed that there was no significant difference in the happening of leucopenia between NPE+RT scheme and NP+RT scheme (OR=0.83, 95%CI (0.35, 1.94)) (Figure 6).

Only two RCTs (Ma et al., 2005; Liu et al., 2009) reported thrombocytopenia after treatment and the combined results of these trials revealed that the difference of the happening of thrombocytopenia between NPE+RT treatment and NP+RT treatment was no significant (OR=0.78, 95%CI(0.19,3.16) (Figure7). Two studies (Ma et al., 2005; Liu et al., 2009) reported the cases of undergoing radioactive esophagitis after treatment, and the analysis results suggested that there was no significant difference in the happening of radioactive esophagitis between NPE+RT and NP+RT (OR=1.00, 95%CI(0.40, 2.49) (Figure 8) .

Four RCTs (Han et al., 2009; Lou et al., 2010; Di et al., 2011; Jiang et al., 2011) reported response rate after treatment and Combined results of these studies revealed thatthere was a signifcant difference in RR between TPE scheme and TP scheme(OR=2.22, 95%CI (1.32, 3.75)) (Figure 9) .

Three (Liao et al., 2009; Xie et al., 2009; Zhao et al., 2011) reported response rate after treatment in TPE and TP arms and there was a signifcant difference (OR=2.02, 95%CI(1.11, 3.68)) (Figure 10).

There was a significant difference (OR=2.49,

Table 4. Comparison of RR, TTP and Adverse Responses Between Treatment and Control Arms

Cases	Inventions	RR	TTP(month)	Leukopenia	Reduced hemoglobin	Thrombocyto penia	Nausea, vomit	Treatment-related death
Chen Shaojun et al.	NOE/ NO	P<0.05	6.6/3.7	P>0.05	P>0.05	P>0.05	P>0.05	None
XieYanru et al.	GPE/ GP	P>0.05	7/4.5	P>0.05	P>0.05	P>0.05	P>0.05	None
ZhangTe et al.	GPE/ T	P<0.05	Not reported	P>0.05	Not reported	P>0.05	P>0.05	Not reported
Tang Zhi et al.	TCE/ TC	P<0.05	Not reported	P>0.05	Not reported	Not reported	P>0.05	Not reported
Han Lichun et al.	TPE/ TP	P<0.05	Not reported	P>0.05	P>0.05	P>0.05	P>0.05	None
Liu Jing et al.	TE/T	P<0.05	Not reported	P>0.05	P>0.05	P>0.05	P>0.05	Not reported

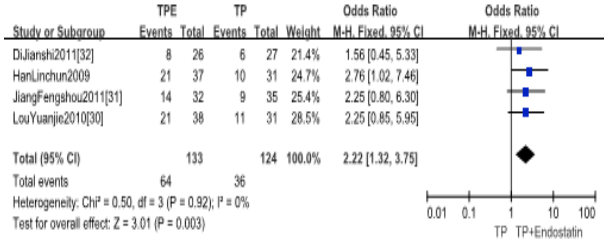

Figure 9. Meta-analysis of the RR (CR+PR) Between TP plus Endostar and TP Alone

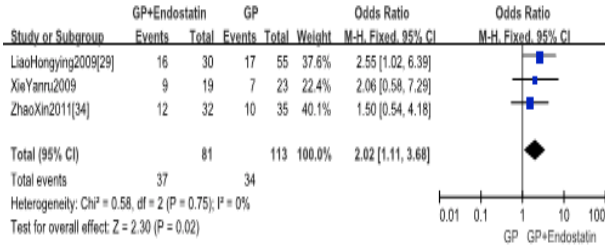

Figure 10. Meta-analysis of the RR (CR+PR) Between GP plus Endostar and GP Alone

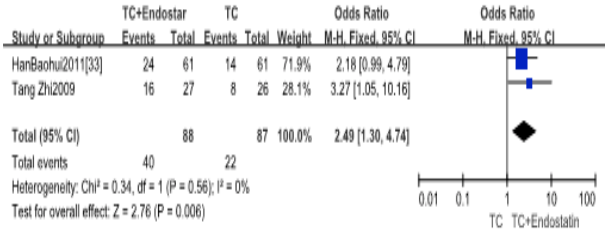

Figure 11. Meta-analysis of the RR (CR+PR) Between TC plus Endostar and TC Alone

95%CI(1.30, 4.74)) (Figure 11) between TCE and TC and only two studies were included in this comparison (Tang et al., 2009; Han et al., 2011).

There was only one trial in some inventions, so they could not be analyzed. After using different inventions to each group, all these studies reported RR and had used statistical analysis as well as adverse responses. More information was included in Table 4.

Discussion

All studies compared chemotherapy plus Endostar with chemotherapy alone, and 8 were the comparison between NPE scheme and NP scheme, 2 RCTs (Ma et al., 2005; Liu et al., 2009) were the comparison between NPE plus Radiotherapy and NP plus Radiotherapy.

Moderate bias may occur in these included studies. Because the medical treatment characteristics of oncology, it is difficult to fully blind and hide random, so bias in this clinical drugs treatment research was acceptable.

Meta-analysis included a total of 915 cases of patients showed that there were significant differences in RR between NPE program and NP program, but there were no significant differences in severe leucopenia, severe thrombocytopenia, nausea and vomiting.

Compared with NP scheme, NPE scheme could improve recent response rate in advanced NSCLC, while did not increase the adverse response. However, long-term effect was not reported, whether there were advantage benefits in overall survival were not known.

Two RCTs (Ma et al., 2005; Liu et al., 2009) reported response rate after treatment. 108 advanced NSCLC patients were included in this meta-analysis, and there was no significant difference in RR as well as leucopenia, thrombocytopenia and radioactive esophagitis between NPE+RT and NP+ RT. Only one study reported one-year progression-free survival rate, one-year survival rate and quality of life (Ma et al. 2005).There were 46 confirmed advanced NSCLC cases involved in this study. The one-year survival rate in NPE+RT and NP+RT were 74.1 % (17/23) and 65.4 %(15/23), the one-year progression-free survival rate in NPE+RT and NP+RT was 56.7 %(13/23) and 52.3 %(12/23). These two data in the experimental arm were higher than those in control arm, but there was no significant difference.

Conclusion based on the current clinical studies, platinum-based chemotherapy is regarded as one of the first-line treatment options for advanced NSCLC patients. Endostar combined with platinum-based chemotherapy could be regarded as a new standard treatment for advanced NSCLC patients. In the clinical treatment, NP plus Endostar could significantly increase term effect, while don't increase the incidence of adverse response. This evidence suggests that endostar should be added to platinum-based chemotherapy in the treatment of advanced NSCLC to improve term effect and life quality.

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