Comparison of amlodipine versus nifedipine for hypertension during pregnancy: a systematic review and meta-analysis

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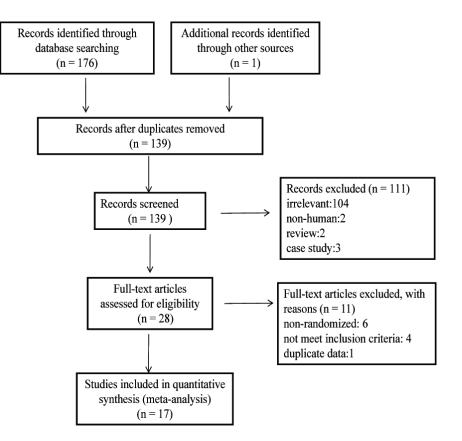
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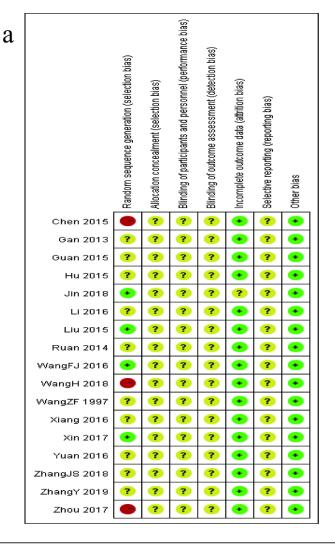
Abstract

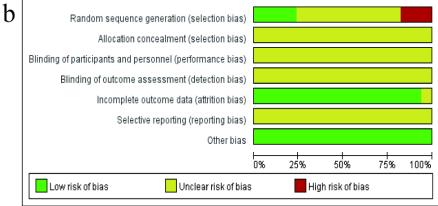
Backgroud: There is a lack of sufficient evidence regarding efficacy and safety of amlodipine on treating hypertension during pregnancy. Objective: To compare the efficacy and safety of amlodipine with nifedipine on hypertension during pregnancy. Search strategy: PubMed, Embase, Cochrane Library, clinicaltrials.gov, Chinese National Knowledge Infrastructure, Wanfang Database and China Biology Medicine disc were searched from inception to April 15, 2021. Selection criteria: Randomised controlled trials were included. Data collection and analysis: Data extraction was carried out by one researcher and checked by another. Results were reported as risk ratios (RR) for dichotomous outcomes or mean differences (MD) for continuous outcomes, with 95% confidence intervals (CI). Results: Seventeen RCTs were included. Amlodipine was found the efficacy is slightly superior to nifedipine on treating hypertension during pregnancy (RR 1.06, 95% CI 1.01 to 1.10) with a decreased risk for maternal side effects (RR 0.42, 95% CI 0.29 to 0.61). Subgroup analysis found amlodipine can get a better control on SBP (RR -11.68, 95% CI -17.98 to -5.37) and DBP (RR -7.44, 95% CI -13.81 to -1.06) compared with extended release nifedipine. In addition, there was no difference between amlodipine and nifedipine on pregnancy outcomes including caesarean section, premature labour, placental abruption, FGR, fetal distress, neonatal asphyxia. Conclusions: Given the results of this systematic review and meta-analysis, amlodipine can be effectively and safely used for hypertension during pregnancy. Key words: Amlodipine, Nifedipine, Hypertension during pregnancy, Meta-analysis Tweetable abstract: This review found that amlodipine is noninferior to nifedipine in managing hypertension during pregnancy.

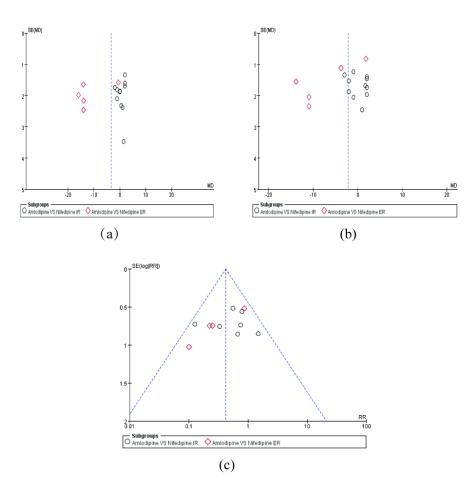
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Comparison of amlodipine versus nifedipine for hypertension during pregnancy a systematic review and me available at https://authorea.com/users/732554/articles/710840-comparison-of-amlodipine-versus-nifedipine-for-hypertension-during-pregnancy-a-systematic-review-and-meta-analysis









(a)

	Amlodip Events	Total	Nifedipir		Moinht		isk Ratio Fixed, 95% Cl	Risk Ratio M-H, Fixed, 95% Cl
Study or Subgroup								M-R, FIXEU, 95% CI
Chen 2015	20	21	16	21	4.9%		25 [0.97, 1.62]	
Gan 2013	37	40	36	38	11.3%		98 [0.87, 1.10]	
Guan 2015	23	24	22	24	6.7%		05 [0.90, 1.21]	
Hu 2015	53	55	52	55	15.9%	1.	02 [0.94, 1.11]	
Liu 2015	45	48	44	48	13.5%	1.	02 [0.91, 1.14]	
Ruan 2014	42	45	43	45	13.2%		98 [0.88, 1.08]	
WangZF 1997	42	45	28	34	9.8%		13 [0.95, 1.35]	
	42	40	20 59					
Xin 2017		. –		72	18.1%		14 [1.00, 1.29]	
Yuan 2016	23	24	22	24	6.7%	1.	05 [0.90, 1.21]	
Total (95% CI)		374		361	100.0%	1.0	06 [1.01, 1.10]	◆
Total events	352		322					
Heterogeneity: Chiª	² = 8.75, df = 8	3 (P = 0	.36); I ^z = 9	1%				0.7 0.85 1 1.2 1.5
Test for overall effe	ct: Z = 2.43 (F	P = 0.02)					0.7 0.85 1 1.2 1.5 Favours nifedipine Favours amlodipine
b)								
,	Amlodipi			lipine			Mean Difference	Mean Difference
Study or Subgroup 1.2.1 Amlodipine VS N	Mean Sl	D Total	Mean	SD	Total V	Veight	IV, Random, 95% Cl	IV, Random, 95% Cl
Gan 2013		6 40	131	8	38	6.5%	2.00 [-1.15, 5.15]	+
Guan 2015	133	7 24	133	6	24	6.3%	0.00 [-3.69, 3.69]	_
Hu 2015	128	9 55	129	10	55	6.4%	-1.00 [-4.56, 2.56]	-
Li 2016		6 47	131	7	47	6.6%	2.00 [-0.64, 4.64]	
Liu 2015 Ruan 2014		8 48 7 45	130 130	9 9	48 45	6.4% 6.4%	-2.00 [-5.41, 1.41] 2.00 [-1.33, 5.33]	
WangFJ 2016		/ 45 8 20	130	9	45	6.0%	2.00 [-1.33, 5.33] 1.00 [-3.66, 5.66]	_ _
WangZF 1997	126.75 17.2	5 45	125.25	13.5	34	5.3%	1.50 [-5.28, 8.28]	_
Yuan 2016	127.53 6.1	4 24		8.23	24	6.2%	-0.99 [-5.10, 3.12]	- <u>+</u>
ZhangJS 2018 Zhou 2017	128.36 8.0 131	3 19 8 47	127.86 131	6.14 10	19 47	6.1% 6.3%	0.50 [-4.05, 5.05] 0.00 [-3.66, 3.66]	
Subtotal (95% CI)	131	8 47 414	131	10		68.6%	0.56 [-0.54, 1.66]	
Heterogeneity: Tau ² = Test for overall effect: 3		41, df = 1	0 (P = 0.7)	8); I² = I				
		,						
1.2.2 Amlodipine VS N								
Jin 2018	123.6 6.		137.8	8.6	43	6.5%	-14.20 [-17.42, -10.98]	
WangH 2018 Xiang 2016	132.9 132 1		133.5 146	8 9	51 30	6.5% 6.0%	-0.60 [-3.71, 2.51] -14.00 [-18.81, -9.19]	T
Xin 2017	132.72 11.2			12.54	72	6.3%	-15.95 [-19.84, -12.06]	I
ZhangY 2019	132	9 35	146	9	35	6.2%	-14.00 [-18.22, -9.78]	
Subtotal (95% CI)		231				31.4%	-11.68 [-17.98, -5.37]	-
Heterogeneity: Tau ² = Test for overall effect: 2	47.79; Chi [#] = 5 7 - 2.62 /P - 0	6.31, df	= 4 (P < 0.)	00001)	; I* = 93%	,		
reaction overall effect.	2 = 3.03 (1 = 0	.0003)						
Total (95% CI)		645			632 1	00.0%	-3.35 [-6.60, -0.11]	◆
		83.91, d	f=15 (P <	0.0000	01); I ^z = 9	2%		-20 -10 0 10 20
Heterogeneity: Tau ² =	39.84, Chi+= 1					96		Favours amlodipine Favours nifedipine
Heterogeneity: Tau ² = Test for overall effect: 3 Test for subaroup diffe	Z = 2.02 (P = 0	.04)	df = 1 (P = 1	0.0002). I* = 92.	~~~		
Test for overall effect : Test for subaroup diffe	Z = 2.02 (P = 0 erences: Chi ² =	.04) : 14.05. (). I* = 92.!			
Test for overall effect : Test for subaroup diffe C)	Z = 2.02 (P = 0 erences: Chi ² = Amlodip	.04) : 14.05. (ine	Nifed	ipine			Mean Difference	Mean Difference
Test for overall effect : Test for subaroup diffe C) Study or Subgroup	Z = 2.02 (P = 0 erences: Chi ^z = Amlodip Mean SI	.04) : 14.05. (ine) Total		ipine), * = 92.! <u>otal VV</u> e		Mean Difference IV, Random, 95% Cl	Mean Difference IV. Random, 95% Cl
Test for overall effect : Test for subdroup diffe C) <u>Study or Subgroup</u> 1.3.1 Amlodipine VS Gan 2013	Z = 2.02 (P = 0 erences: Chi ^z = Amlodip Mean SI	.04) : 14.05. (ine <u>) Total</u>	Nifed	ipine	otal We	ight	IV, Random, 95% Cl 2.00 [-1.41, 5.41]	
Test for overall effect. Test for subaroup diffe C) Study or Subgroup 1.3.1 Amiodipine VS Gan 2015	Z = 2.02 (P = 0 erences: Chi ² = <u>Amlodip</u> <u>Mean SI</u> 5 Nifedipine <u>SI</u> 82	.04) : 14.05. (<u>o Total</u> 6 40 9 24	Nifed Mean 80 82	ipine <u>SD T</u> 9 8	otal We 38 6 24 5	ight 1.2% 1.5%	V, Random, 95% Cl 2.00 [-1.41, 5.41] 1.00 [-3.82, 5.82]	
Test for overall effect : Test for subaroup diffe C) Study or Subgroup 1.3.1 Amlodipine VS Gan 2015 Guan 2015 Hu 2015	Z = 2.02 (P = 0 erences: Chi ² = <u>Mean SI</u> 5 Nifedipine IR 83 80	.04) = 14.05. (<u>) Total</u> 6 40 9 24 7 55	Nifed <u>Mean</u> 80 82 81	ipine <u>SD T</u> 9 8 6	otal We 38 6 24 5 55 6	ight .2% .5%	V, Random, 95% CI 2.00 [-1.41, 5.41] 1.00 [-3.82, 5.82] -1.00 [-3.44, 1.44]	
Test for overall effect : Test for subaroup diffe C) Study or Subgroup 1.3.1 Amlodipine VS Gan 2015 Hu 2015 Li 2016	Z = 2.02 (P = 0 erences: Chi ² = Mean Si 5 Nifedipine IR 82 83 80 82	.04) :14.05.0 <u>ine</u> <u>0 Total</u> 6 40 9 24 7 55 6 47	Nifed Mean 80 82	ipine <u>SD T</u> 9 8	otal We 38 6 24 5 55 6 47 6	ight .2% .5% .6%	N, Random, 95% Cl 2.00 [-1.41, 5.41] 1.00 [-3.82, 5.82] -1.00 [-3.44, 1.44] 2.00 [-0.86, 4.86]	
Test for overall effect : Test for subaroup diffe C) Study or Subgroup 1.3.1 Amiodipine VS Gan 2013 Guan 2015 Hu 2015 Li 2016 Liu 2015 Ruan 2014	Z = 2.02 (P = 0 erences: Chi ^z = <u>Mean St</u> Shifedipine IR 82 83 80 82 83 83	.04) = 14.05. (<u>) Total</u> - - - - - - - - - - - - -	Nifed Mean 80 82 81 80 85 85	ipine <u>SD T</u> 8 8 8 8 8 8 8	otal We 38 6 24 5 55 6 47 6 48 6 45 6	ight .2% .5% .6% .5% .4%	V. Random, 95% Cl 2.00 [-1.41, 5.41] 1.00 [-3.82, 5.82] -1.00 [-3.44, 1.44] 2.00 [-0.86, 4.86] -2.00 [-5.01, 1.01] 2.00 [-0.76, 4.76]	
Test for overall effect. Test for subaroup diffe C) <u>Study or Subaroup</u> Gan 2013 Guan 2015 Li 2016 Liu 2015 Ruan 2015 Ruan 2014 Ruan 2015	Z = 2.02 (P = 0 erences: Chi [#] = <u>Mean SI</u> 5 Nifedipine IR 83 80 82 83 83 83 83 83	.04) = 14.05. (ine 5 Total 6 40 9 24 7 55 6 47 7 48 5 45 6 20	Nifed Mean 80 82 81 80 85 81 84	ipine <u>SD T</u> 8 8 8 8 8 8 7	otal We 38 6 24 5 55 6 47 6 48 6 45 6 20 5	ight .2% .5% .6% .5% .5% .5%	V, Random, 95% Cl 2.00 [-1.41, 5.41] 1.00 [-3.82, 5.82] -1.00 [-3.44, 1.44] 2.00 [-0.86, 4.86] -2.00 [-5.01, 1.01] 2.00 [-0.76, 4.76] -1.00 [-5.04, 3.04]	
Test for overall effect: Test for subaroup diffe C 1.3.1 Amlodipine VS Gan 2013 Guan 2015 Hu 2015 Liu 2016 Liu 2016 Ruan 2014 WangFJ 2016 WangFJ 2016	Z = 2.02 (P = 0 erences: Chi [≇] = <u>Mean SI</u> 8 Nifedipine IR 82 80 83 83 83 83 83 83 84 4.	.04) = 14.05.0 ine 5 6 40 9 24 7 55 6 47 7 48 5 45 6 20 5 45 6 20	Nifed Mean 80 82 81 80 85 81 81 84 87 6	ipine <u>SD T</u> 8 8 8 8 8 8 8	otal We 38 6 24 5 55 6 47 6 48 6 48 6 20 5 34 6	ight .2% .5% .6% .5% .5% .5%	N, Random, 95% Cl 2.00 [-1.41, 5.41] 1.00 [-3.82, 5.82] -1.00 [-3.44, 1.44] 2.00 [-0.86, 4.86] -2.00 [-5.04, 1.01] 2.00 [-0.76, 4.76] -1.00 [-5.04, 3.04] -3.00 [-5.62, -0.38]	
Test for overall effect: Test for subgroup diffe C Study or Subgroup 1.3.1 Antiodipine VS G an 2015 G an 2015 Li 2015 Li 2015 Ruan 2014 Wang J 2016 Wang J 2016 Wang J 2016	Z = 2.02 (P = 0 erences: Chi [₽] = Mean SI 5 Nifedipine IR 82 83 83 83 83 83 83 83 83 83 83 83 83 83	.04) = 14.05.0 ine D Total 6 40 9 24 7 55 6 47 7 48 5 45 6 20 5 45 6 24 5 45 6 20 5 45 6 24	Nifed 80 82 81 80 85 81 84 84 87 6 84	ipine <u>SD T</u> 9 8 6 8 8 8 7 .75 7	otal We 38 6 24 5 55 6 47 6 48 6 45 6 20 5 34 6 24 6	ight .2% .5% .6% .5% .5% .6% 6%	V, Random, 95% Cl 2.00 [-1.41, 5.41] 1.00 [-3.82, 5.82] -1.00 [-3.44, 1.44] 2.00 [-0.86, 4.86] -2.00 [-5.01, 1.01] 2.00 [-0.76, 4.76] -1.00 [-5.04, 3.04] -3.00 [-5.62, -0.38] -2.00 [-5.69, 1.69]	
Test for overall effect: Test for subaroub diffe C) Study or Subgroup Gan 2013 Guan 2015 Hu 2015 Hu 2015 Ruan 2014 WangFJ 2016 WangZF 1997 Yuan 2016 ZhangJS 2018 Zhou 2017	Z = 2.02 (P = 0 erences: Chi [₽] = <u>Mean SI</u> 83 81 83 82 83 83 83 83 83 83 83 83 83 83 83 83 83	.04) = 14.05.0 Total - - - - - - - - - - - - -	Nifed 80 82 81 80 85 81 84 84 87 6 84	ipine <u>SD T</u> 8 6 8 8 7 .75 7 .21 10	otal We 38 6 55 6 47 6 48 6 45 6 34 6 20 5 34 6 24 6 19 6 47 6	ight .2% .5% .6% .5% .5% .6% .6% .1% .3% .0%	V. Random. 95% Cl 2.00 [+1.41, 5.41] 1.00 [-3.44, 1.44] 2.00 [-0.82, 5.82] -1.00 [-3.44, 1.44] 2.00 [-5.01, 1.01] 2.00 [-5.01, 1.01] -1.00 [-5.04, 3.04] -3.00 [-5.62, -0.38] -2.00 [-5.69, 1.69] 1.70 [-1.81, 5.01] 2.00 [-1.85, 5.85]	
Test for overall effect. : Test for subaroub diffe C) <u>Study or Subaroup</u> (an 2013 Guan 2015 Li 2016 Li 2016 Li 2016 Kwang 2014 Wang 2014 Wang 2014 Zhang 2018 Zhang 2018 Zhang 2018 Zhang 2018 Zhang 2018 Zhang 2018	Z = 2.02 (P = 0 erences: Chi ^P = Mean SI 6 Nifedipine IR 83 80 83 83 83 83 83 84 83 83 84 83 83 84 83 83 84 83 83 84 83 83 84 83	.04) :14.05.0 ine D Total 6 40 9 24 7 55 6 47 7 48 5 45 6 20 5 45 6 20 5 45 6 24 2 19 9 47 414	Nifed 80 82 81 80 85 81 84 87 84 82.36 80 80	ipine <u>SD</u> T 9 8 6 8 8 7 .75 .75 .21 10	otal We 38 6 24 5 55 6 47 6 48 6 45 6 20 5 34 6 24 6 19 6 47 6 47 6	ight .2% .5% .6% .5% .6% .6% .1% .3%	V, Random, 95% Cl 2.00 [-1.41, 5.41] 1.00 [-3.82, 5.82] -1.00 [-3.44, 1.44] 2.00 [-0.86, 4.86] -2.00 [-5.01, 1.01] 2.00 [-0.76, 4.76] -1.00 [-5.02, -0.38] -2.00 [-5.62, -0.38] -2.00 [-5.69, 1.69] 1.70 [-1.61, 5.01]	
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Test for overall effect: Test for subaroub diff C C Study or Subaroub Gan 2013 Guan 2015 Li 2016 Li 2016 Li 2016 Ruan 2014 WangF J 2016 WangF J 2016 WangF J 2016 WangF J 2016 WangF J 2016 WangF J 2016 Tagang S 20 Subtolal (95% C) Heterogeneity: Tag Test for overall effect 1.3.2 Amodgipine VS	Z = 2.02 (P = 0 erences: Chi ² = Amlodip Mean Si S Nifedipine IR 82 83 84 83 84 84 84.06 5. 84 84.06 5. 82 = 1.83; Chi ² = 5. Nifedipine EF	.04) :14.05.0 ine 5 6 40 9 24 7 55 6 47 5 45 6 24 5 45 6 24 2 19 9 47 5 6 20 5 45 6 20 20 3 3 8 3 45 6 20 20 3 3 3 3 3 3 3 3 3 3 3 3 3	Nifed Mean 80 81 85 81 84 87 86 84 82.36 5 80 1f = 10 (P =	ipine <u>SD</u> T 9 8 8 8 7 .75 7 .21 10 .0.09);	otal We 38 8 24 5 55 6 47 6 48 6 45 6 20 5 34 6 20 5 34 6 21 6 47 6 401 6 8 %	ight .2% .5% .5% .5% .3% .3% .3% .3% .3% .3% .3%	$\label{eq:response} \begin{array}{c} \textbf{W}, \textbf{Random}, \textbf{95\% C1} \\ \textbf{2.00} [-1, 41, 5, 41] \\ 1.00 [-3, 82, 5 82] \\ -1.00 [-3, 82, 5 82] \\ -1.00 [-3, 63, 64, 86] \\ -2.00 [-5, 63, 4, 86] \\ -2.00 [-5, 63, -0, 38] \\ -3.00 [-5, 63, -0, 38] \\ -3.00 [-5, 63, -1, 69] \\ -3.00 [-5, 63, -1, 69] \\ -3.00 [-1, 18, 5, 129] \\ \textbf{0.06} [-1, 18, 1, 29] \end{array}$	
Test for overall effect: Test for subaroup diff C) Study or Subaroup Gan 2013 Guan 2013 Guan 2015 Hu 2015 Li 2016 Li 2016 Li 2016 Li 2016 Mang2F 1997 Yuan 2016 Zhang3F 1997 Subtotal (95% C) Heterogeneity, Tau ² Test for overall effec 1.3.2 Annoteipine V5 Jin 2018	Z = 2.02 (P = 0 prences: Chi ^P = Mean Si S Nitedipine IR 82 82 83 83 84 84 84 84 82 84.06 52 84 82 84 82 84 82 84 82 84 82 84 82 84 82 84 82 83 83 84 82 84 82 84 82 83 83 84 82 84 82 84 82 83 83 84 82 84 82 83 83 84 82 84 82 83 83 84 82 84 82 83 83 84 82 84 82 83 83 84 82 84 82 83 83 84 82 84 82 83 83 84 82 84 82 84 82 83 83 84 82 84 82 84 82 84 82 83 83 84 82 83 83 84 82 84 82 83 83 84 85 85 85 85 85 85 85 85 85 85	.04) :14.05.0 ine 5 Total 6 40 9 24 7 55 6 40 9 24 7 55 6 40 9 24 7 48 5 45 6 20 5 45 6 20 5 45 6 20 5 45 6 24 1 1 1 1 1 1 1 1	Nifed Mean 80 82 81 80 85 81 84 82.36 84 84 82.36 5 80 1f = 10 (P = 95.2	ipine <u>SD T</u> 9 8 8 8 7 .75 7 .21 10 .0.09); 8.3	otal We 38 6 24 5 55 6 47 6 45 6 20 5 34 6 24 6 24 6 45 6 24 6 45 6 45 6 45 6 45 6 45 6 45 6 47 6 47 6 47 6 47 6 47 6 47 6 47 6 47	ight .2% .5% .5% .5% .5% .3% .3% .3% .3% .3% .3% .3% .3	M. Random. 95% C1 2.00 [-1.41, 5.41] 1.00 [-3.82, 582] -1.00 [-3.82, 582] -1.00 [-3.82, 582] -2.00 [-5.68, 4.86] -2.00 [-5.68, 4.86] -2.00 [-5.68, 4.86] -1.00 [-5.04, 3.04] -3.00 [-5.68, 1.69] -2.00 [-5.68, 1.69] -2.00 [-1.68, 5.85] 0.06 [-1.18, 1.29]	
Test for subaroup diffe (C) <u>Study or Subaroup</u> 1.3.1 Amodpine VS Gan 2013 Guan 2015 Hu 2015 Liu 2015 Liu 2015 Ruan 2014 Wang J 2016 Zhang J2 201	Z = 2.02 (P = 0 rences: Ch ² = Amlodip Mean SI Nifedpine IR 83 83 83 84 84 84.06 82 =1.63, Ch ² = =1.63, Ch ² = 5. Nifedpine EF 81.3 5. 82.5 4.	.04) :14.05.0 ine 5 Total 6 40 9 24 7 55 6 40 9 24 7 55 6 20 5 45 6 20 5 45 6 24 2 19 9 47 16.18, d :0.93) 8 9 43 2 51	Nifed Mean 80 82 81 84 84 82 86 84 82 86 87 87 87 87 81 87 81 81 81 82 80 7 80 7	ipine <u>50 T</u> 9 8 6 8 8 7 .75 7 .21 10 .0.09); 8.3 4.1	otal We 38 6 24 55 45 6 47 6 45 6 20 5 24 6 34 6 47 6 401 68 19 58% 43 6 51 51	ight .2% .5% .6% .5% .3% .3% .3% .3% .3% .3% .3% .3	M. Random, 95% Cl 2.00 [-1 41, 5.41] 1.00 [-3 82, 582] -1.00 [-3 42, 582] -1.00 [-3 42, 142] 2.00 [0 86, 486] -2.00 [-5 66, 476] -1.00 [-5 66, -0.38] -2.00 [-5 65, -0.38] -2.00 [-5 65, -0.38] -2.00 [-1 85, 5.65] 0.00 [-1.18, 1.29] 13.90 [-16.94, -10.86] 1.80 [0.19, 3.41]	
Test for subaroup diff C) Study or Subaroup Gan 2013 Guan 2015 Hu 2015 Li 2016 Li 2016 Li 2016 Li 2016 Chan 2015 Chan 201	Z = 2.02 (P = 0 rences: Ch [#] = Medean SI Midedipine HS 82 83 83 83 83 84 84 84 84 84 84 84 84 85 82 83 83 83 83 83 83 83 83 83 83	.04) = 14.05.0 ine 7 Total - - - - - - - - - - - - -	Nifed Mean 80 82 81 84 85 84 87 84 82.36 84 87 80 95.2 80.7 92	ipine <u>SD T</u> 9 8 8 8 7 .75 7 .21 10 .0.09); 8.3	otal We 38 € 24 5 6 47 6 48 6 45 6 20 6 34 6 24 6 19 6 47 6 47 6 47 6 47 6 47 8 47 8 47 8 47 8 47 8 47 8 47 8 47 8	ight .2% .5% .5% .5% .3% .1% .3% .3% .3% .3% .3% .5% .5%	M. Random, 95% C1 2.00 [-1.41, 5.41] 1.00 [-3.82, 582] -1.00 [-3.82, 582] -1.00 [-3.86, 4.86] -2.00 [-5.66, 4.86] -2.00 [-5.66, 4.76] -1.00 [-5.62, -0.38] -2.00 [-5.63, 1.89] -2.00 [-1.65, -0.38] -2.00 [-1.65, -0.38] 1.70 [-1.61, 5.01] 2.00 [-1.85, 5.55] 0.06 [-1.16, 4.4] 13.90 [-16.94, -10.86] 13.90 [-16.94, -10.86] -1.00 [-1.56, -6.42]	
Test for sverall effect: Test for subaroup diff C Study or Subaroup Gan 2013 Guan 2015 Hu 2015 Li 2016 Li 2016 Li 2016 Li 2016 Li 2016 Kuan 2017 Subdotal (95% CI) Test for overall effect 1.3.2 Amtodipine VS Jin 2018 WangJH 2018 Xiang 2016 Xiang 2016 Xiang 2016 Xiang 2018 Xiang 2018 Xiang 2018 Xiang 2018 Xiang 2018 Xiang 2018 Xiang 2018	$\label{eq:rescaled} \begin{array}{c} Z = 2.02 \ (P=0 \\ \text{arences: } Ch^{P} = \\ \hline \\ \text{Amotofin} \\ \text{Meant} \\ \text{SN interduptine iR} \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ $.04) = 14.05.0 ine D Total - - - - - - - - - - - - -	Nifed Mean 80 82 81 84 85 84 87 84 82.36 84 87 80 95.2 80.7 92	ipine <u>SD T</u> 9 8 6 8 8 8 7 7 7 7 7 7 7 7 7 7 7 7 10 .0 9 8 .21 10 .9 8 8 8 8 8 8 8 8 8 8 8 8 8	otal We 38 € 24 5 55 € 47 € 48 € 48 € 48 € 49 € 19 € 401 € 47 € 19 € 47 € 19 € 47 € 19 € 47 € 19 € 47 € 19 € 47 € 10 € 47 € 10 € 47 € 10 € 1	ight .2% .5% .5% .6% .6% .3% .0% .3% .0% .3% .6% .6% .6% .6% .6%	M. Random, 95% C1 2.00 [-1.41, 5.41] 1.00 [-3.82, 582] -1.00 [-3.82, 582] -1.00 [-3.82, 582] -1.00 [-3.68, 4.86] -2.00 [-5.68, 4.86] -2.00 [-5.68, 4.86] -3.00 [-5.68, -0.38] -2.00 [-5.68, -0.38] -2.00 [-1.85, 5.63] 0.00 [-1.18, -10.86] 13.90 [-16.84, -10.86] 13.90 [-16.84, -10.86] -3.78 [-5.99, -1.59] -1.00 [-1.98, -6.42] -3.78 [-5.99, -7.01]	
Test for sverall effect: Test for subaroup diff (C) <u>Study or Subaroup</u> 1.3.1 Amiodipine VS Gan 2013 Guan 2015 Hu 2015 Hu 2015 Hu 2015 Ruan 2016 Wang/J 2016 ZhangJS 2016 ZhangJS 2018 ZhangJS 2018 ZhangJS 2018 ZhangJS 2018 Yuan 2016 Test for overall effect Jin 2018 Wang/H 2018 Xiang 2016 Xiang 2018 Xiang 20	Z = 2.02 (P = 0 rences: Ch ² = Annotig Meant Sis S Nifedipine IR 92 93 93 93 93 93 93 93 94 94 94 94 95 95 95 96 97 97 97 97 97 97 97 97 97 97	.04) :14.05.0 	Nifed Mean 80 82 81 80 84 84 82.36 84 84 82.36 5 84 84 82.36 5 84 87 84 87 80 10 (P = 95.2 93.14 7 92 7 92 7	ipine <u>SD T</u> 9 8 8 8 8 8 7 7 7 21 10 .21 10 .21 10 .009); 8.3 4.1 8 8.3 8.3 8 .3 5 8 8 .3 10 10 10 10 10 10 10 10 10 10 10 10 10	otal We 38 € 55 € 47 € 48 € 20 € 34 € 20 € 34 € 20 € 34 € 19 € 47 € 401 6 47 € 401 6 47 € 47 € 47 € 47 € 47 € 47 € 47 € 401 € 30 € 51 € 30 € 53 € 22 4 € 30 € 53 € 55 € 47 € 48 € 55 € 47 € 48 € 55 € 47 € 48 € 55 € 47 € 48 € 55 € 55 € 47 € 48 € 55 € 55 € 48 € 55 € 55 € 55 € 55 € 55 € 55 € 55 € 5	iaht .2% .5% .6% .5% .5% .6% .3% .0% .3% .0% .3% .0% .5% .3% .0% .5% .5% .5% .5% .5% .5% .5% .5	M. Random. 95% CI 2.00 [-1.41, 5.41] 1.00 [-3.82, 5.62] -1.00 [-3.48, 1.44] 2.00 [-0.68, 4.86] 2.00 [-0.68, 4.86] -2.00 [-6.64, 3.04] -3.00 [-5.63, -0.38] 1.70 [-1.63, 5.85] 0.06 [-1.18, 1.29] 1.300 [-16.94, -10.86] 1.80 [0.19, 3.41] -1.100 [-5.6, 6.42]	
Test for overall effect: Test for subaroub diff C) Study or Subaroup Gan 2013 Guan 2013 Guan 2015 Hu 2015 Li 2016 Li 2016 Kuan 2016 Kuan 2016 Zhang 2016 Zhang 2016 Zhang 2016 Subout 2017 Subtotal (95% C) Heterogeneiky, Tau ² Test for overall effect 1.3.2 Antiodepine VS Jin 2018 Wang J 2018 Xiang 2016 Xiang 2016 Xiang 2016	Z = 2.02 (P = 0 rences: Ch ² = Amiodig Mean SI 8 Nifedipine IR 82 83 83 83 83 83 83 83 83 83 83	.04) = 14.05.0 5 Total 6 40 9 24 7 55 6 47 7 48 5 45 6 20 5 45 6 24 4 2 19 9 47 4 16 .18, d 3 9 43 2 51 16 .18, d 3 9 43 2 51 16 .18, d 3 9 43 2 51 16 .18, d 16 .18, d 17 .18, d 18 .18, d 	Nifed Mean 80 82 81 80 84 84 82.36 84 84 82.36 5 84 84 82.36 5 84 87 84 87 80 10 (P = 95.2 93.14 7 92 7 92 7	ipine <u>SD T</u> 9 8 8 8 8 8 7 7 7 21 10 .21 10 .21 10 .009); 8.3 4.1 8 8.3 8.3 8 .3 5 8 8 .3 10 10 10 10 10 10 10 10 10 10 10 10 10	otal We 38 € 55 € 47 € 48 € 20 € 34 € 20 € 34 € 20 € 34 € 19 € 47 € 401 6 47 € 401 6 47 € 47 € 47 € 47 € 47 € 47 € 47 € 401 € 30 € 51 € 30 € 53 € 22 4 € 30 € 53 € 55 € 47 € 48 € 55 € 47 € 48 € 55 € 47 € 48 € 55 € 47 € 48 € 55 € 55 € 47 € 48 € 55 € 55 € 48 € 55 € 55 € 55 € 55 € 55 € 55 € 55 € 5	iaht .2% .5% .6% .5% .5% .6% .3% .0% .3% .0% .3% .0% .5% .3% .0% .5% .5% .5% .5% .5% .5% .5% .5	M. Random, 95% C1 2.00 [-1.41, 5.41] 1.00 [-3.82, 582] -1.00 [-3.82, 582] -1.00 [-3.82, 582] -1.00 [-3.68, 4.86] -2.00 [-5.68, 4.86] -2.00 [-5.68, 4.86] -3.00 [-5.68, -0.38] -2.00 [-5.68, -0.38] -2.00 [-1.68, -0.38] -2.00 [-1.68, 5.85] 0.00 [-1.18, -10.86] 13.90 [-16.84, -10.86] 13.90 [-16.84, -10.86] -3.78 [-5.99, -1.59] -1.100 [-1.98, -7.01]	
Test for overall effect: Test for subaroub diff C) <u>Study or Subaroup</u> 1.3.1 Amiodipine VS Gan 2013 Guan 2015 Liu 2015 Liu 2015 Liu 2015 Zhou 2015 Zhou 2017 Subtolal (95% C) Heterogeneity, Tau ² Test for overall effect Nan 2018 Viang 2018 V	Z = 2.02 (P = 0 rences: Ch ² = Amiodig Mean SI 8 Nifedipine IR 82 83 83 83 83 83 83 83 83 83 83	0.40) ine 3 Total 6 400 9 245 6 400 9 245 6 407 7 48 5 455 6 47 7 48 5 455 6 24 2 19 9 47 8 41 8 42 9 47 8 41 8 40 9 47 8 41 8 40 9 47 8 41 8 40 9 47 8 40 8 40 9 47 8 40 8	Nifed Mean 80 82 81 80 84 84 82.36 84 84 82.36 5 84 84 82.36 5 84 87 6 84 87 84 87 80 10 (P = 95.2 93.14 7 92 7	ipine 50 Ti 9 8 8 8 8 8 7 7 .21 10 .0.09); 8.3 8.3 4.1 8 .95 8 < 0.000	otal We 38 6 24 6 55 6 47 6 45 6 20 5 34 6 20 24 6 34 47 6 401 64 30 6 31 6 30 5 231 3 001); P 2	ight 55% 55% 55% 55% 55% 55% 55% 55% 13% 3.5% 5.4% 3% 5.5% 5.6% 5.5% 5.6% 5.5% 5.6% 5.5% 5.6% 5.5% 5.6% 5.6	$\begin{array}{c} \textbf{M}, \textbf{Random}, \textbf{95\% Cl} \\ \textbf{2.00} [-1.41, 5.41] \\ 1.00 [-3.82, 5.82] \\ -1.00 [-3.82, 5.82] \\ -1.00 [-3.82, 5.82] \\ -2.00 [-5.63, 4.76] \\ -2.00 [-5.63, 4.76] \\ -3.00 [-5.63, -0.36] \\ -2.00 [-5.69, 1.69] \\ -3.00 [-5.69, 1.69] \\ -2.00 [-1.85, 5.85] \\ \textbf{0.06} [-1.18, 1.501] \\ 2.00 [-1.85, 5.85] \\ \textbf{0.06} [-1.18, 1.501] \\ -3.00 [-5.63, -4.21] \\ -3.78 [-5.59, -4.59] \\ -3.78 [-5.59, -4.59] \\ -3.78 [-5.99, -1.59] \\ -7.44 [-13.81, -1.06] \end{array}$	
Test for sverall effect. Test for subaroup diff (C) <u>Study or Subaroup</u> 1.3.1 Amiodipine VS Gan 2013 Guan 2015 Li 2016 Li 2016 Li 2016 Li 2016 Zhan 2014 Zhan 2014 Zhan 2014 Zhan 2018 Subtotal (95% C) Heterogeneity: Tau ² Jin 2018 Viang 201	$\label{eq:2.2} Z = 2.02 \ (P = 0 \ erecces: Ch^2 = 0 \ erecces: $		Nifed Mean 80 81 81 84 82 84 82.36 6 84 82.36 6 87 6 87 80 7 95.2 93.14 7 92 93.14 7 92,4 7 93,14 7 92,7 93,14 7 92,7 93,14 7 92,7 93,14 7 95,2 93,14 7 95,2 93,14 7 95,2 93,14 7 95,2 93,14 7 95,2 93,14 7 95,2 93,14 7 95,2 93,14 7 95,2 93,14 7 95,2 93,14 7 95,2 93,14 7 95,2 93,14 7 95,2 93,14 7 95,2 95,2 95,2 95,2 95,2 95,2 95,2 95,2	ipine 5D Ti 9 8 6 8 8 7 7 7.21 10 0.09); 8.3 4.1 8 8.3 4.1 8 8.3 4.1 8 8.3 4.1 8 8.3 4.1 8 8.3 4.1 8 8.3 4.1 8 8.3 4.1 8 8.3 4.1 8 8.3 8 8.3 8 8.3 8.3 8.3 8.3 8.3 8.3 8	otal We 38 6 24 6 55 6 47 6 20 6 34 6 24 6 24 6 24 6 24 6 34 6 47 6 401 6 51 6 30 6 25 6 201); I*= 6	ight 5.2% 5.5% 5.5% 5.5% 5.5% 1.4% 5.5% 1.9% 5.8% 1.9% 5.8% 1.9% 5.8% 1.9% 5.8% 1.9% 5.8% 1.9% 5.8% 1.9% 5.8% 1.9% 5.8% 1.9% 5.9% 5.9%	M. Random, 95% C1 2.00 [-1.41, 5.41] 1.00 [-3.82, 582] -1.00 [-3.82, 582] -1.00 [-3.82, 582] -1.00 [-3.68, 4.86] -2.00 [-5.68, 4.86] -2.00 [-5.68, 4.86] -3.00 [-5.68, -0.38] -2.00 [-5.68, -0.38] -2.00 [-1.68, -0.38] -2.00 [-1.68, 5.85] 0.00 [-1.18, -10.86] 13.90 [-16.84, -10.86] 13.90 [-16.84, -10.86] -3.78 [-5.99, -1.59] -1.100 [-1.98, -7.01]	

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