

**WORKSHEET for Evidence-Based Review of Science for Emergency Cardiac Care****Worksheet author(s)**

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**Clinical question.**

In infants and children with cardiac arrest (P), does the use of tracheal drug delivery (I) compared to intravenous drug delivery (C) worsen patient outcome (eg. ROSC, survival to hospital discharge (O)

**Is this question addressing an intervention/therapy, prognosis or diagnosis? Intervention/Therapy**

**State if this is a proposed new topic or revision of existing worksheet:** revision of existing guideline from 2004

**Conflict of interest specific to this question**

Do any of the authors listed above have conflict of interest disclosures relevant to this worksheet? No

**Search strategy (including electronic databases searched).**

Medline searches (1966-2009) Last search was run September 29, 2009

1. Search (epinephrine OR "adrenaline"[All fields] OR lidocaine OR "lignocaine"[All Fields] OR naran OR vasopressin OR atropine) 236691
2. Search ("Heart Arrest"[Mesh] OR "Cardiopulmonary Resuscitation"[Mesh]) 29608
3. Search trachea\* OR endotrachea\* OR intratrachea\* 84935
4. Search #1 AND #3 AND #2 190
5. Search #1 AND #3 AND #2 Limits: All Child: 0-18 years 54
6. Search #1 AND #3 3570
7. Search #1 AND #3 Limits: Publication Date from 2003/1/1 to 2008/12/12 552

AND

EMBASE search (1966-2009)

1. 'heart'/syn AND arrest 38,480
2. 'epinephrine'/syn OR 'adrenaline'/syn OR 'lidocaine'/syn OR 'lignocaine'/syn OR 'naran'/syn OR 'vasopressin'/syn OR 'atropine'/syn 283,073
3. trachea\* OR endotrachea\* OR intratrachea\* 110,067
4. Search # 1 AND #2 AND #3 448
5. #1 AND #2 AND #3 AND [humans]/lim AND ([newborn]/lim OR [infant]/lim OR [preschool]/lim OR [school]/lim OR [child]/lim OR [adolescent]/lim) 82
6. #2 AND #3 limit publication years [2003-2008] 2,076

In addition, the following databases will be searched: Cochrane database for systematic reviews and Central Register of Controlled Trials, the National Guideline Clearinghouse™, the AHA Master Library. References of relevant review articles and most relevant research articles will be reviewed, along with citation reports for most relevant articles (using ISI Web of Science citation reports).

- **State inclusion and exclusion criteria**

Inclusion criteria: Prospective and retrospective case-control studies, case series and meta-analysis will be reviewed

Exclusion criteria: Studies published only in abstract form, articles not peer reviewed, and articles that do not answer the PICO question will be excluded. Case reports or case series will be excluded from detailed analysis if they are redundant to the reviewed literature.

- **Number of articles/sources meeting criteria for further review:**

24 articles met criteria for further review. Of these, 0 were LOE 1 (RCT), 1 was LOE 3 (retrospective controls), 0 were LOE 4 (no controls), and 23 were LOE 5 (4 neonatal, 7 adult, 12 animal studies)

# Summary of evidence

## Evidence Supporting Clinical Question

<b>Good</b>					[Niemann, 2002, 153-7]A,B,C [Barber, 2006, 1028-34]A,B,C,D <i>[Kleinman, 1999, 2748-54]E</i>
<b>Fair</b>					[Niemann, 2000, 1815-9]A,B,C
<b>Poor</b>					
	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>
<b>Level of evidence</b>					

A = Return of spontaneous circulation

B = Survival of event

C = Survival to hospital discharge

D = Intact neurological survival

E = Other endpoint

*Italics = Animal studies*

## Evidence Neutral to Clinical question

<b>Good</b>					<i>[Kofler, 2000, 1445-9]A</i> <i>[Jasani, 1994, 1174-80]A</i> <i>[Hornchen, 1992, 85-91]A</i> <i>[Quinton, 1987, 828-9]A,B,C</i>
<b>Fair</b>					<i>[Chen, 2008, 722-4]A,E</i> <i>[Schwab, 1994, F213-7]E</i> <i>[McDonald, 1985, 914-5]E</i> <i>[Ralston, 1984, 79-86]A,E</i>
<b>Poor</b>					
	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>
<b>Level of evidence</b>					

A = Return of spontaneous circulation

C = Survival to hospital discharge

E = Other endpoint

B = Survival of event

D = Intact neurological survival

*Italics = Animal studies*

## Evidence Opposing Clinical Question

<b>Good</b>					<i>[Rabitsch, 2003, 27-32]A,B,C</i> <i>[Brown, 1982, 43-5]A</i> <i>[Hornchen, 1987, 1037-9]A,B</i> <i>[Ralston, 1985, 1044-8]A</i> <i>[Wenzel, 1997, 1375-81]A</i> <i>[Redding, 1967, 253-8]E</i> <i>[Yang, 1991, 986-91]A</i>
<b>Fair</b>			[Guay, 2004, 373-8]A,B,C		[Lindemann, 1984, 210-2]B [Schmidbauer, 2000, 89]A [Battin, 2007, 504]A
<b>Poor</b>					[Tandberg, 1982, 443-5]E
	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>
<b>Level of evidence</b>					

A = Return of spontaneous circulation

C = Survival to hospital discharge

E = Other endpoint

B = Survival of event

D = Intact neurological survival

*Italics = Animal studies*

**REVIEWER'S FINAL COMMENTS AND ASSESSMENT OF BENEFIT / RISK:**

The 2005 ILCOR recommendations for drugs administered via a tracheal tube during cardiac arrest are summarized as follows: 1) IV or IO drug injection is preferred over drug administration via a tracheal tube and 2) the recommended dose of epinephrine administered via the tracheal route is 0.1 mg/kg. Since publication of these recommendations, no randomized controlled trials comparing intravenous vs. tracheal epinephrine administration in human subjects have been performed. Additionally, no further animal studies comparing resuscitation outcomes between the two routes of administration have been published. There are few published studies that address tracheal drug delivery via airway adjuncts, such as the laryngeal mask airway (LMA) and the tracheo-esophageal airway (Combitube). Similarly, few studies have reviewed the outcomes of neonates treated with epinephrine administered via an endotracheal tube (ETT). Thus in the following paragraphs I will summarize the published evidence regarding 1) absorption of drugs via the tracheal route in the setting of cardiac arrest, 2) efficacy of epinephrine administered via airway adjuncts in the setting of cardiac arrest, and 3) outcomes (ROSC, survival) after tracheal drug delivery. It should be noted that the majority of published clinical studies administered epinephrine via the tracheal route at a dose of 0.01 mg/kg, ten-times lower than the dose recommended by ILCOR in the 2005.

1. Absorption of drugs after administration via the tracheal route in cardiac arrest

**Epinephrine**

Animal models of cardiac arrest, including ventricular fibrillation or asphyxia, demonstrated elevated plasma drug levels or cerebral blood flow changes after tracheal instillation of epinephrine in a dose of 0.1 mg/kg [Hornchen, 1992, 85-91, Jasani, 1994, 1174-80, Kofler, 2000, 1445-9, Ralston, 1984, 79-86]. In only one animal model, administration of tracheal epinephrine in a dose of 0.01 mg/kg did not significantly increase plasma epinephrine levels and did not have an effect on blood pressure [Kleinman, 1999, 2748-54].

A study in neonates requiring ETT epinephrine for resuscitation (dose 0.2 mg/kg) documented increased plasma epinephrine levels after ETT administration [Schwab, 1994, F213-7].

In adults with cardiac arrest, one study showed that administration of ETT epinephrine did not change plasma epinephrine levels compared with baseline, while IV epinephrine administration raised plasma epinephrine levels significantly [Quinton, 1987, 828-9].

**Lidocaine**

In an animal study of ventricular fibrillation, both IV and ETT lidocaine administration (dose 2 mg/kg) led to similar serum levels, which were elevated as compared with controls [Brown, 1982, 43-5].

Lidocaine administration via ETT in adults with ventricular fibrillation in a dose of 1.5 mg/kg resulted in levels that were not consistently in therapeutic range [McDonald, 1985, 914-5].

**Naloxone**

ETT administration on naloxone in a patient with severe bradycardia resulted in measurable serum levels [Tandberg, 1982, 443-5].

These studies provide evidence that epinephrine in a dose of 0.1 mg/kg is absorbed via the tracheal route in the setting of cardiac arrest. There is limited evidence (animal studies only) that lidocaine in a dose of 2-3 mg/kg is absorbed from the trachea during cardiac arrest. A study from one patient provides limited evidence that naloxone is absorbed from trachea. There are no human or animal studies documenting serum drug levels of atropine or vasopressin after tracheal instillation in the setting of cardiac arrest.

Animal studies suggest that lower epinephrine (0.01-0.05 mg/kg) concentration when the drug is delivered via the tracheal tube may produce transient deleterious  $\beta$ -adrenergic effects resulting in hypotension, and lower coronary artery perfusion [Efrati, 2003, 572-6, Elizur, 2003, 271-6, Manisterski, 2002, 1037-41, table of contents, Orlowski, 1990, 103-13, Paret, 1997, 77-82, Vaknin, 2001, 1408-12].

2. Administration of tracheal drugs via airway adjuncts

Administration of epinephrine via the Laryngeal Mask Airway (LMA) and Esophageal-Tracheal Combitube airway adjuncts has been studied over the last decade.

One animal study demonstrated that ROSC was similar after administration of epinephrine by Combitube or ETT. To obtain comparable serum levels to the ETT administration, doses ten times higher were administered via the Combitube (0.5 mg/kg) [Kofler, 2000, 1445-9].

Another animal study demonstrated that epinephrine administered via a catheter placed in the LMA produced similar plasma epinephrine levels as ETT administration of epinephrine [Chen, 2008, 722-4].

The only human study assessing the efficacy of epinephrine administration via airway adjuncts in cardiac arrest demonstrated that epinephrine administered via Combitube in adults with CA (0.1 mg/kg) resulted in similar survival rates as epinephrine administered via ETT (0.01 mg/kg) [Rabitsch, 2003, 27-32].

### 3. Outcomes (ROSC, survival) after tracheal drug delivery during cardiac arrest

#### *Epinephrine*

There is adequate evidence in **animal models** of asphyxial and ventricular fibrillation cardiac arrest that ROSC is similar in animals receiving epinephrine via ETT or IV [Ralston, 1985, 1044-8, Redding, 1967, 253-8, Yang, 1991, 986-91, Hornchen, 1987, 1037-9].

However, the limited studies in **adults** in the setting of cardiac arrest are flawed because of the small number of subjects and the inconsistency in the epinephrine dose used in the studies.

- Administration of epinephrine via Combitube (0.1 mg/kg) resulted in a ROSC of 85%, a survival to ED of 38%, a survival to ICU of 10%, and a survival to discharge of 6% [Rabitsch, 2003, 27-32]. Combitube administration was compared with ETT administration in this study and led to similar outcomes.

- Administration of epinephrine via ETT or IV (0.01 mg/kg) resulted in increased ROSC after IV medications in three studies; survival to hospital discharge was similar between groups in two studies and better for the IV group in another study [Quinton, 1987, 828-9, Niemann, 2000, 1815-9, Niemann, 2002, 153-7].

- ETT epinephrine at 2.5 or 5 mg was administered to 57 patients in a randomized fashion. ROSC was obtained in 14/32 (43%) of the patients that received 2.5 mg epinephrine and in 16/25 (50%) of the patients that received 5 mg epinephrine [Schmidbauer, 2000, 89].

ETT epinephrine administered to **asphyxiated neonates** resulted in successful resuscitation in two studies (0.02-0.04 mg/kg, in 100% of patients, n=10) [Lindemann, 1984, 210-2] and in 28/39 (71%) [Battin, 2007, 504].

A retrospective review of 44 neonates resuscitated in the delivery room initially with epinephrine via ETT (0.01mg/kg) followed by IV epinephrine for non-responders, showed that 14/44 (33%) of the patients responded to ET epinephrine. Of non-responders, 23/30 responded to IV epinephrine, while 7/30 had no ROSC [Barber, 2006, 1028-34].

In a retrospective study examining 203 **children** with in-hospital cardiac arrest, survival was comparable between children who received IV or endotracheal epinephrine (0.01 mg/kg) (7% vs. 13.3%) [Guay, 2004, 373-8].

#### *Lidocaine*

In an animal study of ventricular fibrillation, both IV and ETT lidocaine administration (dose 2mg/kg) led to similar rate of cardioversion, which was significantly higher in comparison with controls [Brown, 1982, 43-5].

#### *Atropine*

Epinephrine and atropine administered via the ETT or IV to adult patients with cardiac arrest resulted in increased ROSC in the group that received IV medication; survival to hospital discharge was similar between groups in one study and better in the IV group in another study [Niemann, 2000, 1815-9, Niemann, 2002, 153-7].

#### *Vasopressin*

An animal model evaluated the effect of ETT vasopressin compared with normal saline. The animals treated with vasopressin had a higher ROSC as compared with controls [Wenzel, 1997, 1375-81].

#### **Acknowledgements:**

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### *Citation List*

Barber CA, Wyckoff MH. Use and efficacy of endotracheal versus intravenous epinephrine during neonatal cardiopulmonary resuscitation in the delivery room. *Pediatrics*. 2006;118(3):1028-34.

*A retrospective review of 44 neonates resuscitated in the delivery room initially with epinephrine via ETT (ET epi) (0.01mg/kg, 1 cc NS flush) followed by iv epinephrine for non-responders. 14/44(33%) patients responded to ET epi. Of non-responders, 23/30 responded to iv epi, while 7/30 had no ROSC.*

*Limitations include: low dose epinephrine used, small sample size, low volume of NS flush. Pathophysiology related to ineffective neonatal transition that limits pulmonary absorption of the drug (L-R intracardiac shunts such as PDA and PFO) may also be a confounding factor.*

*LOE: 5 (neonates-different patient population)*

*Quality of evidence: Good*

*Evidence: supportive (0.01 mg/kg epinephrine given)*

Battin M, Page B, Knight D. Is there still a place for endotracheal adrenaline in neonatal resuscitation? J Paediatr Child Health. 2007;43(6):504.

1034-4810 (Print)

Comment

Letter

*Retrospective review, neonatal resuscitations in the delivery room from 2003-2006. 39 resuscitations reviewed, 28/39 newborns responded to one or two ETT epinephrine administered. Limitations include no controls, and unknown time of resuscitation before epinephrine administration.*

*LOE 5 (neonates, different patient population)*

*Quality of evidence: Fair*

*Evidence: opposing (epinephrine dose is not specified)*

Brown LK, Diamond J. The efficacy of lidocaine in ventricular fibrillation due to coronary artery ligation: endotracheal vs intravenous use. Proc West Pharmacol Soc. 1982;25:43-5.

0083-8969 (Print)

Journal Article

Research Support, Non-U.S. Gov't

*Animal study, rabbit ventricular fibrillation cardiac arrest. Compares IV vs. ETT lidocaine (dose 2mg/kg) absorption and rate of cardioversion. Animals treated with IV or ETT lidocaine had faster rates of cardioversion compared with controls.*

*LOE 5*

*Quality of Evidence: Good*

*Evidence: opposing (lidocaine dose 2 mg/kg)*

Chen KT, Lin HJ, Jeng HW, Lin CC, Guo HR. The pharmacological effect of epinephrine administration via laryngeal mask airway in a porcine model of asphyxial cardiac arrest. Emerg Med J. 2008;25(11):722-4.

Journal Article

*Animal study, ventricular fibrillation cardiac arrest in piglets, compares plasma levels of epinephrine after three routes of administration: ETT, LMA via catheter, and direct LMA. ETT and LMA via catheter administration resulted in comparable plasma epinephrine levels; lower levels were obtained after direct LMA administration. This study demonstrates absorption of epinephrine from trachea. Outcomes were not measured.*

*LOE:5*

*Quality of evidence: fair*

*Evidence: neutral (epinephrine dose 0.05 mg/kg)*

Efrati O, Barak A, Ben-Abraham R, Modan-Moses D, Berkovitch M, Manisterski Y, et al. Should vasopressin replace adrenaline for endotracheal drug administration? Crit Care Med. 2003;31(2):572-6.

Comparative Study  
Journal Article

Elizur A, Ben-Abraham R, Manisterski Y, Barak A, Efrati O, Lotan D, et al. Tracheal epinephrine or norepinephrine preceded by beta blockade in a dog model. Can beta blockade bestow any benefits? Resuscitation. 2003;59(2):271-6.

Comparative Study  
Journal Article

Guay J, Lortie L. An evaluation of pediatric in-hospital advanced life support interventions using the pediatric Utstein guidelines: a review of 203 cardiorespiratory arrests. Can J Anaesth. 2004;51(4):373-8.

Evaluation Studies  
Journal Article

*Retrospective study examining 203 children with in-hospital CA. Survival was comparable between children who received iv or endotracheal epinephrine (7% vs. 13.3%). Of note, survival of children that did not receive epinephrine was 50%. Number of children who received ETT epinephrine is not reported. Mean dose of tracheal epinephrine was 0.01 mg/kg. Limitations are: very small sample size; duration of cardiac arrest before epinephrine administration is not reported.*

*Evidence: Opposing*

*Quality of Evidence: Fair*

*Level of Evidence: 3 (dose of epinephrine: 0.01 mg/kg)*

Hornchen U, Schuttler J, Stoeckel H, Eichelkraut W, Hahn N. Endobronchial instillation of epinephrine during cardiopulmonary resuscitation. Crit Care Med. 1987;15(11):1037-9.

Journal Article

*Animal study. ROSC after administration of epinephrine IV (0.01 mg/kg) or endotracheally (0.1 mg/kg) was improved compared with controls.*

*Evidence: Opposing*

*Quality of Evidence: Good*

*Level of Evidence: 5 (dose of epinephrine: 0.1 mg/kg)*

Hornchen U, Schuttler J, Stoeckel H. Influence of the pulmonary circulation on adrenaline pharmacokinetics during cardiopulmonary resuscitation. Eur J Anaesthesiol. 1992;9(1):85-91.

Journal Article

Research Support, Non-U.S. Gov't

*Animal study, pig VF model. Plasma epinephrine levels after IV and ETT administration were compared. Both IV and ETT administration resulted in elevated epinephrine levels and increased ROSC.*

*Evidence: Neutral*

*Quality of Evidence: Good*

*Level of Evidence: 5 (dose of epinephrine: 0.1 mg/kg)*

Jasani MS, Nadkarni VM, Finkelstein MS, Mandell GA, Salzman SK, Norman ME. Effects of different techniques of endotracheal epinephrine administration in pediatric porcine hypoxic-hypercarbic cardiopulmonary arrest. *Crit Care Med.* 1994;22(7):1174-80.

Comparative Study

Journal Article

Research Support, Non-U.S. Gov't

*Animal study, asphyxial cardiac arrest. Compares different modalities of epinephrine administration via ETT (direct, via side port, via catheter). There were no differences between groups in success of resuscitation.*

*Evidence: Neutral*

*Quality of Evidence: Good*

*Level of Evidence: 5 (dose of epinephrine: 0.1 mg/kg)*

Kleinman ME, Oh W, Stonestreet BS. Comparison of intravenous and endotracheal epinephrine during cardiopulmonary resuscitation in newborn piglets. *Crit Care Med.* 1999;27(12):2748-54.

Comparative Study

Journal Article

Research Support, Non-U.S. Gov't

*Animal study, VF cardiac arrest in newborn pigs. Serum epinephrine levels and blood pressure were assessed after epinephrine administered iv (0.01 mg/kg) and ETT (0.01 mg/kg). While IV administration of epinephrine produced increase in plasma epinephrine level, this dose of ETT epinephrine did not significantly increase plasma epinephrine levels or blood pressure.*

*Evidence: Supporting*

*Quality of Evidence: Good*

*Level of Evidence: 5 (dose of epinephrine: 0.01 mg/kg)*

Kofler J, Sterz F, Hofbauer R, Rodler S, Schuster E, Winkler M, et al. Epinephrine application via an endotracheal airway and via the Combitube in esophageal position. *Crit Care Med.* 2000;28(5):1445-9.

Comparative Study

Journal Article

Research Support, Non-U.S. Gov't

*Animal study, ventricular fibrillation in pigs. Epinephrine administration via ETT (0.05 mg/kg) vs. Combitube (0.05 mg/kg and 0.5mg/kg). Epinephrine administration via Combitube necessitated ten times the ETT dose to produce the same plasma epinephrine levels. There was no difference between groups in ROSC.*

*Evidence: Neutral*

*Quality of Evidence: Good*

*Level of Evidence: 5 (dose of epinephrine: 0.5 mg/kg)*

Lindemann R. Resuscitation of the newborn. Endotracheal administration of epinephrine. *Acta Paediatr Scand.* 1984;73(2):210-2.

Journal Article

*Subjects: Persistently bradycardic neonates (n=10) successfully resuscitated with epinephrine administered via ETT, 0.02-0.04 mg/kg.*

*Evidence: Opposing*

*Quality of Evidence: Fair*

*Level of Evidence: 5 (dose of epinephrine: 0.02-0.04 mg/kg, neonates- different population)*

Manisterski Y, Vaknin Z, Ben-Abraham R, Efrati O, Lotan D, Berkovitch M, et al. Endotracheal epinephrine: a call for larger doses. *Anesth Analg*. 2002;95(4):1037-41, table of contents.

Journal Article

McDonald JL. Serum lidocaine levels during cardiopulmonary resuscitation after intravenous and endotracheal administration. *Crit Care Med*. 1985;13(11):914-5.

0090-3493 (Print)

Journal Article

*Prospective study (not controlled) assessed lidocaine levels in adults resuscitated from ventricular fibrillation cardiac arrest with lidocaine via either IV or ETT (1.5 mg/kg). IV but not ETT administration of lidocaine resulted in therapeutic lidocaine levels.*

*Evidence: Neutral*

*Quality of Evidence: Fair*

*Level of Evidence: 5 (dose of lidocaine: 1.5 mg/kg, adults- different population)*

Niemann JT, Stratton SJ. Endotracheal versus intravenous epinephrine and atropine in out-of-hospital "primary" and postcountershock asystole. *Crit Care Med*. 2000;28(6):1815-9.

Clinical Trial

Comparative Study

Journal Article

*Retrospective study (subjects are adults with cardiac arrest) assessing the efficacy of atropine and epinephrine via ETT vs IV. ROSC was higher in IV groups as compared with ETT groups. There was no difference in survival between groups. Limitations: low dose epinephrine used, small sample size.*

*Evidence: Supporting*

*Quality of Evidence: Fair*

*Level of Evidence: 5 (dose of epinephrine 0.02 mg/kg, adults-different population)*

Niemann JT, Stratton SJ, Cruz B, Lewis RJ. Endotracheal drug administration during out-of-hospital resuscitation: where are the survivors? *Resuscitation*. 2002;53(2):153-7.

Comparative Study

Journal Article

*Retrospective study (adults with cardiac arrest) comparing the effect of IV vs. ETT epinephrine on outcome after cardiac arrest. IV administration of epinephrine resulted in higher rate of ROSC and survival to hospital discharge. Limitations include low dose of ETT epinephrine used (0.02 mg/kg) and possibly higher morbidity in the ETT group (older, more residents from nursing homes).*

*Evidence: Supporting*

*Quality of Evidence: Good*

*Level of Evidence: 5 (dose of epinephrine 0.02 mg/kg, adults-different population)*

Orlowski JP, Gallagher JM, Porembka DT. Endotracheal epinephrine is unreliable. *Resuscitation*. 1990;19(2):103-13.

Journal Article

Paret G, Vaknin Z, Ezra D, Peleg E, Rosenthal T, Vardi A, et al. Epinephrine pharmacokinetics and pharmacodynamics following endotracheal administration in dogs: the role of volume of diluent. *Resuscitation*. 1997;35(1):77-82.

Comparative Study  
Journal Article

Quinton DN, O'Byrne G, Aitkenhead AR. Comparison of endotracheal and peripheral intravenous adrenaline in cardiac arrest. Is the endotracheal route reliable? *Lancet*. 1987;1(8537):828-9.

Clinical Trial  
Comparative Study  
Journal Article  
Randomized Controlled Trial

*Prospective randomized study (asystolic cardiac arrest, n=12) assessing the ROSC and epinephrine levels after IV or ETT epinephrine. ROSC was higher in the IV epinephrine group. Survival to hospital discharge was similar (n=0) in both groups. Plasma epinephrine levels were not detectable in the ETT group. Limitations: small sample size.*

*Evidence: Neutral*

*Quality of Evidence: Good*

*Level of Evidence: 5 (dose of epinephrine not specified, study in adults- different population)*

Rabitsch W, Schellongowski P, Staudinger T, Hofbauer R, Dufek V, Eder B, et al. Comparison of a conventional tracheal airway with the Combitube in an urban emergency medical services system run by physicians. *Resuscitation*. 2003;57(1):27-32.

Clinical Trial  
Comparative Study  
Journal Article  
Randomized Controlled Trial  
Research Support, Non-U.S. Gov't

*Prospective RCT trial (adults with cardiac arrest) compared the efficacy of epinephrine administration via conventional ETT (ETC) vs. Esophageal-Tracheal Combitube (ETA). Dose of epinephrine via ETT was 0.01 mg/kg; via Combitube 0.1 mg/kg. There was ROSC within 3 min after administration in 43/49 cases (ETC) versus 39/46 cases (ETA), with no difference between groups. Survival to hospital discharge was 3% (2 patients) in the ETA group and 6% (5 patients) in ETC group, did not reach statistical significance.*

*Evidence: Opposing*

*Quality of Evidence: Good*

*Level of Evidence: 5 (epinephrine dose 0.1 mg/kg via ETC, 0.01 mg/kg via ETA, wrong control group: ETC)*

Ralston SH, Voorhees WD, Babbs CF. Intrapulmonary epinephrine during prolonged cardiopulmonary resuscitation: improved regional blood flow and resuscitation in dogs. *Ann Emerg Med*. 1984;13(2):79-86.

Journal Article  
Research Support, U.S. Gov't, P.H.S.

*Animal study (canine cardiac arrest) assessing blood flow to organs (heart, brain, adrenal glands, kidneys, GI tract) in response to ETT epinephrine 0.1 mg/kg. Organ blood flow was modified in response to epinephrine, as evidence of absorption of epinephrine in the tracheobronchial tree during cardiac arrest.*

*Evidence: Neutral*

*Quality of Evidence: Fair*

*Level of Evidence: 5 (epinephrine dose 0.1 mg/kg)*

Ralston SH, Tacker WA, Showen L, Carter A, Babbs CF. Endotracheal versus intravenous epinephrine during electromechanical dissociation with CPR in dogs. *Ann Emerg Med.* 1985;14(11):1044-8.

Comparative Study

Journal Article

Research Support, U.S. Gov't, P.H.S.

*Animal study (canine cardiac arrest) compared the efficacy of IV and ETT epinephrine. ROSC was similar in animals receiving epinephrine 0.1 mg/kg via ETT or 0.01 mg/kg via IV.*

*Evidence: Opposing*

*Quality of Evidence: Good*

*Level of Evidence: 5 (epinephrine dose 0.1 mg/kg)*

Redding JS, Asuncion JS, Pearson JW. Effective routes of drug administration during cardiac arrest. *Anesth Analg.* 1967;46(2):253-8.

0003-2999 (Print)

Journal Article

*Animal study (canine asphyxial cardiac arrest) compared ROSC after 1 mg epinephrine administered via multiple routes. ROSC was similar for ETT, intravenous and intracardiac administration of epinephrine.*

*Evidence: Opposing*

*Quality of Evidence: Good*

*Level of Evidence: 5 (epinephrine dose 0.1 mg/kg)*

Schmidbauer S, Kneifel HA, Hallfeldt KK. Endobronchial application of high dose epinephrine in out of hospital cardiopulmonary resuscitation. *Resuscitation.* 2000;47(1):89.

0300-9572 (Print)

Clinical Trial

Comparative Study

Journal Article

Randomized Controlled Trial

*Prospective RCT trial in adult patients with cardiac arrest, comparing the efficacy of two doses of epinephrine via ETT: 2.5 and 5 mg. ROSC was obtained in 14/32 (43%) patients that received 2.5 mg epinephrine and 16/25 (50%) of patients that received 5 mg epinephrine. The difference was not significant. Limitation is small sample size and epinephrine dose administered only 2 times and 4 times the IV dose.*

*Evidence: Neutral*

*Quality of Evidence: Fair*

*Level of Evidence: 5 (epinephrine dose 2.5 and 5 mg, adults- different population; two doses of ETT epinephrine- wrong control)*

Schwab KO, von Stockhausen HB. Plasma catecholamines after endotracheal administration of adrenaline during postnatal resuscitation. *Arch Dis Child Fetal Neonatal Ed.* 1994;70(3):F213-7.

1359-2998 (Print)

Journal Article

*Prospective study in neonates requiring ETT epinephrine for resuscitation. This study documents increased plasma epinephrine levels after ETT administration.*

*Evidence: Neutral*

*Quality of Evidence: Fair*

*Level of Evidence: 5 (epinephrine dose 0.2 mg/kg, neonates- different population)*

Tandberg D, Abercrombie D. Treatment of heroin overdose with endotracheal naloxone. *Ann Emerg Med.* 1982;11(8):443-5.

Case Reports

Journal Article

*ETT administration on naloxone in a patient with severe bradycardia resulted in measurable serum levels.*

*Evidence: Opposing*

*Quality of Evidence: Poor*

*Level of Evidence: 5 (naloxone, adult patient- different population)*

Vaknin Z, Manisterski Y, Ben-Abraham R, Efrati O, Lotan D, Barzilay Z, et al. Is endotracheal adrenaline deleterious because of the beta adrenergic effect? *Anesth Analg.* 2001;92(6):1408-12.

Journal Article

Wenzel V, Lindner KH, Prengel AW, Lurie KG, Strohmenger HU. Endobronchial vasopressin improves survival during cardiopulmonary resuscitation in pigs. *Anesthesiology.* 1997;86(6):1375-81.

Comparative Study

Journal Article

Research Support, Non-U.S. Gov't

*Animal model (pig ventricular fibrillation cardiac arrest) evaluates the effect of ETT vasopressin compared with NS. The animals treated with vasopressin had a higher ROSC compared with controls.*

*Evidence: Opposing*

*Quality of Evidence: Good*

*Level of Evidence: 5 (dose of vasopressin 0.8 U/kg)*

Yang LY, He CQ, Zhang ZG. Endotracheal administration of epinephrine during cardiopulmonary resuscitation. *Chin Med J (Engl).* 1991;104(12):986-91.

Case Reports

Comparative Study

Journal Article

*Animal study (asphyxial cardiac arrest in dogs) compared ROSC between epinephrine 0.09 mg/kg administered via IV, ETT and ETT via catheter. There was no difference between treatment groups in rate of ROSC.*

*Evidence: Opposing*

*Quality of Evidence: Good*

*Level of Evidence: 5 (dose of vasopressin 0.8 U/kg)*