# 文献精读（2014-10-30）


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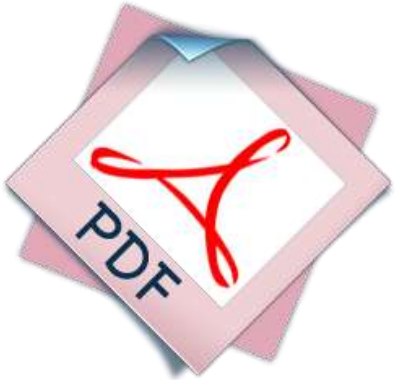
- Dexamethasone pretreatment for 24 h versus 6 h for prevention of postextubation airway obstruction in children: a randomized double-blind trial

- 提前24h与6h给予地塞米松预防儿童拔管后气道梗阻的随机双盲对照研究



# 研究背景

- Postextubation airway obstruction (PEAO) is common in pediatric intensive care units (PICUs). About 10–13 % of children intubated for >24–48 h require reintubation. Thus may increase morbidity, mortality, and cost of care.

- 拔管后气道梗阻在儿童重症监护病房中较为常见
- 插管时间>24–48小时的儿童中，约有10–13 % 需要再插管
- 并发症的发生率，死亡率以及治疗费用增高

# 研究背景

- Steroid pretreatment is effective in preventing PEAO among high-risk adult patients intubated for>36–48h. However, there is no consensus regarding the best approach for preextubation steroid therapy in critically ill children.

- 类固醇激素干预
  - 能有效预防成人拔管后气道梗阻的发生
  - 缺乏在危重症患儿中的确切研究

# 研究目的

- Reducing incidence of PEAO and thus preventing reintubation may improve outcome and reduce cost of acute care
  - reduce PICU stay
  - making more PICU beds available for salvageable critically ill patients

- 预防拔管后气道梗阻的发生，减少再插管几率，缩短PICU的住院时间——改善预后，降低治疗费用

# 研究方法—研究对象

- age>3 months and ≤12 years, intubation for ≥48 h, and anticipated first planned extubation during the next 24 h
- Excluded: congenital anomalies, burns, trauma and surgery involving airway, history of previous tracheal intubation or tracheostomy, chronic lung disease, contraindications for steroid, gastrointestinal bleeding, steroid treatment in preceding 7 days

- 入组： 年龄>3 个月 ≤12 岁，插管时间≥48 小时，预计未来24小时首次拔管
- 排除：先天性气道发育异常，烧伤，气道创伤或气道手术，既往行气管插管或气管切开，慢性肺疾病，类固醇激素禁忌症，胃肠道出血，1周内使用过激素

# 研究方法—分组

- 24-h pretreatment with dexamethasone (24hPD) and 6-h pretreatment with dexamethasone (6hPD)
  - age group (<1 year, 1 to <5 years, and ≥ 5 years)
  - duration of intubation (≤ 72 h, >72 h but ≤ 7 days, and >7 days)

- 随机分为24小时和6小时干预组
  - 年龄分组： <1 岁, 1 到 <5 岁, 和≥ 5岁
  - 插管时间： ≤ 72 小时, >72 h 至≤ 7 天, 以及>7 天

# 研究方法—干预

- 24hPD patients received six doses of intravenous dexamethasone (0.5 mg/kg/dose, maximum 8 mg/dose): the first dose 24 h before anticipated extubation and then every 6 h for a total of six doses. Extubation was done in the morning immediately after fifth dose.
- 6hPD patients received intravenous sterile water in equal volume for initial three doses, followed by dexamethasone (0.5 mg/kg/dose) for next three doses: 1st dose 6 h prior to and 2nd dose at extubation, and 3rd dose 6 h after extubation.

- 24小时干预组：iv地塞米松6次（ 0.5 mg/kg/次，最大剂量8 mg/次），预备拔管前24小时给予首次干预，其后每6小时给药1次，总共6次，第5次给药后立即拔管。
- 6小时干预组：前3次iv等量灭菌水，其后 iv地塞米松3次（ 0.5 mg/kg/次）。第1次于拔管前6小时，第2次于拔管时，第3次为拔管后6小时。

# 监测指标——Westley’s croup score (mWCS)评估气道梗阻情况

**拔管后0分，30分，1、2、3、6、12、24、36和48小时**

**Table 1** Modified Westley’s croup score [21] (mWCS)

| Clinical finding | Score |
|---|---|
| Inspiratory stridor | |
| None | 0 |
| Stridor audible with stethoscope at rest | 1 |
| Stridor audible without stethoscope | 2 |
| Air movement | |
| Normal | 0 |
| Decreased | 1 |
| Markedly decreased | 2 |
| Retractions | |
| None | 0 |
| Mild (alar flaring) | 1 |
| Moderate (suprasternal and intercostals) | 2 |
| Severe (all accessory muscles used) | 3 |
| Maximum total score | 7 |
| Need for adrenaline nebulization | 4 |
| Need for reintubation | 7 |

| 临床表现 | 分值 |
|---|---|
| 吸气性哮鸣音 | |
| 无 | 0 |
| 使用听诊器可闻及 | 1 |
| 不用听诊器可闻及 | 2 |
| 通气状态 | |
| 正常 | 0 |
| 降低 | 1 |
| 显著降低 | 2 |
| 呼吸动度 | |
| 无异常 | 0 |
| 轻度异常（鼻翼煽动） | 1 |
| 中度异常（胸骨上凹和肋间隙凹陷） | 2 |
| 重度异常（所有的辅助肌参与） | 3 |
| 最高分值 | 7 |
| 需要肾上腺素雾化吸入 | ≥4 |
| 需要再插管 | 7 |

# 研究方法

- mWCS ≥4 led to administration of nebulized L-epinephrine(1 ml = 1 mg; 2.5 ml in 2 ml normal saline) every 20 min until improvement in obstructive signs
- Patients were reintubated after failure of nebulized epinephrine as evidenced by audible stridor, markedly decreased air entry and severe chest retractions and/or respiratory acidosis (pH <7.35 and PaCO2>45 mmHg), SpO2<90 % at FiO2 40%, bradycardia or clinical impression of impending respiratory fatigue.

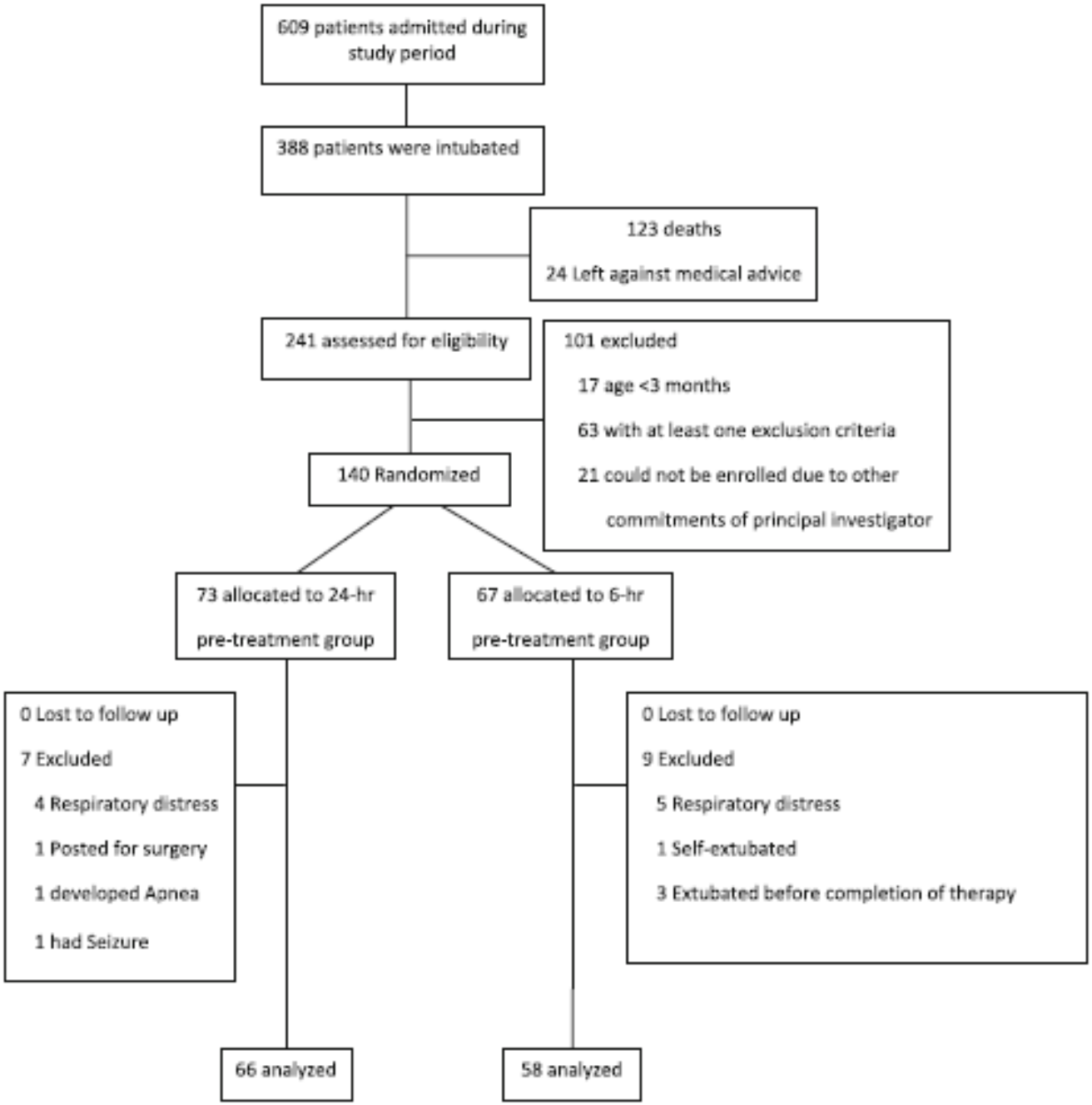
- mWCS ≥4需要肾上腺素雾化吸入（ 2.5 mg 溶于 2 ml NS），20分钟重复1次直到气道梗阻症状缓解(mWCS ≤2)
- 再插管：明显哮鸣音，通气量降低，严重的呼吸困难，呼吸性酸中毒，心动过缓或呼吸衰竭
- 出现以上2种情况，则认为发生拔管后气道梗阻

# 主要研究结果

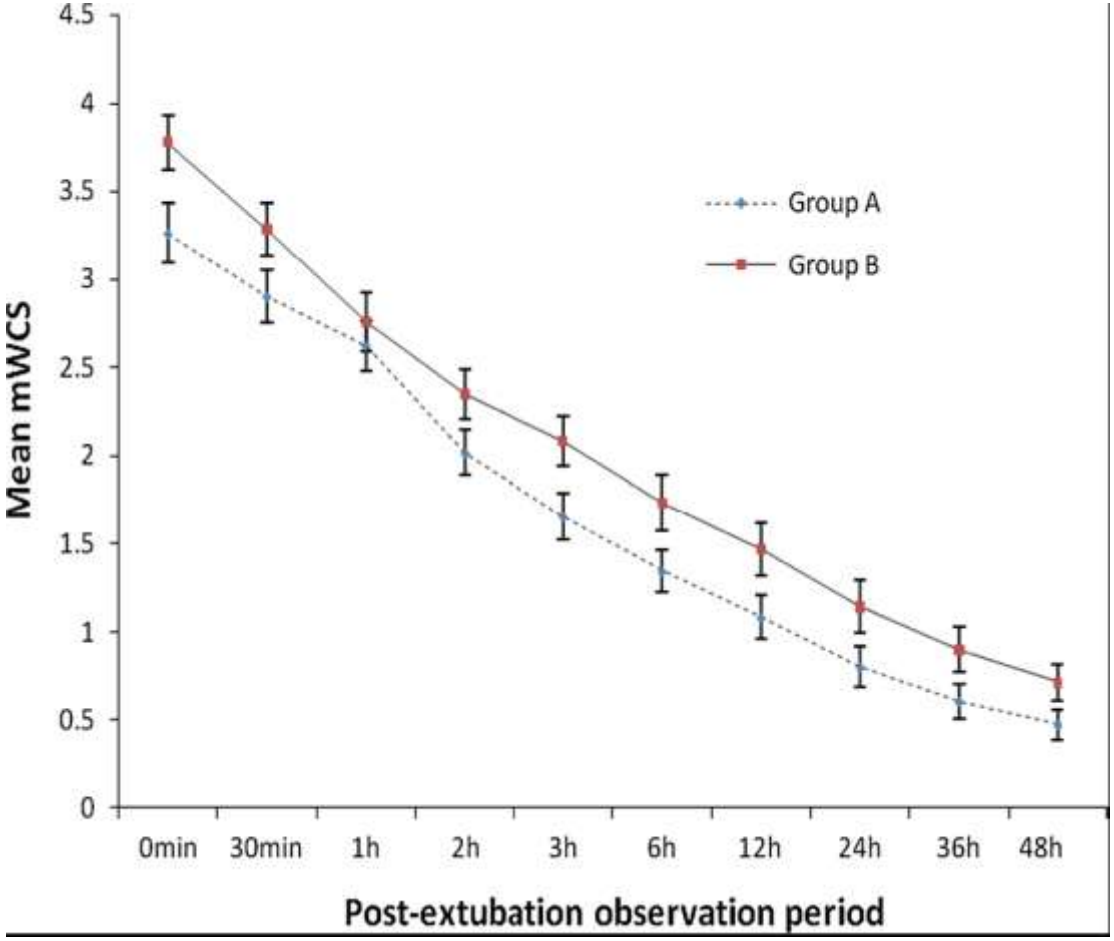
Mann–Whitney U test for continuous variables

$X^2$ test (and Fisher exact test if necessary) for categorical variables

Analysis of variance (ANOVA) was used for intergroup comparisons


609 patients admitted during study period
388 patients were intubated
123 deaths
24 Left against medical advice
241 assessed for eligibility
101 excluded
17 age <3 months
63 with at least one exclusion criteria
21 could not be enrolled due to other commitments of principal investigator
140 Randomized
73 allocated to 24-hr pre-treatment group
67 allocated to 6-hr pre-treatment group
0 Lost to follow up
7 Excluded
4 Respiratory distress
1 Posted for surgery
1 developed Apnea
1 had Seizure
0 Lost to follow up
9 Excluded
5 Respiratory distress
1 Self-extubated
3 Extubated before completion of therapy
66 analyzed
58 analyzed

# 研究结果




[mean ± standard error on the mean (SEM)]

A组： 24hPD
B组： 6hPD

repeated-measures ANOVA,
interactional p = 0.0001

与6小时干预组相比，24小时地塞米松干预显著降低48小时观测期内mWCS的分值

# 研究结果

- 24hPD reduced the incidence of PEAO (43/66 versus 48/58; p = 0.027) with absolute risk reduction of 17 %.
- Consequently, it reduced the number of patients requiring adrenaline nebulization [24hPD, 64 %; 6hPD, 84 %; p = 0.02].
- Once patients required adrenaline nebulizations to mitigate PEAO, there was no difference in the number of nebulizations needed in the two groups [mean (SD); 2.28 (1.59) versus 2.39 (1.53); p = 0.78].

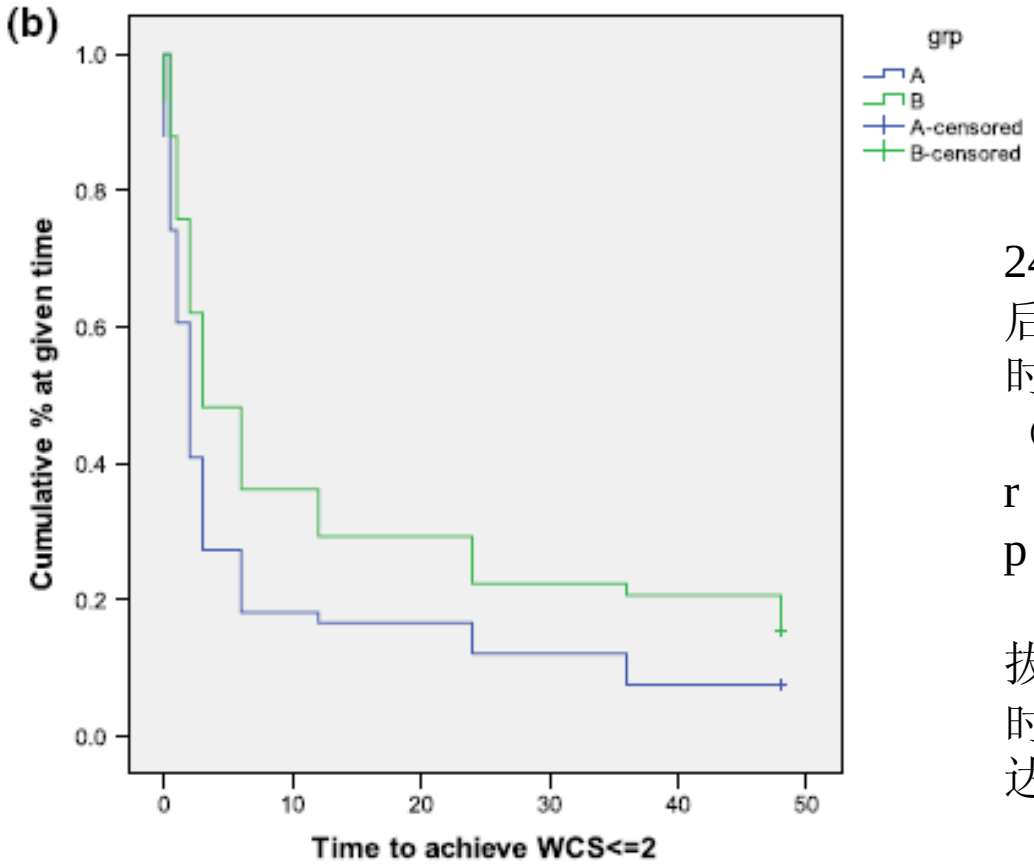
- 与6小时干预相比，24小时干预显著降低了拔管后气道梗阻的发生率（82% *VS.* 65%），具体的风险下降了约17%
- 与6小时干预相比，24小时干预减少需要了肾上腺素雾化治疗的患儿数量[24hPD, 64 %; 6hPD, 84 %; p = 0.02].
- 对于采用肾上腺素雾化治疗缓解病情的患儿，2组间雾化的次数无显著差异

# 研究结果

- It also reduced the incidence of reintubation, though nonsignificantly.
- Also, 24hPD delayed reintubation as well, with a median gap of 12 h (range 3–13 h) since extubation among 24hPD patients, versus 6 h (range 0 min to 36 h) among 6hPD patients.

- 24小时干预组患者再插管的发生率（8%）比6小时干预组（16%）降低了一半，然而这一差异缺乏统计学意义
- 24小时地塞米松干预显著推迟了患者发生再插管的时间，拔管后12小时 *VS.* 6小时

# 研究结果




A组： 24hPD
B组： 6hPD

24小时干预组患儿拔管后气道梗阻病情缓解的时间低于6小时干预组（ mWCS ≤2）（log-rank test，p = 0.016）

拔管后3小时内， 24小时干预组有更多的患儿达mWCS ≤2的标准

# 研究结果

- Univariate analysis identified longer (>7 days) intubation, cuffed tracheal tube, airway manipulation >1, pre-PICU intubation duration >1 day, and not having received 24hPD as risk factors for PEAO.
- Presence of hypoalbuminemia (p = 0.06), pedal and/or truncal edema at extubation were other risk factors

- 单因素分析证实：插管时间>7天，带套囊的气管导管，气道操作次数>1，入PICU前插管时间大于1天，没有接受24小时地塞米松干预均为拔管后气道梗阻的危险因素。
- 拔管时患儿存在低蛋白血症，四肢及躯干水肿也是拔管后气道梗阻的危险因素。

# 研究结果

| Independent risk factors | Regression coefficient (SE) | *p*-Value | Odds ratio (95 % CI) |
|---|---|---|---|
| Independent risk factors identified on multivariate analysis ($n = 124$) | | | |
| Intervention group (24-h versus 6-h pretreatment) | 0.96 (0.48) | 0.043 | 2.61 (1.03–6.61) |
| Duration of intubation (≤7 days versus >7 days) | 1.79 (0.48) | <0.001 | 6.00 (2.33–15.46) |
| Tracheal tube (uncuffed versus cuffed) | 1.14 (0.48) | 0.018 | 3.12 (1.22–8.01) |

- Multivariate analysis identified intubation >7 days as the most important independent risk factor, others being cuffed tracheal tubes and not having received 24hPD

- 多因素分析证实，插管时间>7天，带套囊的气管导管和没有接受24小时地塞米松干预均是拔管后气道梗阻发生的危险因素，其中插管时间>7天是最重要的独立危险因素

# 主要结论

- 24hPD reduced the incidence and severity of PEAO as well as the time to recover from it among patients in the study setting. This may help reduce PICU stay and its consequences. It also revealed a positive trend toward reintubation benefit. Intubation duration >7 days and cuffed tracheal tubes seem to be major independent predictors of PEAO. Other potential risk factors were the number of airway manipulations, longer pre-PICU intubation duration, and presence of hypoalbuminemic edema.

- 本研究结果提示24小时地塞米松干预可降低拔管后气道梗阻的发生率及严重程度，缩短其缓解时间。有利于减少再插管的几率。
- 拔管后气道梗阻发生的危险因素包括：进行气道操作的次数，入PICU前插管时间较长以及低蛋白水肿。而插管时间>7天是最重要的独立危险因素

# 局限性

- mWCS was used to improve the objectivity of croup evaluation, but assessment of the involved clinical signs itself was fairly subjective.
- Lack of measurement of observer agreement is another limitation of this study.

- 本文采用mWCS作为客观评价指标，然而其中包含的临床表现本身具有较强的主观性
- 本文同样缺乏有效标准来评估观察者的一致性

# 研究意义及展望

- While improving airway management skills will be a long-term goal, 24hPD should be considered among the select group of high-risk patients in the meantime. Further studies with larger sample sizes and in PICUs with different socioeconomic background, utilizing more objective ways of assessing airway obstruction, are desirable to validate these findings.

- 提高气道管理的技术是一个长远的目标，对于存在高危因素的患者我们可以考虑采用24小时地塞米松干预的方式。
- 开展不同社会背景下的大样本量的深入研究，采用更为客观的气道评估方法，将为本次的研究发现提供更有效的依据


Thank You!