

Evidence-Based Medicine

**Applications in prevention of
adverse effect of
indomethacin therapy
in patent ductus arteriosus (PDA)**

高醫小兒科部新生兒科

Patient profile

- Name: 陳 x x
- one day old male
- Mother history
 - G7P3A4
 - Gestational age : 30 weeks
 - Delivery method: cesarean section

Chief complaint

**dyspnea immediately
after birth**

Present illness

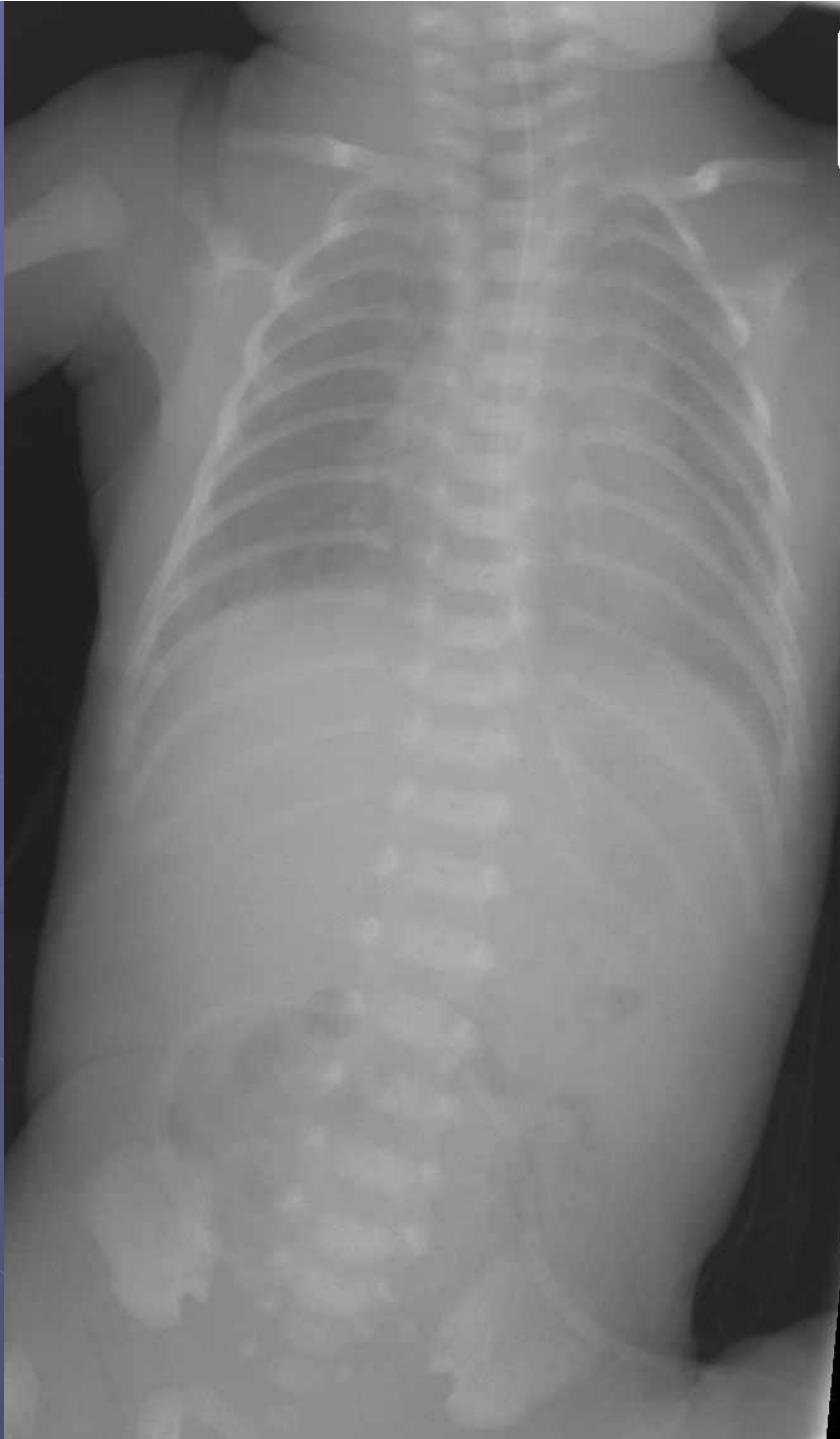
- No abnormality during prenatal examination.
- Mother had frequent uterine contraction and received tocolysis
- Ineffective tocolysis and Breech position
→ emergent C/S
- delay of initial crying , lip cyanosis, bradycardia

Physical examination

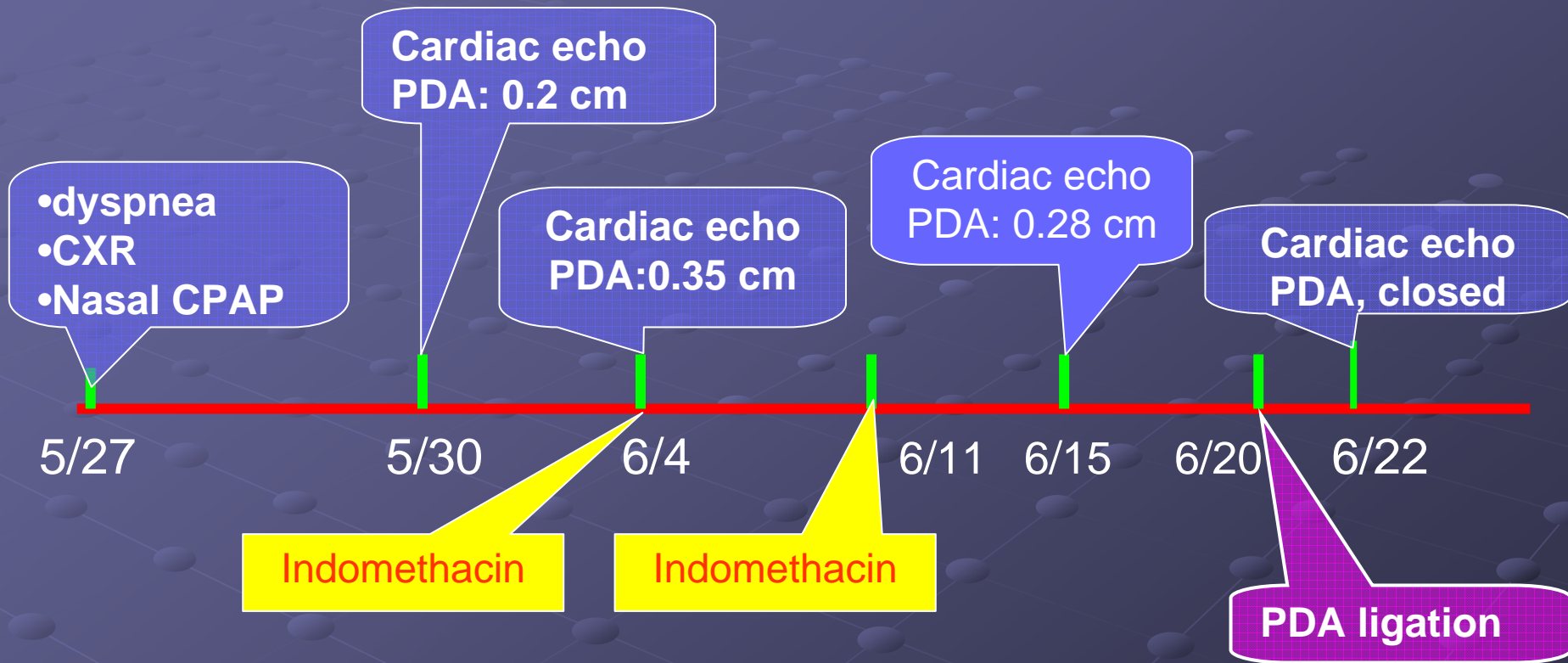
- Vital signs: BP:58/44mmHg HR: 160bpm **RR: 64cpm** BT: 37°C
 - HC: 29.5 cm (75-80 percentile)
 - BW: 1550 gm (25-50 percentile)
 - BL: 44 cm (75-90 percentile)
- Conscious : alert
- Anterior fontanel: not bulging
- Face: no dysmorphism
- Chest: symmetric expansion, **Sub costal retraction (+)**
 - H.S.: no murmur,regular heart beat
 - B.S.: coarse
- Abdomen: soft
 - bowel sound: normoactive
- L/L: no pitting edema

WBC	Blood	6.41
RBC	Blood	4.84
Hgb	Blood	17.0
Hct	Blood	49.9
MCV	Blood	103.1
MCH	Blood	35.1
MCHC	Blood	34.1
PLT	Blood	172
RDW -CV	Blood	14.1
RDW -SD	Blood	51.1
NEUT	Blood	45.2
EOSIN	Blood	1.1
BASO	Blood	0.5
LYMPH	Blood	47.9
MONO	Blood	5.3

CRP (定量)	Blood	<0.20
Urea N	Blood	3.5
Creatinine	Blood	0.6
NA	Blood	139
K	Blood	4.5
SGOT	Blood	37
SGPT	Blood	5
Temperature	Blood	37.0
pH	Blood	7.441
pCO2	Blood	32.6
pO2	Blood	39.7
HCO3-	Blood	21.7
Total CO2	Blood	18.8
Base excess	Blood	-1.5
SBC	Blood	23.1
BEecf	Blood	-2.4
%sO2c	Blood	76.7
Ca++(ionized)	Blood	5.22



- 96.5.27
- Respiratory distress syndrome ,grade II



實證醫學五大步驟

- 整理出一個可以回答的問題
(Asking an answerable question)
- 尋找文獻證據
(Tracking down the best evidence)
- 嚴格評讀文獻
(Critical appraisal)
- 應用於病人身上
(Integrating the appraisal with clinical expertise & patients' preference)
- 對過程進行稽核及評估
(Auditing performance and evaluation)

Asking

- P: prevent renal dysfunction in indomethacin therapy for closure patent ductus arteriosus
- I: Dopamine treatment
- C: no treatment
- O: outcome

Acquire

- Key word :indomethacin ,renal dysfunction
- Database :*The Cochrane Library*2007, Issue 2
- Topic :
Dopamine versus no treatment to prevent renal dysfunction in indomethacin-treated preterm newborn infants (Review)

Background

- Indomethacin therapy for closure of PDA frequently causes **oliguria**, and occasionally more **serious renal dysfunction**.
- **Low dose dopamine** has been suggested as a means for preventing this side effect.

Selection criteria

- Randomized or quasi-randomized studies of the effects of dopamine on **urine output, glomerular filtration rate, fluid balance or incidence of renal failure**, in preterm newborn infants receiving indomethacin.

Types of participants

- Preterm infants, ≤ 36 weeks gestation at birth receiving indomethacin for either PDA closure or prophylaxis, during the first month of life.

Types of intervention

- Dopamine compared to no treatment.

Main results

- Three studies were found (total number randomized patients, 75) which fulfilled the entry criteria for this review. All were single center trials which enrolled NICU patients receiving indomethacin for symptomatic PDA
- There are no results for effects of dopamine on several of the primary outcomes, including death before discharge, serious intraventricular hemorrhage, cystic periventricular leukomalacia, or renal failure.
- Dopamine improved urine output ,but mild .

Reviewers' Conclusions

- There is **no** evidence from randomized trials to support the use of dopamine to prevent renal dysfunction in indomethacin-treated preterm infants.

Can the results be applied to my patient?

- Dopamine has **not** been shown to prevent adverse effects of indomethacin on the kidneys of preterm babies

Asking

- P: prevent side effect and morbidity in indomethacin therapy for closure patent ductus arteriosus
- I: Furosemide treatment
- C: no treatment
- O: side effect and morbidity prevention

Acquire

- Key word :indomethacin ,side effect prevention
- Database *Cochrane Database of Systematic Reviews* 2001, Issue 3.
- Topic: **Furosemide for prevention of morbidity in indomethacin treated infants with PDA (Review)**

Background

- **Inhibition of prostaglandin synthesis** mediates closure of the ductus arteriosus and renal side effects after indomethacin administration.
- Because **furosemide increases prostaglandin production**, it could potentially help prevent indomethacin-related toxicity but also decrease ductal response to indomethacin.

Types of participants

- Preterm infants with a symptomatic PDA who were to receive at least one dose of indomethacin.

Types of intervention

- Patients were randomly allocated to receive either indomethacin alone or indomethacin preceded by or immediately followed with furosemide.

Review method

- Definition of the subsets:
 - Classify patients into two subsets based on their individual BUN/creatinine ratio before initiating indomethacin.

Main results

- Furosemide administration did **not** significantly increase the risk of failure of ductal closure
- Furosemide increased urine output regardless of the initial BUN/creatinine ratio, leading to a 5% weight loss during a 3-dose course, **an undesired effect in patients with initial BUN/creatinine ratio >20 mg/mg.**
- Furosemide increased creatinine clearance **only** in patients with initial BUN/creatinine ratio <20 mg/mg

Reviewers' Conclusions

- There is **not** enough evidence to support the administration of furosemide to premature infants treated with indomethacin for symptomatic **PDA**.
- Furosemide appears to be **contraindicated** in the presence of dehydration in those infants.



Thank you for your
attention !