

Proton Pump Inhibitors prescription patterns and associated complications in the paediatric intensive care unit

BACKGROUND

- ✓ Proton Pump Inhibitors (PPIs) are regularly prescribed in Paediatric Intensive Care Unit (PICU)
- ✓ **Indications** : Gastroesophageal Reflux Disease (GERD), Upper gastro-intestinal bleeding management, **Stress ulcer prophylaxis**
- ✓ Risk factors associated with Upper gastro-intestinal bleed (UGIB) are : **PRISM** (Pediatric Risk of Mortality) > 10, **Coagulopathy** (INR > 1.5, Fibrinogen < 2g/L, Thrombopenia < 100 G/L = 100,000/mm³), **Need for mechanical ventilation**
- ✓ Lack of evidence regarding the efficacy of stress ulcer prophylaxis for prevention of upper gastro-intestinal bleeding in the PICU
- ✓ Recent studies have associated the use of PPIs with a higher risk of nosocomial infection in the ICU and hyponatremia

OBJECTIVES

- ✓ Describe PPI prescription patterns in our PICU
- ✓ Explore potentially associated clinical complications like nosocomial infections and hyponatremia

METHODS

- ✓ Single-centre retrospective cohort study
- ✓ CHU de Caen Paediatric intensive care unit
- ✓ 2 Year period from January 1st 2017 to december 31st 2018
- ✓ Approved by CHU de Caen ethics board
- ✓ Data were retrieved from medical records with a standardised case report form

RESULTS

Population characteristics		PPIs Group		Non – PPIs group		P-value
Total	N(%)	231	30,6	523	69,4	
Age (years)	median [IQR]	10	[1-15]	2	[0-11]	<.0001
Age (years) < 2	N (%)	65	28,1	252	48,1	<.0001
Female	N (%)	100	43,3	206	39,4	0,3145
Weight (kg)	median [IQR]	31	[10-48]	12	[6-32]	<.0001
Premature	N (%)	42	18,2	98	18,7	0,8563
PRISM Score	median [IQR]	2	[0-7]	1	[0-6]	0,3256
Immunosuppression	N (%)	81	35,1	270	51,6	<.0001
Reason for hospitalisation <.0001						
Programmed surgery	N (%)	87	37,7	89	17,2	
Urgent surgery	N (%)	19	8,2	31	5,9	
Medicine	N (%)	94	40,7	328	62,7	
Traumatology	N (%)	31	13,4	75	13,3	
Surgery	N (%)	137	59,3	195	37,3	<.0001
Invasive devices						
Central venous line	N (%)	46	19,9	15	2,9	<.0001
Parenteral nutrition	N (%)	20	8,7	3	0,6	<.0001
Mechanical ventilation	N (%)	107	46,3	202	38,6	0,0476
Urinary catheter	N (%)	80	34,6	54	10,3	<.0001
At least 1 Invasive device	N (%)	159	68,3	239	45,7	<.0001
+ Surgery	N (%)	122	52,8	124	23,7	<.0001
Duration of stay in PICU	median [IQR]	6	4-11	4	2-6	<.0001

PPI and Non PPI population characteristics

Prescribed PPI	Esomeprazole	Pantoprazole	Lansoprazole	Oméprazole	Total
N (%)	221 (95,7)	7 (3)	2 (0,9)	1 (0,4)	231 (100)
Intravenous (n (%))	122 (55,2)	6 (85,7)	0	1 (100)	129
Dosing regimen (mg/kg/day)	1,02	0,94	---	0,54	---
Mean Duration (days)	7,39	10,17	---	3	7,49
Oral (n (%))	99 (44,8)	1 (14,3)	2 (100)	0	102
Dosing regimen (mg/kg/day)	0,95	0,68	0,29	---	---
Mean Duration (days)	10,04	8	7	---	9,96

PPI Prescription patterns

Indication	N = 231 (%)
Stress ulcer prophylaxis	177 (76,6%)
Gastro intestinal reflux	20 (8,6%)
Cystic fibrosis	5 (2,1%)
Stridor	5 (2,1%)
Oesophageal atresia	2 (0,9%)
Unknown	17 (7,3%)
Gastro intestinal bleeding	5 (2,1%)

PPI Indication

42 (23,7%) had 2+ UGIB risk factors
58 (11%) had 2+ UGIB risk factors in the non PPI group

	PPI Group	Non-PPI Group	P-value
Nosocomial infection (n (%))	21 (9)	9 (1,7)	<.001
Pulmonary Infection	10	4	---
Urinary tract infection	4	2	---
Surgical site infection	3	2	---
Sepsis	2	1	---
Others (Candidiasis and colitis)	2	0	---

RR = 3,4 [IC95% = 1,76 - 6,57] ; p < 0,05

Logistical regression independantly associated proton pump inhibitors with **nosocomial infection**: OR_a = 2,42 [IC95% = 1,17 – 5,14] ; p = 0,02

PPI Exposure was associated with a **higher risk of hyponaetremia** :

RR = 5,18 [IC95% = 2,16 – 12,43] p < 0,05

Propensity score matching analysis results : matched 183 patients, nosocomial infection rate was still higher in the PPI Group

	Unadjusted			Matched		
	IPP (n=231)	No IPP (n=523)	p*	IPP (n=183)	No IPP (n=183)	p*
Nosocomial infections, n(%)	19 (8)	11 (2)	<0.001	12 (7)	3 (2)	0.031
Duration of hospitalisation (days), median (IQR)	12 (7 - 22)	6 (4 - 11)	<0.001	11 (6 - 20)	7 (4 - 11)	<0.001

LIMITS

- ✓ Retrospective
- ✓ Single Center
- ✓ Confusion Bias : potential confounders adjusted with the logistical regression
- ✓ Indication Bias : a sicker population received PPIs → Resolved with propensity score matching analysis

CONCLUSION

- ✓ Overuse of PPIs
- ✓ Poorly documented medical indications
- ✓ Potential increase in the risk of nosocomial infection and hyponaetremia

- ✓ Risk – benefit ratio impossible to evaluate given the low incidence of UGIB in the PICU, the poorly documented efficacy of PPIs and risk of complications.
- ✓ Need for prospective multicentric studies and clinical practice guidelines