OPIOIDES EN INDUCCIÓN ANESTESICA PEDIÁTRICA: REMIFENTANIL y FENTANILO

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ALGUNAS VECES EMPIEZAS ASI!!!

EL CULPABLE

Y OTRAS TERMINAS AQUÍ!!!

SUEÑO o REALIDAD con los fármacos que utilizamos hoy?

DE QUE DEPENDE MI RESULTADO?

Es cierto que la experiencia tiene mucho que ver con lo anterior ?

Todo es una cascada de eventos para lograr un objetivo

Pre-medicación: efecto negativo de midazolam??

Preparación pre- operatoria

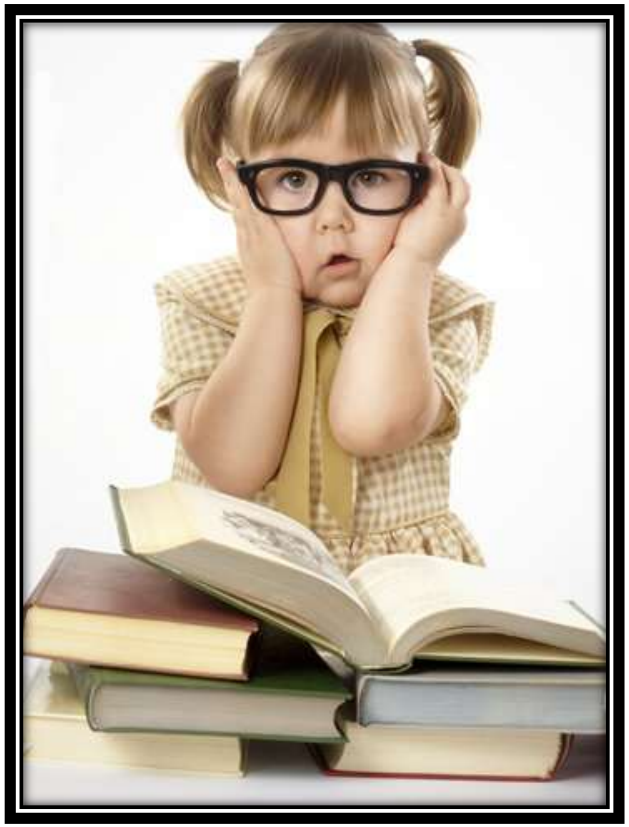
INTRODUCCION

- Cambios y adelantos importantes en la práctica anestésica, el abordaje hoy debe ser integral (período perioperatorio).
- variabilidad farmacocinética y farmacodinamia en los niños durante su desarrollo (fisiología, fisiopatología y las patologías pediátricas).
- El incremento de cirugía ambulatoria (60-80% CX en niños) trae consigo un campo de actos.
- La pre medicacion deberia ser individual antes de la IOT y dirigida por objetivos especificos.

INTRODUCCION

- Hoy extrapolamos nuestra experiencia de adultos a niños, se puede hacer ello con todos?
- Ventajas del opiode: menos delirium, depresion cardiovascular, tachycardia, respuesta al estimulo noxious, y un despertar suave.
- Guinsburg et al, los opioides decrementan el catabolismo, efecto de estabilizacion clinica en infantes pre-terminos criticos.

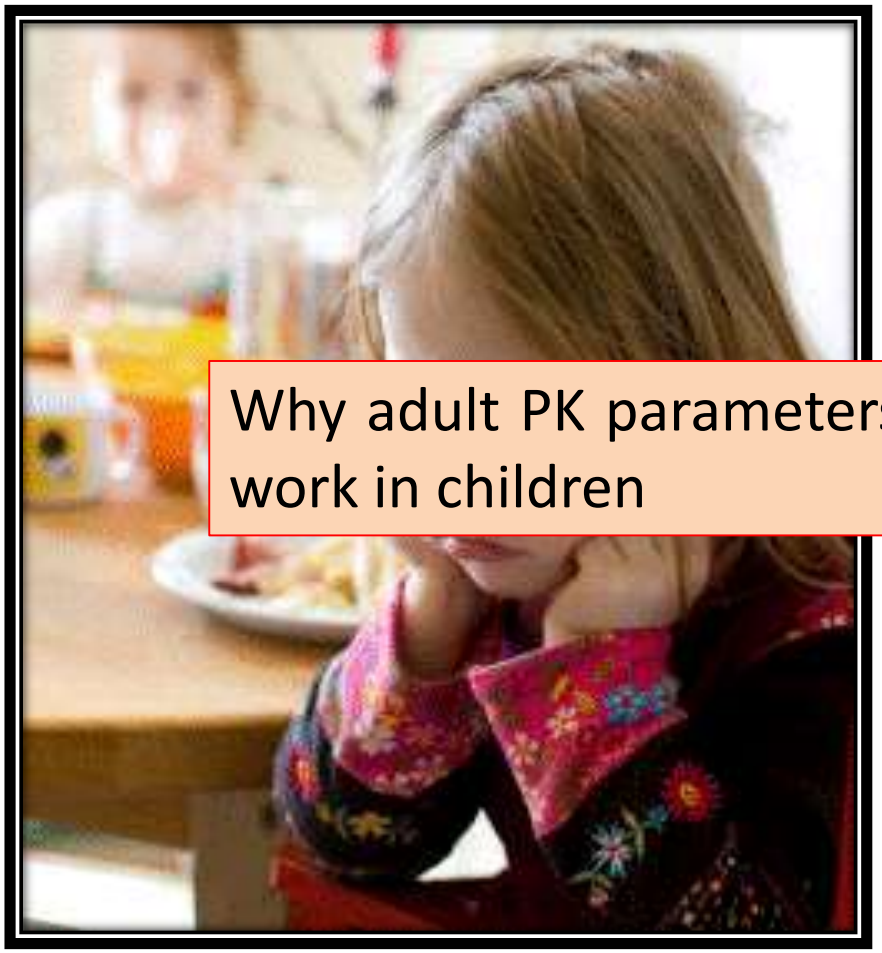
OPIOIDES EN ANESTESIA



¿Se puede administrar remifentanil en bolus?

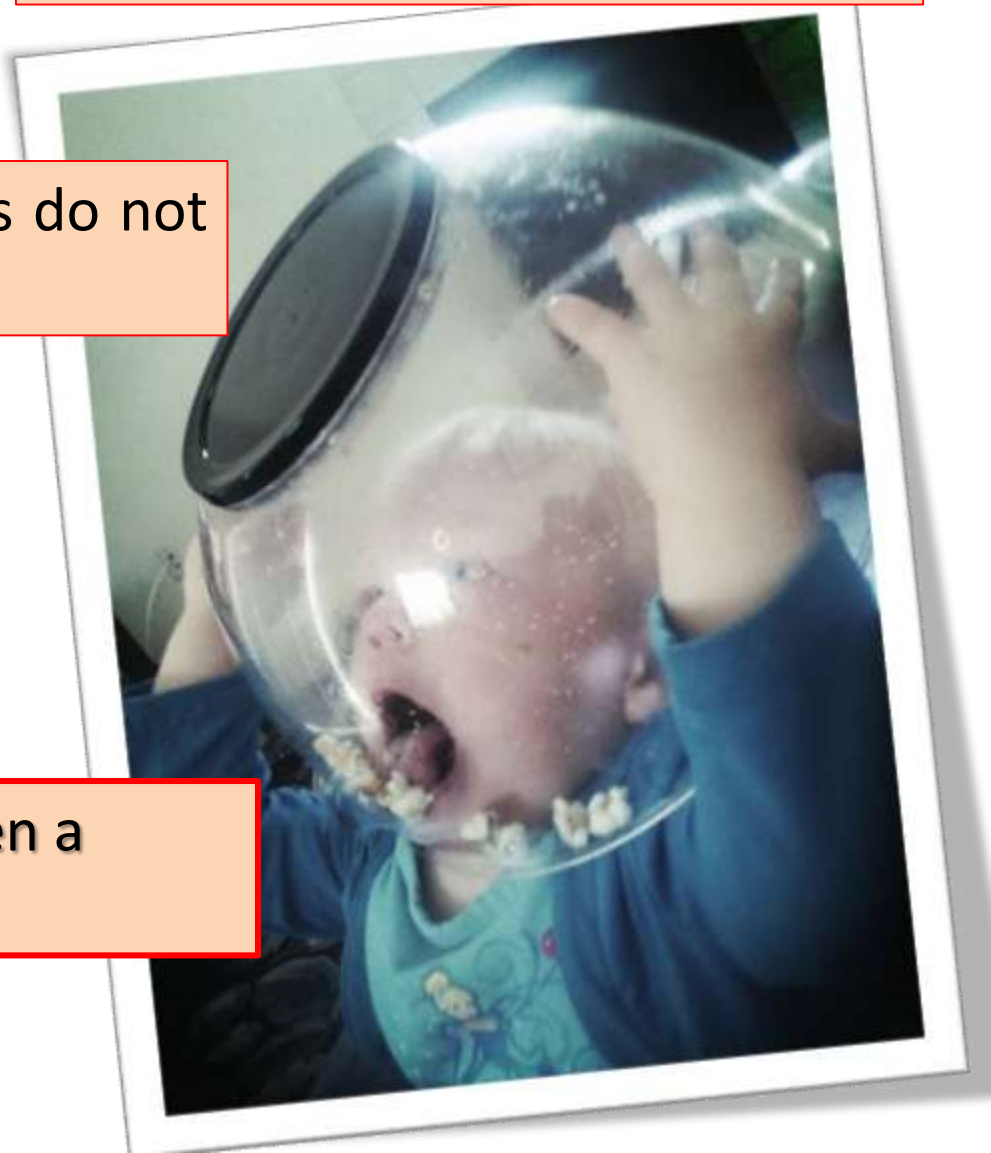
¿Cuál es el riesgo de rigidez muscular torácica por uso de opioides?

¿Infusión vs bolus?
¿Conlleva riesgos cada una de ellas?



¿es verdad que extrapolamos nuestros conocimientos del uso de fármacos de adultos a niños?

Why adult PK parameters do not work in children



Hiperalgesia y emergencia suceden a menudo en nuestros pacientes

Uso de opioides en cirugía ambulatoria

- Infusion de remifentanilo y relacion de Ventilacion espontanea con edad del niño
- Children <3 years tolerated a higher infu
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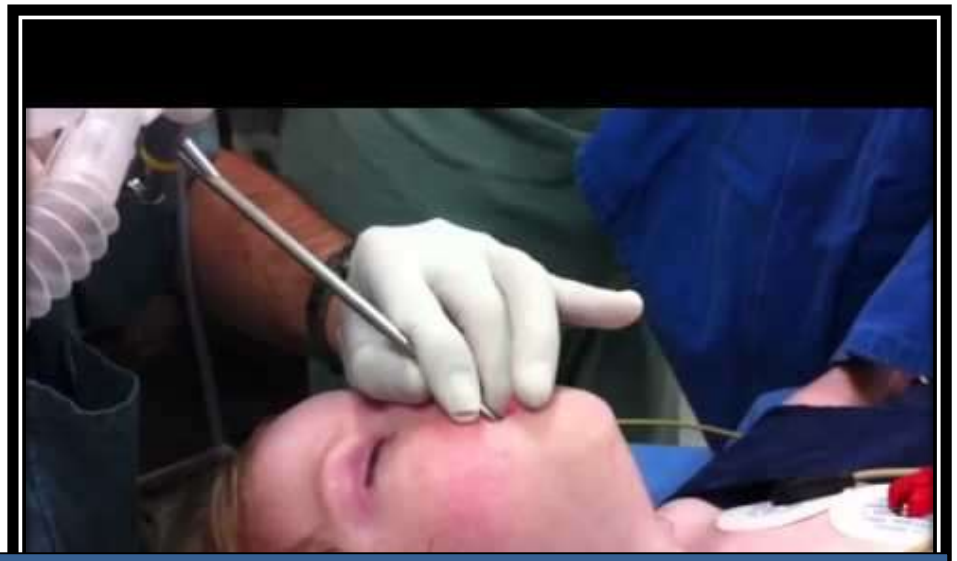

They used respiratory rate as the pharmacodynamics endpoint and found that younger children, especially those < 3 years old, were more tolerant to the respiratory rate depressant effects of remifentanil (fibro-broncoscopia)

REMIFENTANILO Y FENTANILO

Typical pharmacokinetic and physicochemical parameters of some opioid analgesics.

	Relative lipid solubility	Terminal half-life (h)	Clearance (mL min^{-1} kg^{-1})	Volume of distribution (L kg^{-1})	pK_a	% non-ionized (pH 7.4)
Morphine	1	3	15	3.5	7.9	24
Pethidine	28	4	12	4.0	8.7	5
Fentanyl	580	3.5	13	4.0	8.4	9
Alfentanil	90	1.6	6	0.8	6.5	89
Remifentanil	50	0.06	50	0.4	7.1	65
Tramadol	1	5.0	6	3.1	4.5	99

Principles and practice of pharmacology for anaesthetist. Calvin N. 5ta edition.

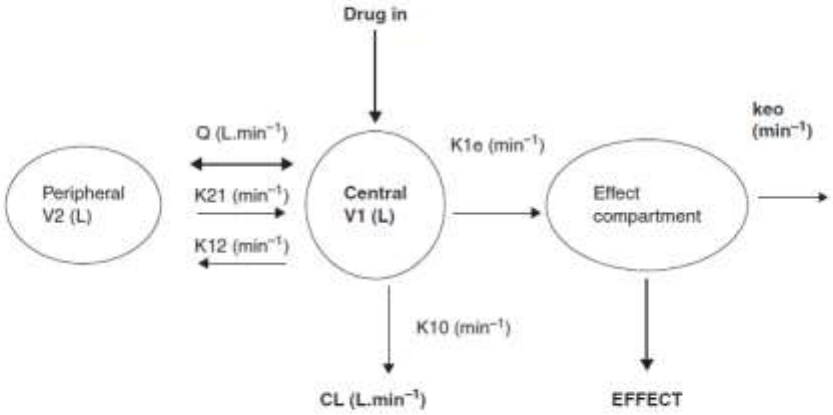

Fig. 1 – Schematic for a drug described
Source: author.

Porque extrapolar esta teoría de adultos en niños?

Table 1
Pharmacokinetic parameters of remifentanil from infants <2 months up to 18 years

	No. of patients	*Age*	*VDss* ($ml \cdot kg^{-1}$)	*CL* ($ml \cdot kg^{-1} \cdot min^{-1}$)	$t_{1/2}\alpha$ *(min)*	$t_{1/2}\beta$ (min)	*CV* ($ml \cdot kg^{-1}$)
Davis *et al.*(11)	6	Neonates	325.33	80.38	0.42	4.38	125.05
Ross *et al.*(12)	8	0–2 months	452.80	90.50	#	5.40	#
	10	2 months–2 years	307.90	92.10	#	3.40	#
	8	2–6 years	240.10	76.00	#	3.60	#
	8	7–12 years	248.90	59.70	#	5.30	#
	5	13–16 years	223.20	57.20	#	3.70	#
	3	16–18 years	242.50	46.50	#	5.70	#

Si sus variables numéricas son distintas y no solo dependen de edad.

REMIFENTANILO

- Tiempo de equilibrio plasma cerebro:1.6 min;
- Vida media de contexto sensible: 3-10 min
- Metabolism independent of kidney and liver functions (ultrashort-acting)
- Permits a profound blockade of sympathetic system response to nociceptive stimulation (potent -opioid agonist)
- Permits rapid emergence.

Dosis de remifentanilo?

- is reportedly similar in infants and children, as it is in adults; effective dose in adults 2.0 to 5.0 µg/kg,
- Pediatrics dose of 1 - 3 µg/kg provides similar intubation conditions to muscle relaxants with minimal side effects.
- the addition of benzodiazepines or a combination of propofol followed by remifentanil may minimise the occurrence of muscle rigidity.

NEONATO: ES EL PACIENTE MAS FRÁGIL O EL MAS RESISTENTE DE TODOS CONTRA TODO??

REMIFENTANILO EN NEONATOS

- Pain treatment is part of the quality of neonatal care.
- The results of some studies demonstrate that there is still a gap between scientific knowledge on neonatal pain, as well as its consequences, and the use of methods for pain assessment and management.

EFECTOS SECUNDARIOS DESPUÉS DEL USO DE REMIFENTANILO Y FENTANILO

TOLERANCIA:
puede darse a 3 hours de infusion aunque es controversial

RIGIDEZ MUSCULAR:
asociado con > 1 ug/kg pretreatment with benzodiazepines o propofol may be effective in preventing opioid induced muscle rigidity (Durmus M et al). **Propofol en < 3 años??**

EFECTOS SECUNDARIOS DESPUÉS DEL USO DE REMIFENTANILO Y FENTANILO

EFECTOS HEMODINAMICOS:

- The mechanism(s) is not clear, but it is not likely caused by histamine release
- possible mechanism for the cardiovascular effects may be via vagal-cardiac activation (hypothesis of vagal-cardiac activation with remifentanil).
- The exact mechanism of the vasodilation is unknown, (presynaptic inhibition of norepinephrine release at the postsynaptic terminal)

Consecuencia de los opioides?

Mala técnica anestésica o producto del uso de opioides

EFECTOS SECUNDARIOS DESPUÉS DEL USO DE REMIFENTANILO Y FENTANILO

HIPERALGESIA:

- Opioids are the most important drugs for the treatment of moderate to severe pain.
- Clinical studies, intraoperative remifentanil may paradoxically enhance postoperative pain and opioid analgesic requirements? activation of (NMDA) receptor system or internalization /inactivation of opioid receptors
- Yuan Y et al, hyperalgesia starts from 2 h after surgery and its peak at 24 to 48 h after surgery.

REMIFENTANILO VS FENTANILO: CUAL FARMACO ES MEJOR PARA EL NIÑO?

Opioides y dolor: existe una diferencia con las edades?

Mi elección de fármaco tendrá relación con el weaning?

DOSIS DE REMIFENTANILO PARA INTUBACION

Study	Number of patients	Ages (years)	Sedative premedicant	Induction of anaesthesia	Dose of remifentanil $\mu g.kg^{-1}$	Remifentanil-intubation time (s)	Conclusions
Batra et al. [19]	40 in two groups	5–10	Pethidine + atropine IM	Propofol 3 $mg.kg^{-1}$	2 3	100	All intubated successfully, 3 $\mu g.kg^{-1}$ better conditions ($p < 0.05$)
Blair et al. [20]	109 in four groups	3–12	none	Propofol 3 $mg.kg^{-1}$ + atropine 10 $\mu g.kg^{-1}$	1 2 3 or Mivacurium 0.2 $mg.kg^{-1}$	60	Optimum dose range 2–3 $\mu g.kg^{-1}$
Crawford et al. (21]	64 in four groups	32 full term infants and 32 children aged 2–5 years	none	Propofol 4 $mg.kg^{-1}$ and glycopyrrolate 10 $\mu g.kg^{-1}$	1.25 1.5 1.75 2	90	ED50 1.7 ± 0.1 $\mu g.kg^{-1}$ ED98 2.88 ± 0.5 $\mu g.kg^{-1}$
Morgan et al. [22]	60 in two groups	2–12	none	Propofol 4 $mg.kg^{-1}$	1.25 or 1 $mg.kg^{-1}$ suxamethonium	30	28/30 remi group intubated on first attempt

DOLOR EN PEDIATRÍA Y RELACIÓN CON OPIOIDES

- The physiologic responses to painful stimuli PAS, FSC y riesgo de hemorragia intracraneal, predispose to hypersensitive pain perception with future experiences and long-term psychophysical sequelae.
- Buscamos use of brief tracheal intubation and extubation por lo que ultra-short-acting agents to facilitate these objectives is of great interest.

CONCLUSIONES

- Remifentanil has gained the confidence of anesthesiologists and has given a real opportunity to change the way anesthesia is given.
- Remifentanil can be considered the ideal opioid despite many obstacles to pediatric use.
- Interest concerning sedation with remifentanil in paediatric and neonatal intensive care unit is increasing, particularly because preterm neonates normally have immature clearance pathways for most drugs, delaying recovery time

CONCLUSIONES

- Nowadays, the dominant role of remifentanil in children and even in neonates is certified by increasing of reports about its unique PK characteristics. However, further studies are needed to evaluate the possible advantages of TCI models in children and infants.
- A number of factors other than size and age contribute to this variability; temperature, pathology, type of surgery, circadian rhythms, pharmacogenomics will all have impact. One factor that is becoming increasingly important is obesity.
- Chest wall rigidity: Despite the reputation of remifentanil to cause chest wall rigidity in adults, this effect is now being questioned. The suggestion is that it is more likely to be due to vocal cord closure.

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