Celocurine versus Rocuronium pour la séquence rapide en obstétrique

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Conflits d’Intérêts

- aucun

Succinlylcholine
Un curare et quelques inconvénients

- Hyperthermie maligne
- Hyperkaliémie
- Spasme masseter
- Curarisation prolongée
- Douleurs musculaires…

Rocuronium et intubation à séquence rapide

- For rapid-sequence induction of anaesthesia, an increased dose of rocuronium (1.0 mg/kg) is recommended to achieve intubating conditions at 60 s comparable with those found with succinylcholine. *Perry J, Lee J, Wells G. Rocuronium versus succinylcholine for rapid sequence induction intubation. Perry et al, Cochrane Database Syst Rev 2003; CD002788*

Rocuronium versus succinylcholine for rapid sequence induction intubation (Review)

- 58 studies identified; 37 combined for analysis.
- Overall, succinylcholine was superior to rocuronium, RR 0.86 (95% confidence interval (95% CI) 0.80 to 0.92) (n = 2690).
- In the group that used propofol for induction, the intubation conditions were superior with succinylcholine (RR 0.88, 95%CI 0.80 to 0.97) (n = 1183)
- No statistical difference in intubation conditions when succinylcholine was compared to 1.2mg/kg rocuronium; however, succinylcholine was clinically superior as it has a shorter duration of action.

Perry et al, *The Cochrane Library* 2008, Issue 1

Rocuronium versus succinylcholine for rapid sequence induction intubation (Review)

Comparison 2. Rocuronium specific dose versus succinylcholine

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Excellent versus other intubation conditions	37	2791	Risk Ratio (M-H, Random, 95% CI)	0.87 [0.81, 0.93]
1.1 Rocuronium 0.6-0.7mg/kg	30	1782	Risk Ratio (M-H, Random, 95% CI)	0.81 [0.73, 0.90]
1.2 Rocuronium 0.9-1.0mg/kg	11	923	Risk Ratio (M-H, Random, 95% CI)	0.96 [0.89, 1.02]
1.3 Rocuronium 1.2mg/kg	3	86	Risk Ratio (M-H, Random, 95% CI)	0.93 [0.75, 1.15]
2 Acceptable versus suboptimal intubation conditions	36	2672	Risk Ratio (M-H, Random, 95% CI)	0.96 [0.93, 0.99]
2.1 Rocuronium 0.6-0.7mg/kg	30	1782	Risk Ratio (M-H, Random, 95% CI)	0.95 [0.90, 1.00]
2.2 Rocuronium 0.9-1.0mg/kg	10	804	Risk Ratio (M-H, Random, 95% CI)	0.98 [0.95, 1.01]
2.3 Rocuronium 1.2mg/kg	3	86	Risk Ratio (M-H, Random, 95% CI)	1.0 [0.80, 1.25]

Rocuronium is less effective than succinylcholine for creating excellent intubation conditions. Rocuronium should therefore only be used as an alternative to succinylcholine when it is known that succinylcholine should not be used.

Perry et al, *The Cochrane Library* 2008, Issue 1

Rocuronium et Obstétrique

- In caesaren section patients, the duration of action of amino-steroidal neuromuscular blocking agents is prolonged. *Pühringer et al, Anesth Analg 1997; 84: 352–4*
- In this specific group of patients, rocuronium 0.6 mg/kg provides, in the presence of a sufficient dose of thiopental, clinically acceptable intubating conditions in 90% of patients. *Abouleish et al, Br J Anaesth 1994; 73: 336–41*

Rocuronium et Obstétrique

- The prolonged action of rocuronium in pregnant and post-partum patients (25%) would support the use of the usual intubating dose of rocuronium (0.6 mg/kg) fo Caesarean section patients. *Pühringer et al, Anesth Analg 1997; 84: 352–4*
- Rocuronium 0.6 mg/kg crosses the placenta with an umbilical vein :maternal vein ratio of 0.16. *Abouleish E, Abboud T, Lechevalier T, Zhu J, Chalian A, Alford K. Rocuronium (Org 9426) for caesarean section. Br J Anaesth 1994; 73: 336–41.*

Sugammadex et Obstétrique

- Sugammadex has been shown to provide a rapid and sustained reversal (TOF ,0.9) of rocuronium at various doses (0.6, 1.0, and 1.2 mg/kg). *Sparr et al, Anesthesiology 2007; 106: 935–43. Pühringer et al, Anesthesiology 2008; 109: 188–97*
- The amount of sugammadex that undergoes placental transfer is thought to be small; however, robust data in human fetal transfer are lacking. *McGuigan et al, BJA doi:10.1093/aer019*

Sugammadex reversal of rocuronium-induced neuromuscular block in Caesarean section patients: a series of seven cases

Table 1 Physical characteristics, dose regimen of anaesthetic agents, and recovery data

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
Age (yr)	29	28	33	26	36	30	39
Weight (kg)	75	103	73	56	92	75	70
Height (cm)	160	170	174	153	173	168	170
ASA class	III	II	II	II	II	II	I
Gestation (weeks)	38	39	38	40	39	38	26
Thiopental (mg kg^{-1})	5.4	5.0	5.4	7.0	5.4	5.5	5.0
Rocuronium (mg kg^{-1})	0.66	0.50	0.66	0.66	0.66	0.66	0.57
Duration of operation (min)	28	53	25	20	38	28	35
TOF value at end of operation (%)	0	3	0	0	0, T_2	0	0
Sugammadex (mg kg^{-1})	4	2	3	4	2	4	4
Time to TOF >0.9 (s)	60	50	90	60	60	50	100

In all cases, live children were born, and the paediatricians observed no signs of neuromuscular weakness in any of them.

After operation, the patients were monitored for 3 h for recurarization, No signs of muscle weakness or recurarization were observed in any of them.

Pühringer et al, British Journal of Anaesthesia 105 (5): 657–60 (2010)

Dose de Sugammadex?

- Profound (deep) block 4 mg/kg.
- Moderate (shallow) block 2 mg/kg.
- Block somewhere between 3 mg/kg ?
- Normal practice involves careful monitoring of neuromuscular function and also bearing in mind the current expense of sugammadex.

Williamson et al, *Acta Anaesthesiol Scand 2012;* ***56: 394–398***
Kessel et al, *Acta Anaesthesiol Scand 2012;* ***56: 394–398***

Rocuronium and sugammadex for rapid sequence induction of obstetric general anaesthesia

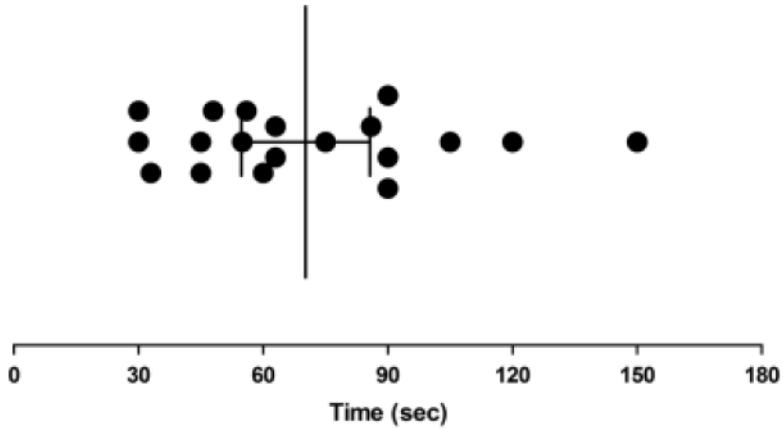


Fig. 1. Time from the administration of rocuronium to ablation of train-of-four ratio response (s). Mean 70 s; 95% CI 55–86 s.

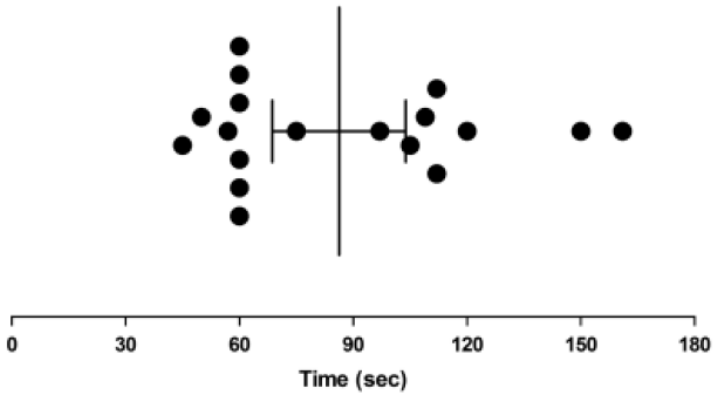


Fig. 2. Time from the administration of sugammadex to recovery of train-of-four ratio ratio ≥ 90% (s). Mean 86 s; 95% CI 69–104 s.

Williamson et al, Acta Anaesthesiol Scand 2011; 55: 694–699

Rocuronium and sugammadex for rapid sequence induction of obstetric general anaesthesia

- 16/ 18 patients intubated at 60 s at the first attempt; 2in the remaining at the second attempt.
- Intubating conditions were excellent in 12/18 and good in 6/18; none were rated as poor or unacceptable
- none of these babies needed a period of ventilation

Williamson et al, Acta Anaesthesiol Scand 2011; 55: 694–699

Rocuronium and sugammadex for rapid sequence induction of obstetric general anaesthesia

- With rocuronium, multiple intubation attempts can occur without any deterioration of the intubating conditions.
- Rocuronium 1.2 mg/kg can be immediately reversed with sugammadex if required at dose of 16 mg/kg.
- This results in a return of neuromuscular function in 2.9 min , faster than the spontaneous offset of suxamethonium (10.9 min)

Williamson et al, Acta Anaesthesiol Scand 2011; 55: 694–699

Rocuronium – Sugammadex et Allergie

Epidémiologie

- Anaphylaxie femme par million *:* *Mertes et al. JACI 2011*
  - tous antigènes : 155
  - curares 250
  - Latex 91
- UK: 0,03/1000 *7 report of maternal death inUK*
- USA : 2,7/100,000 *Mulla et al, AAAI 2010*
- Latex 1/310 *Draisci et al, Int J Obst 2007*
- Antibiotiques 57% des cas *Mulla et al, AAAI 2010*

ansm
Agence nationale de sécurité du médicament et des produits de santé

RÉPUBLIQUE FRANÇAISE

Lettre aux professionnels de santé

Juillet 2012

SUXAMETHONIUM
Respecter strictement la chaîne du froid.

Information destinée aux anesthésistes-réanimateurs, aux urgentistes, aux infirmier(e)s anesthésistes et aux pharmaciens des pharmacies à usage intérieur.

- Ne pas utiliser les lots de Célocurine®, Suxaméthonium Aguettant® et Biocodex® qui ont été conservés à température ambiante ou ont été congelés.
- Seuls les lots conservés entre 2°C et 8°C (au réfrigérateur) doivent être utilisés.
- Ne pas remettre en chaîne du froid des produits qui en sont sortis.
- Vérifier et respecter strictement la date de péremption.

Suxamethonium - Respecter strictement la chaîne du froid

Le 20 Juillet 2012,

Chers (ères) Collègues,

A la suite d'un nombre accru de signalements d'accidents anaphylactiques avec les curares, et notamment avec la succinylcholine,

l'Agence Nationale de Sécurité Sanitaire et des Produits de Santé (ANSM) vient de publier sur son site une lettre rappelant les bonnes pratiques de maintien de la chaîne du froid pour ce produit (1). Le site de la SFAR se fait l'écho de cette information importante en informant les anesthésistes-réanimateurs dès la publication de cette lettre d'information.

La SFAR reste très vigilante sur l'évaluation, la compréhension et le suivi de cet accroissement des signalements. La SFAR rappelle le travail immense que la discipline a réalisé depuis plusieurs années concernant la compréhension, la notification et la prise en charge de ces accidents potentiellement graves. Outre les travaux et les publications de certains collègues concernant la risque anaphylactique (2) mais aussi la curarisation en général (3,4) et qui font référence à l'échelon international, outre la création d'un groupement de centres d'allergo-anesthésie (GERAP) (5), la SFAR a publié récemment une Recommandation Formalisée d'Experts (6) décrivant les règles de bonne pratique, tant en matière de diagnostic que pour la prise en charge clinique.

La SFAR, bien que n'ayant pas participé directement à la rédaction de ce communiqué, se sent investie d'un rôle de partenaire pour analyser et comprendre. Elle peut être le lien entre l'Agence (ANSM) et les praticiens pour diffuser, participer à l'observatoire, à l'analyse des données, ainsi qu'à la réflexion sur l'utilisation des curares.

Pr D Benhamou Pr P M Mertes

Sugammadex in the management of rocuronium-induced anaphylaxis

- 33 ans, laparoscopie, **rocuronium 0,39 mg/kg**, adrénaline 4 mg, m+19 **sugammadex 6,5 mg/kg**, puis adrénaline 0,65 et metaraminol 1 mg *McDonnell et al, BJA 106 (2): 199–201 (2011)*

- 66 ans, cimentoplastie, **rocuronium 0,6 mg/kg**, grade III, adrénaline 0,2 mg, PA remonte à 75 mmhg, **sugammadex 4 mg/kg** reversion du bloc, PA 100 mmHg. *Motamed et al, JACP 2012*

- 47 ans, cholecystectomie, 78 kg, **rocuronium 50mg**, grade III, adrénaline 0,17 mcg/kg/min, transfert en ICU. Après 1 h, **sugammadex 400mg,** réduction des doses d'adrénaline de moitié. Funnel et al, BJA, doi:10.1093/bja/aer211

- 51 ans, hernie ombilicale, 112 kg, **rocuronium 0,45 mg/kg**, grade III, adrénaline 0,5 mg en 15 min, 18 min : adrénaline 0,2 mg et **sugammadex 2000 mg (18 mg/kg)**, amélioration, SE adrénaline 0,5 mg/h sevrée en 60 min. Raft et al, AFAR 31 (2012) 158–161

- 62 ans, mastectomie, 45 kg, **Rocuronium 20 mg**, grade II, pas adrénaline, , 30 min : **sugammadex 200mg**, regression erytheme, Kawano et al., Journal of Clinical Anesthesia (2012) 24, 62–64

Sugammadex and rocuronium-induced anaphylaxis

- Anaphylaxis grade III
- Boluses of epinephrine and steroids / 18 min after induction the patient suddenly and dramatically improved.
- Arterial pressure and the heart rate normalized airway pressures decreased rapidly.
- patient was extubated after a further 15 min of normal ventilation.
- Skin tests + rocuronium, cross-reactivity with steroid and benzyliso

Wordsworth et al doi:10.1093/bja/aer138

Rocuronium / Sugammadex

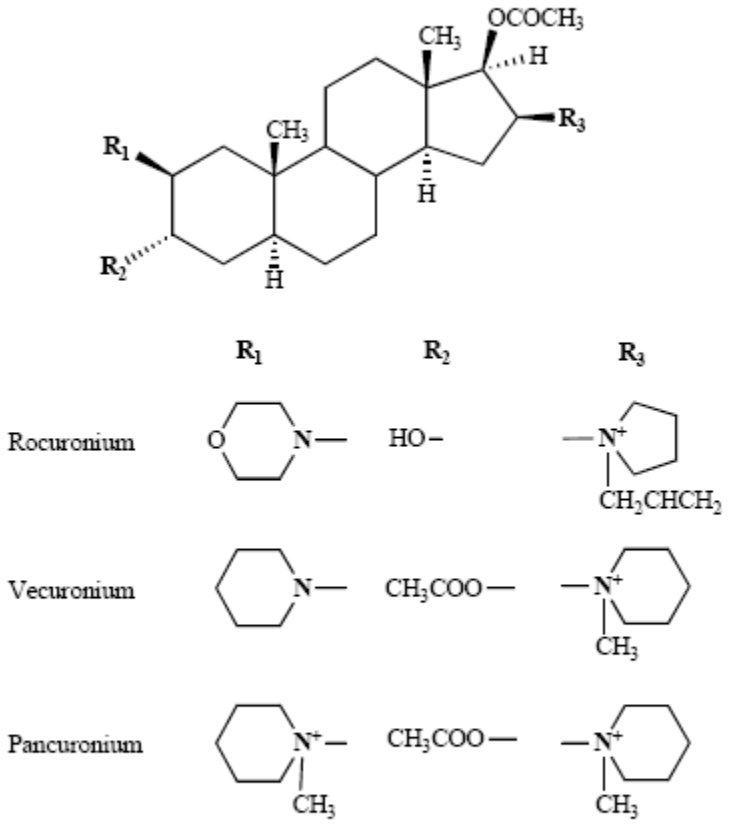
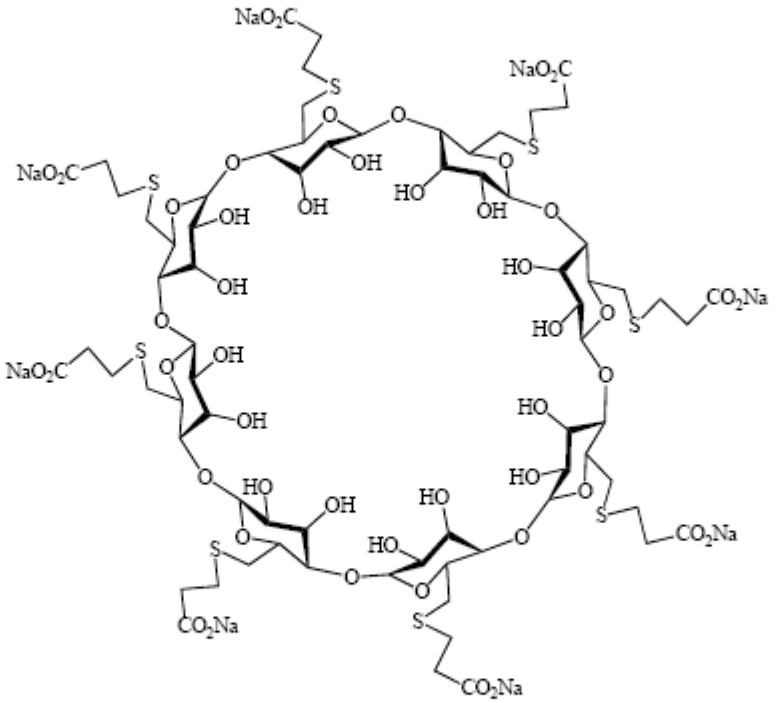


Fig. (2). Structures of the non-depolarizing and competitive aminosteroid neuromuscular blocking drugs rocuronium, vecuronium and pancuronium. Note the morpholino and pyrrolidinium groups at positions 2 and 16 respectively of rocuronium.



Two-dimensional structure of sugammadex, 6-perdeoxy-6-per(2-carboxyethyl)thio-γ-cyclodextrin sodium salt showing the thio(2-carboxyethyl) sodium group linked at position 6 of each of the eight glucopyranose units.

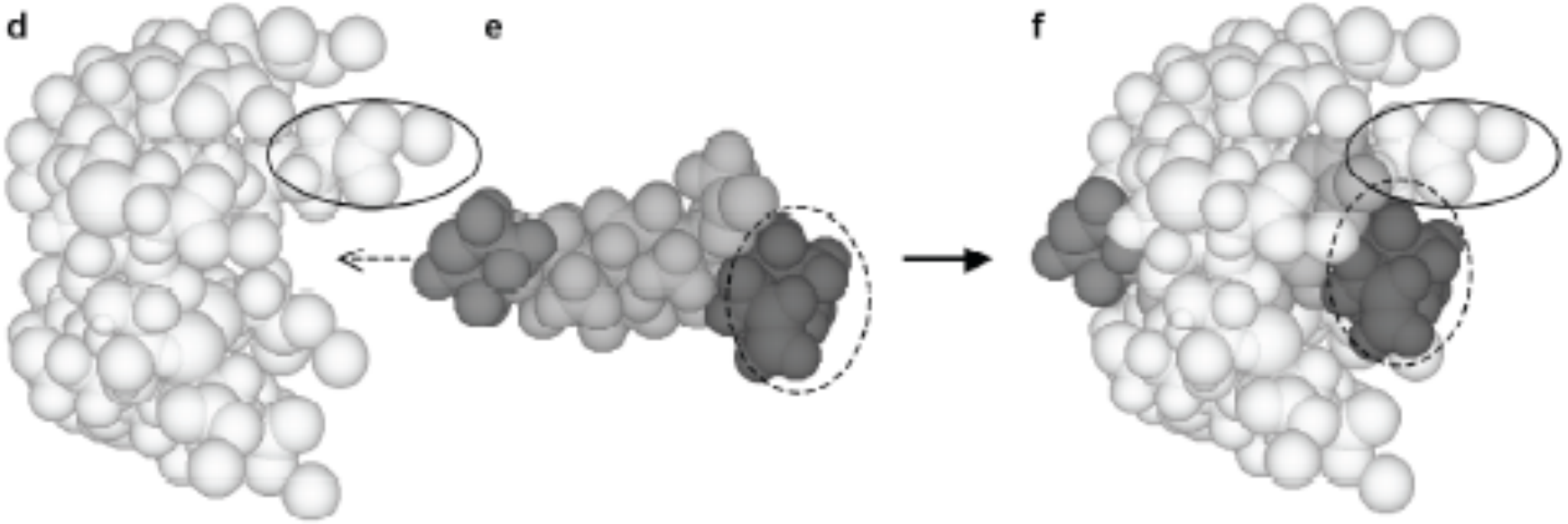


Fig. (6). Space filling ball-and-stick (**a**,**b**,**c**) and CPK (**d**,**e**,**f**) three-dimensional molecular models illustrating the encapsulation of the rocuronium molecule (**b** and **e**) by sugammadex (**a** and **d**) to form the rocuronium-sugammadex inclusion complex (**c** and **f**). The pyrrolidinium quaternary ammonium group (circled) and the tertiary ammonium group, part of the morpholine ring, are shown in dark shading at the right and left hand ends respectively of the rocuronium molecule. In the inclusion complex, the quaternary ammonium group attached to ring D of rocuronium (see Fig. **5**) is visible at the primary rim end (right hand side) surrounded by thio(2-carboxyethyl) sodium groups (**c**,**f**). One of the eight thio(2-carboxyethyl) sodium groups of sugammadex is ringed. The morpholine group containing the tertiary ring nitrogen and attached at position 2 of the rocuronium molecule protrudes from the complex at the secondary rim end (left hand side). The hydroxyl group at position 3 is behind the morpholine ring in the selected view. All four rings A-D of the rocuronium steroid nucleus and the ~11Å C3 -- C16 length are within the sugammadex extended cavity.

Constante d'association:

- rocuronium-sugammadex: Ka $1,8*10^{7}M^{-1}$
- rocuronium-IgE: Ka 10^{10} $10^{11}M^{-1}$?

Rocuronium-induced anaphylaxis is probably not mitigated by sugammadex: evidence from an in vitro experiment

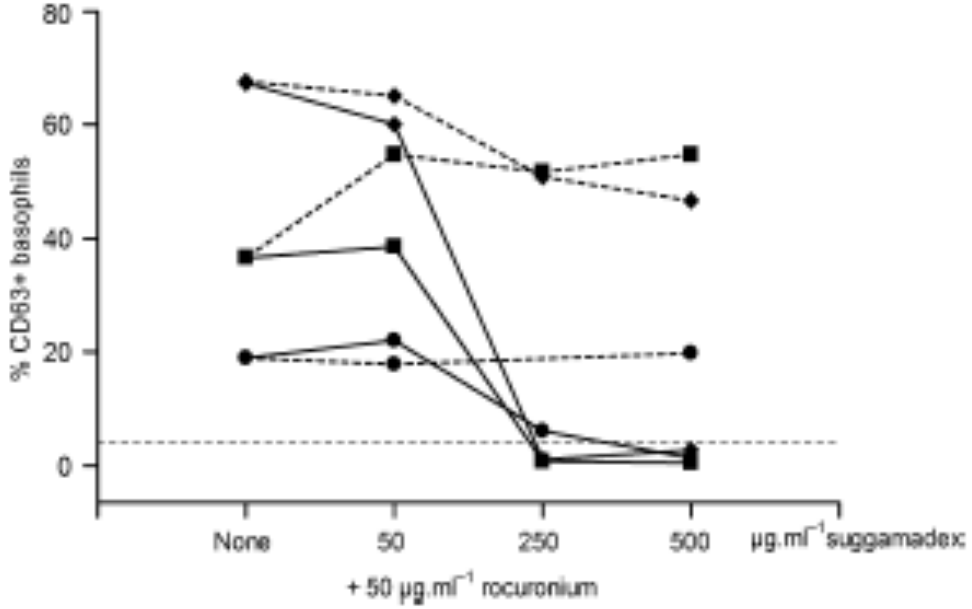


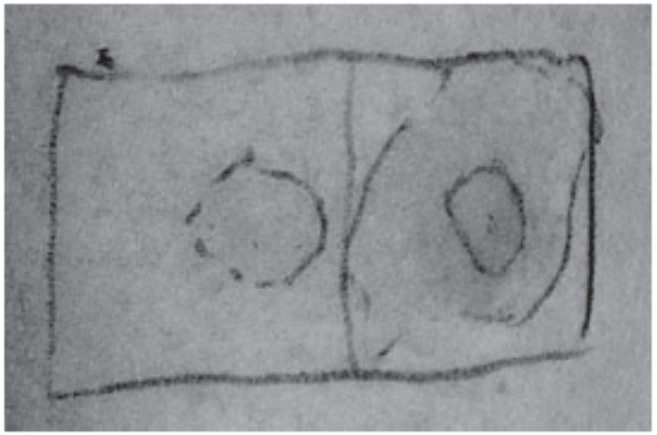
Figure 2 Dose-dependent inhibition of rocuronium-induced basophil activation in three rocuronium-allergic patients. Solid line: pre-incubated mixture of rocuronium and sugammadex. Dotted line: addition of sugammadex after 3 min of activation with rocuronium.

Leysen et al, Anaesthesia, 2011, 66, pages 519–531

Activation des Cellules Effectrices

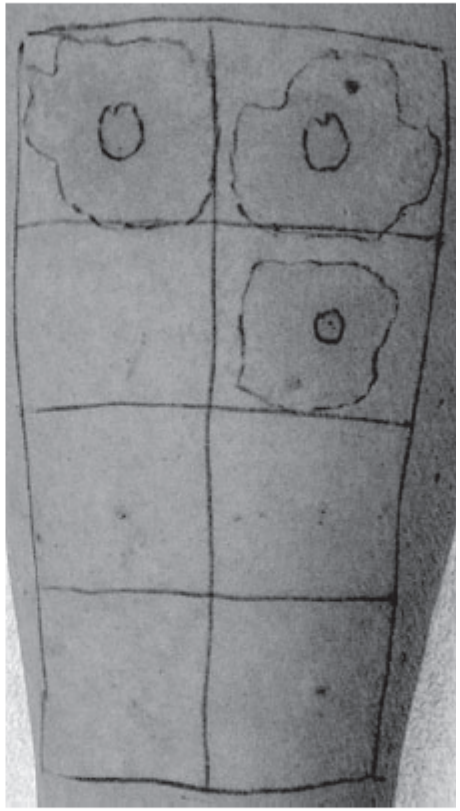
- Voie classique : IgE et récepteur de haute affinité /mastocytes
- Voie alterne : IgG et récepteur de faible affinité FcRIII/macrophages
- PAF et plaquettes
- NO et endothélium
- PI3-K / Akt signalling, cytokines IL-4 et IL-13, sphingosine-1-phosphate et sphingosine kinases

The role of sugammadex in the development and modification of an allergic response to rocuronium: evidence from a cutaneous model



Sugammadex 0.13 mg.ml^{-1} followed by **rocuronium**	**Rocuronium** followed by **sugammadex** 1.3 mg.ml^{-1}

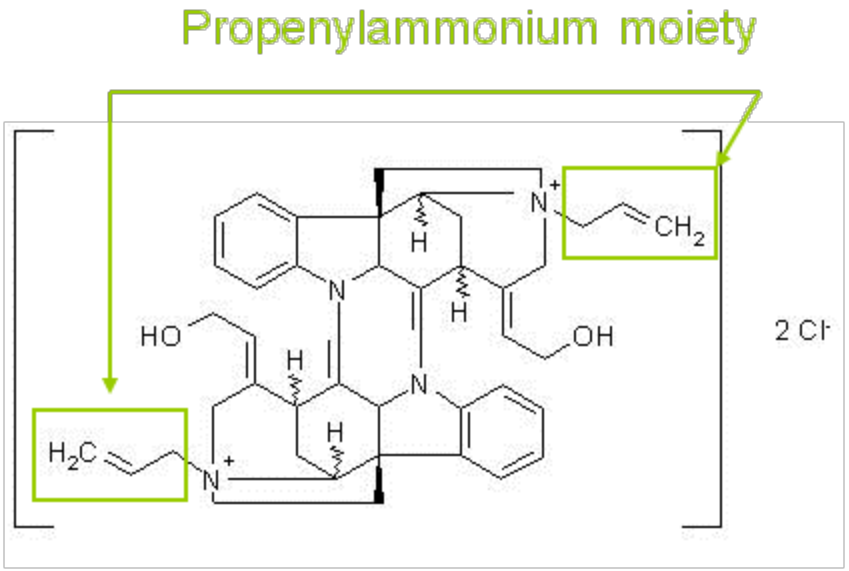
Rocuronium followed by sugammadex 0.13 mg.ml^{-1}	Rocuronium 0.01 mg.ml^{-1}
Saline 0.9%	Histamine
Low-dose sugammadex (0.13 mg.ml^{-1})	Pre-mixed rocuronium with sugammadex (1:4)
High-dose sugammadex (1.3 mg.ml^{-1})	Pre-mixed rocuronium with sugammadex (1:20)



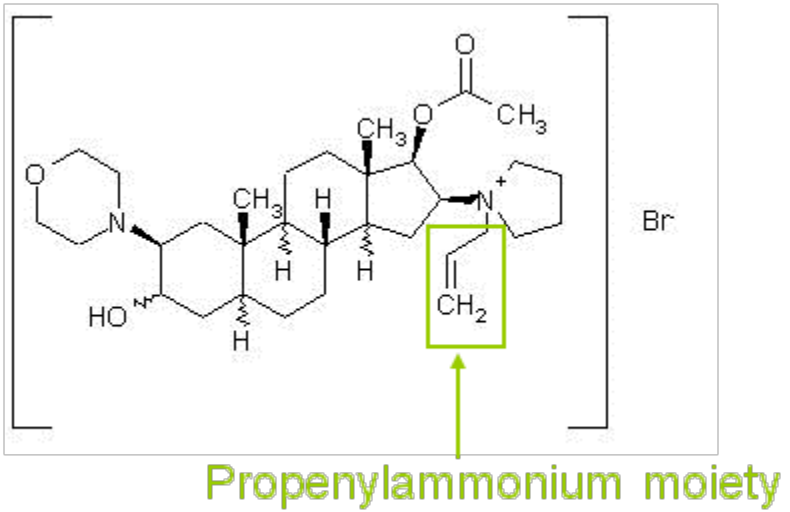
Clarck et al, Anaesthesia 2012, 67, 266–273

Alcuronium - Rocuronium

- The propenylammonium moieties of **alcuronium** are chemically unrelated to the substituted ammonium or amine groups on the other NMBAs but it also occurs on rocuronium.



- As for alcuronium in the late 1970s, **rocuronium** has been claimed to be at high risk for anaphylaxis. If this is true, propenylammonium moieties present in both NMBAs may account for the apparent increased allergenicity.



Quelle dose de Sugammadex en cas d'allergie en obstétrique?

- Constante d'association:
  - rocuronium-sugammadex: Ka $1,8*10^{7}M^{-1}$
  - rocuronium-IgE: Ka 10^{10} $10^{11}M^{-1}$?

- Rocuronium 0.4 à 0.6 mg/kg → Sugammadex 4 à 16 mg/kg

- Rocuronium 1.2 mg/kg → Sugammadex ?

Allergie aux cyclodextrines

- **Allergy to low dose sugammadex.** Homme 17 ans, grade II, prick +; *Menéndez-Ozcoidi Anaesthesia. 2011 Mar;66(3):217-9.*

- **Three cases of suspected sugammadex-induced hypersensitivity reactions.** Grade I prick +, Grade III prick +, Grade II no test. *Godai et al, Br J Anaesth. 2012 Aug;109(2):216-8*

Conclusion

- Rocuronium 1.2 mg/kg proposé en obstétrique
- Rocuronium et succinylcholine = potentiel allergénique voisin
- Sugammadex et allergie au rocuronium :
  - Efficacité à démontrer
  - Retrait de l'allergène tjs intéressant mais rompre la liaison
  - Quelle dose? Constante d'affinité rocuronium - IgE ≠ rocuronium - récepteur
- Coût, allergie, nouveau né?

Merci

de votre

Attention