

Discuss the factors affecting speed of onset of blockade of a major peripheral nerve, with local anaesthetic.

NB: info in italics relevant to duration of action – only written here as a teaching point – not required in answer

Drug Concentration

- \uparrow concentration speeds onset d/t \uparrow diffusion gradient
- total dose and total volume also relevant – *also to duration of action*

Proximity to Nerve

- deposition close to nerve / fully surrounding nerve speeds onset
- benefit of US

Ionisation

- LA needs to be in un-ionised form to cross nerve cell membrane
- when injected into pH 7.4
 - lignocaine (pKa 7.9) is approx. 25% un-ionised
 - bupiv & ropiv (pKa 8.1) are approx. 17% un-ionised
- \therefore lignocaine faster
- if tissue acidotic, % un-ionised will be lower for all LA – slow onset or ineffective

Lipid Solubility

- LA's need to be lipid soluble to cross nerve cell membrane BUT with higher lipid solubility this actually slows onset
- lipid sol \propto potency – if \uparrow potency need less drug so less diffusion gradient
- also, highly lipid soluble LA gets taken up into surrounding peri-neural tissue, and some gets “trapped” inside the lipid bilayer of nerve membrane
- relative lipid solubility (octanol : water)
 - lignocaine 366
 - ropiv 775
 - bupiv 3420 -- hence slower
- *lipid solubility is very relevant for duration of action*

Type of Nerve Fibre

- some fibre types blocked earlier than others (\uparrow susceptibility if smaller, or myelinated fibres)
- onset (first to last) ...
 - see Table 36-3 Miller 8th edition

Proximal vs. Distal

- fibres to hand/foot run in middle of nerve; fibres to shoulder/hip run on outer part
- \therefore block of proximal limb will occur before distal (*and last longer*)

Frequency Dependent Block

- increased LA binding with Na channels in open or inactivated state (c/w resting)

Additives

- sodium bicarbonate – alkalinises LA solution to \uparrow un-ionised fraction and speed onset (caution: can make LA insoluble and precipitate)
- *clonidine causes hyperpolarisation – prolongs duration of action*
- *adrenaline only relevant to duration of action*

Pregnancy

- \uparrow sensitivity of nerves to LA d/t progesterone – faster onset

Elderly

- faster onset – less peri-neural tissue / \uparrow sensitivity of nerve to LA