limited, case reports/series provide low-level evidence that cannot support specific recommendations.

The cardiovascular profile of pancuronium suggests that it can produce cardiovascular stimulation possibly by a direct action and an increased release/decreased reuptake of catecholamines at the adrenergic nerve terminals. β-Adrenoreceptors and M2 muscarinic receptors possibly play a significant role in pancuronium-induced cardiac responses. Pancuronium has been found to have a higher potency for interaction with cardiac muscarinic receptors compared with newer neuromuscular blockers. On the other hand, as shown in Supplementary Table S1 of our review, there is sufficient evidence supporting the lack of significant cardiac effects of newer neuromuscular blockers, such as atracurium, cisatracurium, and rocuronium. Based on the above, we consider that pancuronium is probably not the first-choice neuromuscular blocker for patients with arrhythmogenic syndromes (as ARVD), even though serious adverse effects have not been observed in the authors’ clinical practice, or confirmed in relevant clinical reports.

In conclusion, pancuronium seems to have a less favourable cardiovascular profile compared with newer neuromuscular blockers according to electrophysiological studies. Regarding neuromuscular blockers and ARVD, relevant literature is inadequate to support specific recommendations. On the other hand, as it is prudent for the physicians always to be on the safe side, we consider that neuromuscular blockers with minimal cardiovascular effects should be preferred over pancuronium in patients who are at risk of arrhythmias, as are patients with ARVD.

Declaration of interest
None declared.

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Seizures associated with local anaesthetic intoxication

Editor—We are interested in the study by Griffiths and colleagues which has relevance to a recent case we encountered. A 59-yr-old patient with chronic liver disease was admitted for an acute episode of encephalopathy after an incarcerated inguinal hernia. The patient had Child’s grade C cirrhosis with coagulopathy and chronic ascites treated with regular paracentesis. We elected to undertake surgery for the inguinal hernia repair using a locoregional technique (LA). We performed an ultrasound-guided transversus abdominis plane (TAP) block (30 ml ropivacaine 7.5% injection (3 ml kg⁻¹)). Fifteen minutes later, the patient had seizures. We immediately injected 200 ml (3 ml kg⁻¹ 20% Intralipid solution). It produced a rapid neurological improvement. The plasma ropivacaine concentration at the time of the seizures was 2.8 μg ml⁻¹. Neurological symptoms have been shown to occur at a mean plasma venous concentration of 2.2 μg ml⁻¹. In our case report, LA intoxication was confirmed. Surgery was possible 30 min after the seizures. The patient was transferred to the intensive care unit. Convolusions complicating TAPB had not previously been described. We used a dose of ropivacaine within the normal range (3 ml kg⁻¹), and injected the LA with repeated negative aspiration and ultrasound control. The 15 min delay between injection and onset of seizure was too long for it to be due to direct injection. One of the hypotheses was relative overdose in our patient in relationship with cirrhosis.

Pharmacokinetics of most local anaesthetic drugs is altered by poor liver function and associated alterations in circulation and body fluids. In end-stage liver dysfunction, the clearance of ropivacaine was found to be about 60% lower than that in healthy volunteers, but interestingly, plasma concentrations were similar. The latter finding may depend on increased volumes of drug distribution at the steady state (Vdss) of ropivacaine. Even in end-stage liver dysfunction, α-1 acid glycoprotein is synthesized and thus provides some protection against LA toxicity. In patients with hepatic dysfunction, single-dose blocks can usually be performed safely with normal doses of the LAs. As large doses of LAs are injected in TAPB, systemic toxicity of the LA, as a result of absorption into the circulation, should always be considered. A TAP can potentially cause systemic toxicity of LAs. The vascularity (density of capillaries) and LA binding to the tissues influence the initial rate of absorption into the circulating blood. Cirrhotic patients have a hypervascularization of the abdominal wall after portal hypertension. They can have poor synthesis of binding proteins. Griffiths and colleagues showed that a dose of 3 mg kg⁻¹ may be
excessive in some patients. However, they believed that clinically important toxicity with this technique is infrequent.\textsuperscript{1} Toxicity can occur. In fact, our case report suggests that we should reduce LA dose in the case of specific medical conditions such as Child’s C cirrhosis.

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**Reply from the authors**

Editor—We thank Dr Landy and colleagues for their interest in our paper.\textsuperscript{1} The case they describe appears to support our hypothesis that the transversus abdominis plane (TAP) block has the potential to result in clinical neurotoxicity as a result of local anaesthetic absorption. We would like to comment on a number of interesting features of this case.

First, it is noteworthy that the onset of symptoms is at 15 min post-injection. This corresponds approximately to the peak plasma levels detected in our study. As Dr Landy and colleagues suggest, this is more consistent with absorption of local anaesthetic from the TAP plane rather than inadvertent intravascular injection.

Secondly, it seems likely that the patient’s significant liver impairment will have contributed to the manifestation of clinical toxicity. This supports the proposal that total doses of local anaesthetic should be reduced in ‘at risk’ patient groups. It would be useful to know the unbound level, given that it is the free ropivacaine level that is responsible for clinical manifestations of toxicity and also, because their patient is likely to have had decreased levels of $\alpha$-1 acid glycoprotein, decreased protein binding and therefore, an increased concentration of free ropivacaine for a given total concentration of drug.

We also note that a relatively high concentration of ropivacaine was used (0.75%), presumably in order to obtain surgical anaesthesia rather than postoperative analgesia. While it is clear that for a given regional technique, a higher dose of local anaesthetic results in higher plasma concentrations,\textsuperscript{2} it is unknown to what extent the concentration of injectate directly contributes to the rate or extent of plasma uptake. However, 0.5% ropivacaine is effective for ilioinguinal block and infiltration for inguinal hernia repair.\textsuperscript{3} It has also been shown that there is no additional benefit to using 0.75% ropivacaine compared with 0.5% ropivacaine for interscalene block.\textsuperscript{4}

The anatomical location of the injection in this case is not described, but it seems likely that the total volume of 30 ml was used on one side only (for a unilateral procedure), and presumably only in the posterior (anterior axillary line) rather than spread over a larger area of the TAP (e.g. the subcostal approach).\textsuperscript{5} This larger volume in a smaller plane may also result in a larger ‘hydrostatic’ pressure, facilitating leak into the surrounding tissues. Practitioners using the TAP block will be aware that a proportion of injectate can occasionally be observed leaking from the TAP plane into the surrounding musculature. It is unknown the extent (if any) to which this ‘leak’ may correlate with the degree of systemic absorption and contribute to variability in absorption between blocks.

Again we thank Dr Landy and colleagues for reinforcing that in patients at increased risk of local anaesthetic toxicity either from pharmacokinetic or pharmacodynamics reasons, the total dose should be reduced.

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