IS THERE STILL A PLACE FOR LIDOCAINE IN SPINAL ANAESTHESIA?

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INTRODUCTION

Over the last decade, methods and practice of anaesthesia have changed considerably in favour of regional techniques whenever applicable. Based on data representative for France, which were commissioned by « La Société Française d’Anesthésie et de Réanimation » (SFAR), the percentage of procedures performed under regional anaesthesia has quadrupled between 1980 and 1996 [1]. According to this survey, 16 % of the anaesthetic workload comprised regional anaesthetic techniques among which spinal anaesthesia accounted for the largest part with a share of 37 %. This number represents an estimate of 442,000 spinal anaesthetic procedures performed in 1996 in 1,583 units offering anaesthesia services. Therefore, lack of side-effects attributable to drugs used for spinal anaesthesia is of paramount importance as any postanaesthetic morbidity may impinge on an otherwise rapid postoperative recovery and thus have important economic implications.

This chapter focuses on lidocaine’s potential to cause neurological side-effects or even injury, additional data showing the impact of anaesthetic equipment (i.e., needle size and incidence of post-dural puncture headache) on postoperative morbidity will not be included.

1. LIDOCAINE’S SAFETY RECORD

The safety of neuraxial drug application, be it epidural or spinal, has been the subject of controversy ever since the introduction of spinal anaesthesia into clinical practice by August Bier in 1898. Uncertainties in classifying the aetiology of complications occurring in association with spinal anaesthetic procedures emerged during debates surrounding the Wooley and Roe case [2], and launched a large series of incriminating statements, faulty hypotheses and precipitate conclusions.

Until recently, lidocaine has not been the target of such stunning publicity as was the Wooley and Roe case. For almost 50 years, lidocaine has been enjoying an incredible
popularity as a short-acting local anaesthetic and was considered to represent a standard drug for short surgical procedures performed under spinal anaesthesia. Its reputation was based on a remarkable safety record devoid of reports suggesting a potential for neurotoxicity and the results from a large-scale prospective review [3]. Since then, according to reasonable estimates, lidocaine has been used effectively and safely for spinal anaesthesia in some fifty million patients [4]. Therefore, it is not surprising that publications addressing the issue of local anaesthetic neurotoxicity in general and of lidocaine in particular, have encountered a lot of criticism and overt rejection.

2. LABORATORY EVIDENCE FOR LIDOCAINE’S NEUROTOXIC POTENTIAL

Laboratory set-ups evaluating neurotoxicity of local anaesthetics are based on both in vitro and in vivo models. In an in vitro preparation that uses the sucrose gap method for compound action potential recording, exposure of desheathed frog sciatic nerves to 5 % lidocaine, with or without 7.5 % dextrose, resulted in an irreversible complete loss of conduction. In contrast, nerves exposed to 1.5 % lidocaine recovered partially as evidenced by a 25 % to 50 % residual blockade after 2 to 3 hours of drug washout [5]. In this frog nerve model, lidocaine induced an irreversible ablation of the compound action potential that was concentration-dependent; beginning at a concentration as low as 40 mM, (which corresponds to a 1 % lidocaine solution) and being complete at 80 mM (2 % lidocaine solution) [6].

In an in vivo rat model, persistent sacral sensory deficit, as evaluated by tail-flick latency, was induced by subarachnoid infusion of 5 % lidocaine in 7.5 % dextrose [7], while no such sensory impairment was observed after 0.75 % bupivacaine with 8.25 % dextrose or 0.5 % tetracaine with 5 % dextrose. In a similar rat model, dose-related neurotoxic effects, as evidenced by histological abnormalities and persistent paralysis, have been demonstrated following subarachnoid infusion of 1.5 % lidocaine [8]. However, in this series, the incidence of paralysis did not differ between the study drugs (1.5 % lidocaine, 0.5 % bupivacaine and 2 % chloroprocaine), but increased with the duration of exposure, e.g. higher cumulative dosages.

Data evaluating the effect of additives on the neurotoxic potential of lidocaine are limited. In a rat model, the presence of 7.5 % glucose did not affect the potential of 5 % lidocaine to induce persistent sensory impairment, which is another finding that supports the hypothesis that the neurotoxic potential is related to the local anaesthetic itself [9].

Results of a recent in vivo study in a rat model suggest that the neurotoxic potential of lidocaine does not result from blockade of voltage-gated sodium channels [10]; subarachnoid administration of concentrations of conventional local anaesthetics (lidocaine and bupivacaine) at a tenfold higher concentration than necessary for reversible sensory blockade, induced persistent sensory impairment, whereas tetrodotoxin, a highly selective sodium channel blocker, did not. Of note, histopathological examination revealed that damage was limited to the sacral nerve roots, while the spinal cord was apparently unaffected.

3. CLINICAL EVIDENCE FOR LIDOCAINE’S NEUROTOXIC POTENTIAL

Neurotoxic side-effects of local anaesthetics may include both major permanent injury on one hand and, on the other hand, minor and transient symptoms. Reports of cauda
equina syndrome in association with repetitive subarachnoid administration of high doses of local anaesthetics for continuous spinal anaesthesia in the early 90’s were the immediate cause of increased awareness with regard to the neurotoxic potential of commonly used local anaesthetics [11]. Maldistribution within the subarachnoid space leading to excessive concentrations of local anaesthetic solutions within the sacral area has been implicated in contributing to neurotoxicity. This topic is again being brought back into the focus of public debate by recent reports on permanent neurological deficits following single injection spinal anaesthetics using 5 % hyperbaric lidocaine [12, 13]. In this context, unequivocal editorial recommendations and caveats have been launched [14].

However, lidocaine has also been reported to be associated with less severe, but far more common neurological symptoms. After first being published in 1993 [15], transient neurological symptoms (TNS) have been observed by many anaesthetists in association with the administration of hyperbaric 5 % lidocaine for spinal anaesthesia [16-18]. Typical symptoms consist of pain in the lower back and buttocks that radiates down both legs and lasts for 2 to 5 days, and occurs after a symptom-free interval.

In none of these patients was any objective neurological abnormality observed. In order to evaluate the incidence of TNS and to identify factors potentially contributing to TNS, we addressed this issue in a prospective, blinded, non-randomized study that included 270 gynaecological patients [16]. Approximately one third of the patients receiving hyperbaric 5 % lidocaine for spinal anaesthesia complained of TNS whereas only one patient had numbness of the lateral aspect of one foot in association with hyperbaric 0.5 % bupivacaine. These results were largely confirmed by non-randomized [17] as well as randomized studies [18, 19] performed in different institutions.

The hypothesis that the occurrence of TNS might be related to the high osmolarity of the hyperbaric 5 % lidocaine solution (820 mOsm/l) was not substantiated. In a prospective double-blinded randomized study, no difference in the incidence of TNS was found in patients receiving either the commercially available hyperbaric 5 % lidocaine or a less hyperbaric 5 % lidocaine solution at one half the original osmolarity [20]. As local anaesthetic neurotoxicity may increase with higher drug concentrations [6], the manufacturer of the hyperbaric 5 % lidocaine solution changed the package insert for this preparation recommending dilution of the drug with an equal volume of normal saline or cerebrospinal fluid before subarachnoid administration. However, such recommendations may not be followed or may not even be noticed [13]. Nevertheless, according to two recent studies, the incidence of TNS was unaffected by reducing the concentration of lidocaine from 5 % to 2 % [18, 19].

Patient positioning was suggested as a potentially contributory factor [15]. Results from two recent studies confirmed this initial hypothesis by showing that the incidence of TNS after lidocaine spinal anaesthesia was significantly higher in patients operated on in the lithotomy position [21] or positioned for knee arthroscopy [18] compared with those in the supine position.

**CONCLUSION**

Potential neurotoxicity associated with spinal administration of lidocaine may serve as an example that both scrupulous attention to outcome measures and thorough analysis of side-effects or complications are crucial prerequisites for improving the safety of anaesthetic procedures, reducing concomitant risks and avoiding pitfalls. To date, the
underlying pathophysiology of these neurological sequelae that differ substantially in severity and significance has not been established. It has also not been demonstrated that persistent sacral sensory deficit induced by lidocaine in the rat [7] correlates with TNS lidocaine spinal anaesthesia in humans [15-21]. Therefore, caution should be used in assuming that they share a common mechanism, even if such a concept is very appealing. Despite the fact that neither the pathophysiology of lidocaine-associated neurotoxicity nor the exact molecular mechanisms resulting in nerve and spinal cord injury are fully understood, a cautious approach to drug selection should take into account all information available from case reports, prospective randomized trials and laboratory research in order to reduce the risk of morbidity induced by regional anaesthesia. Furthermore, patients should be informed about the risk of TNS after short procedures. In patients not prepared to take the risk of transient neurological side-effects or presenting for surgery in the lithotomy position, we believe that lidocaine should be completely avoided.

SUMMARY

Almost half a century of uneventful clinical experience with lidocaine spinal anaesthesia certainly can attribute a label of excellency to this local anaesthetic. However, its safety record has been tarnished by recent reports of severe permanent and moderate transient neurological complications. Further, there are experimental in vitro and in vivo findings which indicate that lidocaine is associated with an increased potential for neurotoxicity compared with other local anaesthetics. Therefore, prudence dictates scrutinising the current concepts of neuraxial anaesthesia for their impact on postoperative morbidity and overall outcome.

REFERENCES BIBLIOGRAPHIQUES

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