Epidural test dose: lidocaine 100 mg, not chloroprocaine, is a symptomatic marker of *iv* injection in labouring parturients

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The authors studied the sensitivity (SN) and specificity (SP) of an epidural test dose containing either lidocaine 100 mg or 2-chloroprocaine 100 mg as symptomatic markers of intravascular injection in labouring parturients. In a prospective, double-blind and randomized fashion 48 unmedicated and labouring parturients were equally divided into three groups. After placement of a lumbar epidural catheter the normal saline group (NS) received 5 ml normal saline iv, the lidocaine group (LD) received lidocaine 100 mg iv, and the 2-chloroprocaine group (CH) received 2-chloroprocaine 100 mg iv. All injections were given during uterine diastole. Within the next one to two minutes a blinded observer recorded the patient's perception of the presence of metallic or funny taste, dizziness, and tinnitus. We then calculated SN and SP of each symptom (alone and in combination) along with their positive (+) and negative (−) predictive value (PV). In both groups no symptom alone reached clinically acceptable levels of SN (<87%). Only in the LD group, tinnitus+taste *and* dizziness+taste *reached a SN of 100% with a SP of 81% and 69% respectively. While the −PV was 100% for both groups of symptoms, the +PV reached 42% for* tinnitus+taste *and 30% for* dizziness+taste. *We conclude that lidocaine 100 mg is a sensitive marker of intravascular injection in labouring parturients, and that* tinnitus+taste *is the most reliable indicator of intravenous injection.*

Les auteurs ont étudié la sensibilité et la spécificité d'une dose test péridurale, contenant soit de la lidocaïne 100 mg, soit de la 2-chloroprocaïne 100 mg, comme témoin symptomatique d'une injection systémique, chez des femmes enceintes en cours de travail. Au cours d'une étude prospective, en double aveugle et randomisée, 48 patientes en cours de travail, ne recevant aucun traitement, ont été réparties en trois groupes identiques. Après la mise en place d'un cathéter épidural lombaire, le groupe contrôle reçoit 5 ml de salin isotonique intraveineux, le groupe lidocaïne (LD) reçoit 100 mg de lidocaïne iv et le group 2-chloroprocaïne (CH) reçoit 100 mg de 2-chloroprocaïne iv. L'ensemble des injections fut donné en cours de diastole utérine. Dans les deux minutes qui suivaient, un observateur n'ayant pas connaissance du protocole, recueillait auprès des patientes l'existence des signes suivants = goût métallique ou anormal dans la bouche, somnolence, sensation de vertiges. Nous avons calculé ensuite la sensibilité (SN) et la spécificité (SP) de chaque symptôme (seul et en association) ainsi que leur valeur prédictive positive (PV+) ou négative (PV−). Dans les deux groupes, aucun des symptôme seul n'a atteint une sensibilité de niveau clinique acceptable (<87%). Dans le groupe (LD) uniquement, l'association des signes suivants: vertige−goût *et* somnolence−goût *a atteint une sensibilité de 100% et une spécificité de 81% et 69% respectivement. Alors que la valeur prédictive négative était de 100% pour les deux groupes de symptômes, la valeur prédictive positive a atteint 42% pour le groupe* vertige−goût *et 30% pour le groupe* somnolence−goût. *Nous en concluons que 100 mg de lidocaïne est un marqueur sensible d'injection systémtique chez la femme enceinte et que les signes cliniques:* vertige−goût *constitutent le témoin le plus fiable de cette injection systémique.*

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Local anaesthetics intended for epidural injection may be unintentionally injected intravascularly which may cause seizures and cardiac arrest.[1] To avoid the unintentional *iv* injection of epidural doses of local anaesthetics, the concept of an epidural test dose (ETD) has been developed.

Many agents have been tested as components of an ETD to rule out intravascular injection. Intravenous li-

TABLE I Sensitivity (SN), specificity (SP), and negative and positive predictive value (PV) of each symptom in the lidocaine and chloroprocaine group.

	Lidocaine				*Chloroprocaine*			
	SN	*SP*	*−PV*	*+PV*	*SN*	*SP*	*−PV*	*+PV*
Taste	75%	81%	76%	35%	44%	81%	59%	24%
Dizziness	87%	75%	75%	32%	87%	75%	86%	32%
Tinnitus	87%	94%	88%	66%	56%	94%	68%	56%

Sensitivity: number of true positives divided by the number of true positives plus false negatives.
Specificity: number of true negatives divided by the number of true negatives plus false positives.
Negative predictive value: number of true negatives divided by the number of true negatives plus false negatives.
Positive predictive value: number of true positives divided by the number of true positives plus false positives (assuming a 12% prevalence).

TABLE II Sensitivity (SN), specificity (SP), and negative and positive predictive value (PV) of symptoms used in combination of two in the lidocaine and chloroprocaine group

	Lidocaine				*Chloroprocaine*			
	SN	*SP*	*−PV*	*+PV*	*SN*	*SP*	*−PV*	*+PV*
Dizziness+tinnitus	94%	75%	92%	34%	87%	75 %	86%	32%
Tinnitus+taste	100%	81%	100%	42%	81%	81%	81%	37%
Dizziness+taste	100%	69%	100%	30%	94%	69%	92%	28%

docaine 100 mg and chloroprocaine 100 mg cause predictable symptoms (metallic taste, dizziness, and tinnitus) in unmedicated male volunteers. Therefore, they have been suggested as markers of intravascular injection in epidural analgesia.

We designed this prospective, double-blind and randomized study to evaluate the diagnostic accuracy of lidocaine 100 mg and chloroprocaine 100 mg as detectors of intravascular injection in labouring parturients.

Method

After approval by the Institutional Human Research Committee, 48 consecutive and unmedicated labouring women requesting lumbar epidural analgesia for labour gave informed consent. Their ASA physical status was 1 or 2 following an uncomplicated pregnancy. Cervical dilatation was >4 cm with uterine contractions at three- to four-minute intervals or less. Women with a history of allergy to either lidocaine or 2-chloroprocaine were excluded. A non-invasive blood pressure cuff was used to measure blood pressure every three minutes. Pulse oximetry monitored maternal SpO_2 and HR. Fetal heart rate was displayed continuously. An external tocodynamometer or an internal uterine pressure catheter monitored uterine activity. Each patient received an *iv* infusion of 700–1000 ml crystalloid solution via a peripheral catheter inserted into a vein in the dorsum of the hand in preparation for lumbar epidural analgesia. With the patient in the sitting position a lumbar epidural catheter was inserted and taped.

Parturients were sequentially randomized to one of three groups. Between uterine contractions, one group (NS, 16 patients) received 5 ml of normal saline *iv*, a second group (LD, 16 patients) received lidocaine 100 mg *iv* (2%, 5 ml), and a third group (CH, 16 patients) received chloroprocaine 100 mg *iv* (2%, 5 ml). Within the next one-to-two minutes a blinded observer (an anaesthesiology resident or attending staff) recorded the patient's perception of the presence of metallic or funny taste, dizziness, and tinnitus.

The sensitivity (SN) and specificity (SP) of each symptom, alone and in combination, along with the positive (+) and negative (−) predictive value (PV) was calculated assuming a 12% prevalence of intravascular cannulation.[2]

Results

No adverse effects of any kind were experienced by our parturients during the performance of the study.

Analysis of demographic data (age, height, weight, and parity) confirmed comparability among groups ($P < 0.05$).

In both groups no symptom alone achieved clinically acceptable levels of sensitivity (<87%) (Table I).

Table II shows SN and SP of each group of two symptoms used in combination along with their + and − PV. In the chloroprocaine (CH) or lidocaine (LD) group, the

TABLE III Sensitivity (SN), specificity (SP), and negative and positive predictive value (PV) of the three symptoms used together in the lidocaine and chloroprocaine group

	Lidocaine				*Chloroprocaine*			
	SN	*SP*	*−PV*	*+PV*	*SN*	*SP*	*−PV*	*+PV*
Dizziness Taste Tinnitus	100%	69%	100%	30%	94%	69%	92%	28%

presence of either symptom defined a true positive test and the absence of both defined a false negative test; in the NS group, the presence of either symptom defined a false positive test and the absence of both a true negative. In the CH group, *dizziness+taste* achieved a SN of 94% (95% CI 70–100%), SP was 69% (95% CI 48–93%). In the LD group, *tinnitus+taste* and *dizziness+taste* reached a SN of 100% (95% CI 79–100%) with a SP of 81% (95% CI 54–96%) and 69% (95% CI 41–89%) respectively. While the −PV was 100% for both groups of symptoms, the +PV reached 42% for *tinnitus+taste* and 30% for *dizziness+taste*.

When all three symptoms were used together, sensitivity was 94% (95% CI 70–100%) in the CH group and 100% (95% CI 79–100%) in the LD group. Specificity was 69% (95% CI 41–89%) in both groups (Table III).

Discussion

The incidence of unintentional intravascular cannulation during the placement of a lumbar epidural catheter in parturients ranges between 8% and 16%,[2] and may be related to the presence of dilated epidural vessels in pregnancy.[3] Intravascular injection of epidural doses of local anaesthetics may cause seizures and cardiac arrest and parturients are more sensitive to the toxic effects of local anaesthetics.[1]

The incidence of unintentional intravascular cannulation can be reduced, but not eliminated, by injecting saline in the epidural space via the epidural needle prior to the placement of the catheter.[2]

Aspiration of blood via the epidural catheter confirms the diagnosis of intravascular cannulation, but a negative aspiration does not rule it out. An ETD has been used to detect intravascular as well as intrathecal cannulation for many years. Several agents and techniques have been tested as components of an ETD to rule out intravascular cannulation with variable results.[4-5]

The use of epinephrine as a component of an ETD was introduced by Moore and Batra.[6] They demonstrated a predictable HR increase after *iv* injection of epinephrine, 15 μg, in male volunteers. However, the efficacy of epinephrine as marker of *iv* cannulation in labouring parturients has been questioned because of the wide variability in maternal heart rate.[7] We recently demonstrated the accuracy of epinephrine 10 or 15 μg in detecting intravascular cannulation in labouring parturients.[8] However, the safe use of epinephrine-containing ETDs in patients with compromised utero-placental reserve, as in preeclampsia, has yet to be determined.

Micro bubbles of air have also been found to be reliable markers of intravascular injection in labouring parturients.[9] The technique requires the use of a Doppler monitor located over the maternal precordium. Changes in Doppler heart tones following the injection of micro bubbles via the epidural catheter will identify intravenously located catheters. This air test carries a sensitivity of 100% and a specificity of 98%; however, the +PV for this technique (not provided by the authors) may not differ from other techniques (six false positive of 22 positive tests).[9] A low +PV implies a more frequent unnecessary repetition of the procedure in the presence of a positive test.

The use of local anaesthetics as markers of *iv* cannulation has also been suggested. The *iv* injection of lidocaine 100 mg and 2-chloroprocaine 100 mg causes predictable symptoms in unmedicated male volunteers. In labouring parturients lidocaine 45 mg *iv* failed to elicit reliable symptoms.[10] Our study shows that lidocaine 100 mg, but not 2-chloroprocaine 100 mg, is a clinically acceptable marker of intravascular injection in labouring patients. The inability of 2-chloroprocaine 100 mg to elicit predictable symptoms may be a dose-related phenomenon, and may reflect the different CNS toxicity of the two agents.[11] By using two symptoms (*tinnitus+taste*) in combination, sensitivity with lidocaine was 100% and specificity 81%. The absence of false negative results (−PV 100%) provides support to the safety of this technique. However, a +PV of 42% implies that in the presence of a positive test (patient complaining of tinnitus or funny taste) up to 58% of the catheters may be thought erroneously to be located in a vessel. Even though the overall incidence of positive tests after our ETD (true and false positive) is not known, it may range between 10 to 20%, so that unnecessary replacement of 58% of those catheters may be acceptable. Indeed only about 5–10% of all catheters would be unnecessarily removed.

In parturients the intrathecal injection of lidocaine 100 mg may cause undesirably high levels of spinal anaesthesia. Therefore, the use of lidocaine 100 mg as a marker of *iv* injection mandates exclusion of unintentional subarachnoid cannulation. We suggest that an intrathecal test dose of local anaesthetic should be used (i.e., lidocaine 45 mg) via the epidural catheter and the injection of lidocaine 100 mg should follow a negative intrathecal test dose (no signs of spinal anaesthesia).

Our study shows that the use of *tinnitus+taste* enhances the accuracy of this test. This implies that questioning the patient about symptoms should be limited to tinnitus and taste. Inquiring about *dizziness* reduces the specificity (from 81% to 69%) of the test without increasing its sensitivity (already 100%).

In conclusion, we found that lidocaine 100 mg, but not 2-chloroprocaine, is a sensitive marker of intravascular injection in labouring patients; and that *tinnitus+taste*, but not *dizziness*, are the most reliable indicators of *iv* injection. In the presence of a positive test 58% of epidural catheters may be thought erroneously, to have been located intravascularly.

We suggest that lidocaine 100 mg is a useful test for intravascular cannulation by an epidural catheter in those labouring parturients with any fetal or maternal condition, preeclampsia or reduced utero-placenta reserve, where the use of epinephrine-containing ETD may not be advisable.

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