

The epidural test dose in obstetric anesthesia

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Complications related to anesthesia represent the 6th leading cause of pregnancy-related mortality. In 82% of cases, death occurs during a caesarean section. Often, it is a situation where elective procedures are administered to young female patients whose death could have been prevented by experienced personnel. According to Hawkins,¹ the maternal mortality rate related to anesthesia declined from 4.3 (1979-81) to 1.7 (1988-90) per million live births. This drop in mortality is attributed to the increased use of regional instead of general anesthesia. Closer attention to the toxicity of local anesthetics and the adoption of measures such as use of the test dose and the continuous rather than bolus administration of local anesthetic solutions at low concentrations have contributed to the reduction in mortality. Since test doses came into use 20 years ago, they have been one of the most controversial issues in obstetric anesthesia. As defined by Moore and Batra in 1981, a test dose is the injection in an epidural catheter of 15 µg of adrenaline combined with 3 ml of local anesthetic. The objective is to detect tachycardia within 60 seconds, a sign of an accidental intravenous (IV) injection, thereby avoiding injection of a massive toxic dose of local anesthetic.²

Is the test dose still useful? Should it be redefined? Is there one ideal test dose? Should we abandon it as some authors have recommended? It must not be forgotten that, despite a decline in the incidence of fatal systemic complications related to the IV injection of local anesthetics, this danger lurks in our practice every day.

BACKGROUND

In 1979, Albright reported 5 cases of circulatory collapse following accidental IV administration of bupivacaine to pregnant women, and 1 case following the administration of etidocaine during epidural regional anesthesia. In each case, aspiration prior to the injection was negative for blood return. Fibrillation or ventricular tachycardia, asystolia or complete block occurred quickly, making resuscitation difficult.³ In 1981, in a study of 175 patients, Moore and Batra found that 15 µg of adrenaline increases the heart rate from 79 ± 14 to 111 ± 15 beats per minute in 23 ± 6 seconds, with a return to baseline within 32 ± 33 seconds.² With this study, and Albright's recommendation in 1984, the test dose became routine practice for initiating epidural anesthesia.⁴

In 1990, Guinard et al confirmed Moore and Batra's findings and defined a positive test dose as an increase in heart rate of ≥ 20 beats per minute following injection of 10 to 15 µg of adrenaline, combined with 3 ml of 1% lidocaine. However, these data applied only to young, healthy, nonpregnant, unpremedicated subjects who were not taking beta-blockers.⁵

RISKS ASSOCIATED WITH AN EPIDURAL BLOCK

The risks involved during the epidural injection of a local anesthetic include:

- accidental subdural injection
- subarachnoid injection
- intravenous injection

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TABLE 1: Properties of the ideal test dose

- Detects an IV or subarachnoid injection
- Safe and risk-free for the patient
- Easy to use
- Minimal patient cooperation
- Simple monitoring
- High sensitivity and specificity
- Applicable to all clinical situations
- Requires little time

The test dose with adrenaline is one means of preventing these incidents and ensuring a safe injection of the anesthetic agent.

Subdural injection

Subdural injections are uncommon and difficult to detect because cerebrospinal fluid (CSF) does not flow back freely, as a result, aspiration is rarely positive. A subdural injection is slow to take effect and produces a high degree of sensory block, partly sparing the motor fibers and sacral nerve fibers. Hence, the block is unevenly distributed.

Subarachnoid injection

Puncture of the dura mater is reported in 0.61% to 10% of cases. The most commonly accepted incidence is 1% to 2%. It is easily recognized by a positive CSF return, which contraindicates the injection of a local anesthetic. Migration of an epidural catheter into the subarachnoid space following its insertion or during treatment is harder to detect and occurs in 0.26% to 0.6% of cases. Unidentified intrathecal injection can result in a high degree of sensory and motor block, compromising respiratory function and vital signs.

Intravenous injection

An IV puncture may occur during insertion of the epidural needle or catheter, or by the subsequent migration of the catheter. The incidence ranges from 0.2% to 11% (an average of 2.8% in the general population and 7% to 8.5% in pregnant women). Accidental placement of an intravenous epidural catheter is associated with significant risk because it is difficult to detect and there is the possibility of injecting a large amount of local anesthetic, which can quickly produce a toxic level of the drug.

Properties of the ideal test dose

The ideal test dose should be safe, easy to use, requiring only easily accessible monitoring. It should permit an IV or subarachnoid injection to be detected within a brief period of time and with minimal cooperation from the patient. It should also be safe,

involving no additional risks to the patient, and applicable to all clinical situations. Lastly, it should be characterized by high levels of sensitivity and specificity (Table 1).

SUGGESTED TESTS TO CHECK CATHETER PLACEMENT

The most commonly used tests to check the epidural placement of a catheter are:

- aspiration
- fractioned injection of the anesthetic solution
- injection of a test dose of a local anesthetic
- adrenaline injection

Other, less common tests are:

- air injection
- fentanyl injection
- ephedrine injection
- isoproterenol injection

Aspiration

Aspiration is undoubtedly the first test to perform. Easy to perform, it allows detection of the IV or subarachnoid placement of an epidural catheter. The reliability of the test, however, largely depends on the type of catheter used.

Aspiration with a single-orifice catheter will reveal the presence of blood in 34% to 81% of cases. Aspiration with a multi-orifice catheter, however, will detect 99.5% of potentially hazardous injections.⁶ D'Angelo demonstrated that with a multi-orifice catheter, analgesia is more often adequate. This type of catheter requires little repositioning and leads to better distribution of the anesthetic solution. Yet, the incidence of IV cannulation and catheter migration, or the need to replace it, is the same regardless what type of catheter is used.⁷ Some studies have demonstrated that multi-compartmental placement of a multi-orifice catheter is very rare. In the event of both an epidural and vascular position, the slow injection of local anesthetic with a low concentration (0.125% bupivacaine) will still produce analgesia because the solution preferentially flows through the nearest opening. Conversely, a rapid injection will shoot through all the catheter holes. Note that aspiration is not recommended following the partial withdrawal of a catheter previously in an IV position. Since the incidence of false negatives is then 25%, completely removing the catheter and redoing the procedure is suggested. The use of this test is not recommended when injecting a local anesthetic of high concentration for surgical purposes, such as a caesarean.

Fractioned injection of the anesthetic solution

Fractioned injection is among the recommendations for the safe practice of regional anesthesia. Theoretically, when small doses of a local anesthetic

are accidentally injected intravenously, the patient should describe subjective symptoms before the plasmatic concentration reaches the threshold of toxicity or convulsions. However, what really happens is another story. Cases cited in the literature indicate that some patients who received massive doses of local anesthetics reported no symptoms, while others immediately went into convulsions.⁸

Injection of a test dose of local anesthetic

Injection of a local anesthetic helps rule-out an IV or subarachnoid injection.

Subarachnoid detection

A subarachnoid injection of 3 ml (45 mg) of hyperbaric lidocaine into the lumbar area produces sensory anesthesia affecting the S2 dermatome in 1.45 ± 1.2 minutes before spreading to T9.⁹ An epidural injection, on the other hand, produces a sensory change in the L2 dermatome after 3 minutes. Isobaric bupivacaine, at doses of 8 to 15 mg, has too high a variability in its onset and spread to qualify as an adequate test dose. Norris¹⁰ suggests using a smaller, safer dose of 2.5 mg. The patient then reports a sensation of warmth, little change in terms of sensory perception, a slight motor block, and rapid analgesia. Therefore, it is important to look for signs and symptoms that suggest a subarachnoid injection of bupivacaine. Injection of a test dose into the subarachnoid space involves the non-negligible risks of hypotension and a high degree of sensory block that can extend to C6.¹¹

Intravenous detection

Following an IV injection of lidocaine, symptoms such as tinnitus, perioral paresthesia, a metallic taste, lightheadedness, sedation, and a feeling of relaxation may occur. Unfortunately, depending on the clinical situation and whether or not premedication is a factor, these symptoms are not consistent. Colonna-Romano demonstrated that an injection of 100 mg of lidocaine is a sensitive marker in unpremedicated pregnant patients.¹² For a combination of the following symptoms – tinnitus-metallic taste – the sensitivity associated with an injection of 100 mg of lidocaine is 100% and specificity is 81%. A study by Michels and Lyons in 60 unpremedicated female patients in good health, confirmed the findings. They determined that an injection of 1 mg/kg of lidocaine is more sensitive for detecting an accidental IV injection than 0.5 mg/kg (CI, 85%-100% vs 26%-74%).¹³ Nonetheless, it is imperative to start with a more conservative test dose of lidocaine to rule-out a subarachnoid injection.

Some authors consider it risky to use bupivacaine to detect an accidental IV injection. The ratio of the

dosages required to produce circulatory collapse compared to the toxicity in the central nervous system is higher with lidocaine than with bupivacaine. Lidocaine would therefore seem to be a safer agent.¹³ A study by Mulroy in healthy, unpremedicated, female patients found that 25 mg of bupivacaine and 90 mg of chloroprocaine are alternatives for detecting an IV injection, based on symptoms perceived by the patients.¹⁴ It should be noted that an accidental subarachnoid injection of 25 mg of bupivacaine can cause high spinal anesthesia. As for chloroprocaine, the possibility of neurotoxicity is not ruled-out. In the studies mentioned above, no author has been able to prove that bupivacaine or chloroprocaine are effective for detecting an IV injection in a premedicated female patient.

Air test

The air test involves looking for the presence of intracardiac air by using a Doppler placed on the precordial area (lower sternum) while injecting 1 ml of air into the epidural catheter. In 1990, Leighton and Norris demonstrated that for 313 women in labour, an injection of 1 ml of air after a negative aspiration in a single-orifice epidural catheter was a safe and reliable test with 100% sensitivity and 98% specificity. No patient experienced complications related to the test.¹⁵ Ten years later, Leighton's study of 300 women in labour found that the air test cannot be used with multi-orifice catheters because it will only detect 82% of intravenous locations.¹⁶ In theory, as with liquids, a slow injection of air will exit from the nearest hole. Yet, it is difficult to inject air fast enough for it to escape through more than one hole. Therefore, the test is not reliable when using multi-orifice catheters.

Ephedrine

Ephedrine is used in obstetric regional anesthesia to correct hypotension. It is associated with little change in uteroplacental circulation and uterine contractions. According to a study by Cherala, an injection of 15 mg of ephedrine produces, within 5 minutes, a temporary increase of ≥ 10 mm Hg of systolic arterial pressure for 4.3 ± 1.3 minutes.¹⁷ In 3 of 30 fetuses, it produced transitory tachycardia (averaging 120 to 150 bpm) without negative consequences. Yet, the slowness of the response and the necessity of closely monitoring arterial pressure to detect changes beat by beat make ephedrine a less interesting agent.

Fentanyl

Readily available, non-toxic, rapid-acting, and with no effect on uterine flow, fentanyl has some of the ideal qualities of a test dose. Theoretically, the

plasmatic peak of intravenous fentanyl is immediate and occurs 5 to 10 minutes after an epidural injection. Unfortunately, Yoshii found that 92% of patients in labour injected with 100 µg of fentanyl, intravenously or in the epidural space, were unable to accurately identify the way it was injected, based on a description of the symptoms. Some patients described no symptoms during an IV injection or described symptoms during an epidural injection for a 5% incidence of false positives and 95% specificity.¹⁸ An IV injection of fentanyl 60 minutes earlier or an injection of fentanyl in the epidural space 90 minutes earlier, did not appear to interfere with the test. Yet, the fentanyl test has some disadvantages. If the result is dubious, doing a second test is not desirable due to the superimposition of effects. In addition, fentanyl cannot be used to detect an accidental subarachnoid injection.

Isoproterenol

Isoproterenol is the most powerful of the non-selective beta-adrenergic agonists. Compared to alpha and beta agonists such as adrenaline, it does not cause a biphasic heart rate or bradycardia, reflexes observed in response to the alpha-adrenergic effect. Since its cardiac effects are only slightly altered by the presence of anesthetic agents such as sevoflurane and isoflurane, many studies are trying to demonstrate its effectiveness as a test dose for children or adults under general anesthesia. In pregnant women, the chronotropic effect of isoproterenol is diminished.¹⁹ Moreover, no histopathological document has proven the innocuousness of isoproterenol injected into the subarachnoid or epidural spaces.

Adrenaline injection

Adrenaline injection is a simple test. It requires little equipment, no cooperation from the patient, and monitoring is easily accessible. Nevertheless, some restrictions and contraindications should be noted. General anesthesia, advanced age, and the use of beta-blockers attenuate the response to adrenaline. An increase in oxygen consumption may cause myocardial ischemia and cardiac arrhythmia. In pregnant women, reduced sensitivity to adrenaline has been clearly proven. Moreover, a few clinical situations contraindicate its use (Table 2).

In a study of 20 female patients, Leighton and Norris reported fetal distress in 2 fetuses following the injection of 15 µg of adrenaline.

TABLE 2: Contraindications for adrenaline with pregnant patients

- High blood pressure
- Preeclampsia
- Cardiovascular disease
- Taking beta-blockers
- Tachycardia > 125 bpm
- Cocaine intoxication
- Compromised uteroplacental perfusion
- High uterine contraction frequency (< 1 min.)
- Monitoring impossible

One showed late deceleration for 10 minutes and the other, 4 minutes of bradycardia followed by a decline in the variability of the fetal heart for 7 minutes. In both cases, cardiac variability returned to baseline after 20-25 minutes. The APGAR scores at 5 minutes were nonetheless ≥ 7 .²⁰ Although a normal and healthy fetus can easily tolerate a reduction in uterine flow, a fetus in distress may have a different response. How can the response be predicted? Both distressed fetuses were in good condition at the time of the adrenaline injection. In a pregnant sheep, not in labour, a 55%-65% reduction in uterine flow from base value was observed after injections of 10 and 20 µg of adrenaline. The reduced flow lasted for 3 minutes. The fetal heartbeat, maternal arterial tension, and fetal and maternal arterial blood gases did not change. This reduction in uterine flow is identical to what occurs during a normal uterine contraction. Therefore, such a reduction in uterine flow due to an adrenaline injection superimposed on the effect of a contraction could compromise the integrity of the fetus.²¹ In estimating placental perfusion by measuring the velocity of umbilical cord flow with a Doppler, it was demonstrated that an injection of 8 ml of 1.5% lidocaine with 1/200,000 adrenaline causes a greater decline in umbilical flow if the flow resistance is high at the onset.²²

Adrenaline test positivity criteria

The test dose as defined by Moore and Batra cannot be applied to pregnant women. The great variability in heart rate during labour, along with the reduced sensitivity to catecholamines found in pregnant women, reduce test-dose specificity. In view of these facts, some authors modified the positivity criteria for the test. In 1987, Leighton and Norris found only a 50% sensitivity to the adrenaline test by using an increase in heart rate ≥ 25 bpm over the baseline as positivity criteria.²⁰

In 1992, Colonna-Romano observed that an injection of 10 µg of adrenaline is as effective as 15 µg for identifying an IV injection. With an increase in heart rate ≥ 10 bpm as the positivity criteria, he demonstrated 100% sensitivity, but a positive predictive value of only 55%-73%.²³ Later, the same author defined criteria for a positive adrenaline test by comparing the acceleration phase of tachycardia caused by adrenaline to that caused by a uterine contraction. Since the acceleration phase associated with adrenaline is sharper than that stemming from a uterine contraction, this makes it possible to identify a positive test more accurately.²⁴ In 1998, Colonna-Romano assessed all these criteria in a study involving 198 pregnant patients. He looked for an increase in heart rate to ≥ 10 bpm over the baseline observed one minute before the injection and for acceleration phase ≥ 1.0 bpm. The test showed 100% sensitivity, 96% specificity, a 100% negative predictive value, and a 63% positive predictive value. Since the prevalence of a positive test in the study was 12%, 4.5% of catheters were withdrawn needlessly.²⁵

Therefore, the adrenaline test is 100% sensitive, but lacks specificity. Since repositioning a catheter is not risk-free (puncture of the dura mater: 1%-2%; intravenous puncture: 7%-8%; block failure: 5%), some physicians are reconsidering its use. Moreover, the concept of an acceleration phase is not easy to apply in practice.

Currently, the adrenaline test requires:

- exclusion of some patients (see Table 2)
- lowering the threshold of the increase in heart rate
- monitoring that is capable of detecting a rapid change in the heart rate
- avoiding an injection during a contraction

In view of these constraints, it may be justified not to consider adrenaline as an acceptable alternative for detecting an IV injection. Furthermore, some authors emphasize the limitations of a test dose with adrenaline. For Norris, aspiration of multi-orifice catheters effectively detects most IV punctures (99.5% of cases). Since the prevalence of an IV catheter undetected by aspiration is low, a positive response to adrenaline does not necessarily mean an IV puncture.²⁶ In pregnant women, the effects associated with the injection or perfusion of a diluted mixed solution of local anesthetic (bupivacaine $\leq 0.125\%$) and narcotic are very likely to be limited to regression or failure of the block. Higher doses are necessary to cause cardiac or central nervous

system toxicity. When a block fails, removal of the catheter is recommended rather than injecting a bolus of a higher concentration. Birnbach and Chesnut believe the following questions should be asked before abandoning the adrenaline test.

- Is there an infallible test dose?
- Do changes in the practice of regional anesthesia involving the use of multi-orifice catheters and the slow perfusion of low concentrations of local anesthetics justify abandoning the test dose with adrenaline?
- What do you do if a patient has to undergo an emergency caesarean when it is uncertain that the catheter is properly placed? If the catheter is not correctly positioned, the patient will suffer longer before a decision is made to proceed with a new peridural technique.
- Do anesthesiologists remain at the bedside of patients long enough to observe the response to a therapeutic dose of local anesthetic?
- Is the inconvenience of replacing a properly positioned catheter following a positive test dose with adrenaline greater than the morbidity or mortality associated with the accidental injection of a heavy dose of local anesthetic?²⁷

It seems obvious that there is no perfect test dose. Fentanyl, local anesthetics, and the air test have demonstrated only partial effectiveness for detecting an IV injection. On the other hand, adrenaline injections have 100% sensitivity. Perhaps in some situations, the test dose with adrenaline still represents the most suitable solution. Nevertheless, one must add observation, vigilance, and judgment. Paech, like Norris, argues that a test dose is always indicated if the aspiration test is equivocal or questionable.²⁸

CONCLUSION

In conclusion, these are some recommendations based on the work by Norris:¹⁰

For intrathecal detection

- Start with aspiration.
- Test with 2.5 mg bupivacaine; check for the sensation of heat, slightly altered sensibility, and mild motor block or rapid analgesia. Lidocaine 45 mg and bupivacaine 7.5 mg are not advisable due to the risk of a high block.

For intravenous detection

- Use a multi-orifice catheter.
- Proceed with aspiration (if positive, remove the catheter).

- Use low concentrations of local anesthetics (bupivacaine < 0.125%).
- Consider each dose a test dose.
- Inject 5-ml boluses at most.
- Confirm the analgesia and bilateral sensory change.
- Repeat the peridural if the catheter does not work.

For a caesarean

- First use aspiration.
- If there are no contraindications for injecting adrenaline, 1.5% lidocaine with 1/200,000 (3 ml) adrenaline should precede the fractioned injections of 5 ml of 2% lidocaine.

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