Transient Horner's syndrome following thoracic epidural anesthesia for mastectomy: a prospective observational study

Syndrome de Horner transitoire après anesthésie péridurale thoracique pour mastectomie: étude observationnelle prospective

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Abstract

Purpose Transient Horner's syndrome is an uncommon complication of epidural anesthesia, though its exact incidence in thoracic epidural anesthesia is not clear. Therefore, this study prospectively evaluated the incidence of Horner's syndrome after thoracic epidural anesthesia for mastectomy.

Methods Patients scheduled for mastectomy, with or without breast reconstruction, were enrolled in this prospective observational study from September 2010 to December 2013. Intraoperative thoracic epidural anesthesia was established using 0.375% or 0.5% ropivacaine 15 mL with thoracic epidural analgesia continued postoperatively with a continuous infusion of 0.15% ropivacaine 2 mL·hr⁻¹ with fentanyl 8 µg·hr⁻¹. Signs of Horner's syndrome (miosis, ptosis, and hyperemia) were assessed at one and two hours as well as one, two, and three days postoperatively.

Results Thoracic epidural anesthesia was successful in 439 patients, with six (1.4%) of these patients acquiring Horner's syndrome. All signs of Horner's syndrome

resolved gradually within 180 min of discontinuing the epidural infusion. In one patient with Horner's syndrome, a radiographic contrast injection confirmed that the drug had spread to the cervical epidural level.

Conclusion The incidence of Horner's syndrome following thoracic epidural anesthesia and continuous thoracic epidural analgesia for mastectomy was 1.4%. The mechanism was consistent with cephalic spread of the epidural local anesthetic. This trial was registered at: Clinicaltrials.gov, number: NCT02130739.

Résumé

Objectif Le syndrome de Horner transitoire est une complication rare de l'anesthésie péridurale, bien qu'on n'en connaisse pas précisément l'incidence dans l'anesthésie péridurale thoracique. Cette étude a donc évalué de manière prospective l'incidence du syndrome de Horner après anesthésie péridurale thoracique pour mastectomie.

Méthodes Des patientes devant subir une mastectomie programmée, avec ou sans reconstruction du sein, ont été recrutées dans cette étude observationnelle prospective de septembre 2010 à décembre 2013. L'anesthésie péridurale thoracique peropératoire a été obtenue avec 15 ml de ropivacaïne à 0,375 % ou 0,5 % et l'analgesie péridurale thoracique a été poursuivie en postopératoire avec une perfusion continue de ropivacaïne à 0,15 % à raison de 2 mL·h⁻¹ plus fentanyl 8 µg·h⁻¹. Des signes du syndrome de Horner (myosis, ptose, et hyperhémie) ont été recherchés en postopératoire une et deux heures après l'intervention, puis un, deux et trois jours en post opératoire.

Résultats L'anesthésie péridurale thoracique a été un succès chez 439 patientes, parmi lesquelles 6 (1,4 %) ont éprouvé un syndrome de Horner. Tous les signes du

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syndrome de Horner ont progressivement disparu dans les 180 minutes suivant l'arrêt de la perfusion péridurale. Une radiographie avec injection de produit de contraste a confirmé chez une patiente présentant le syndrome de Horner que le médicament s'était étendu au niveau péridural cervical.

Conclusion *L'incidence du syndrome de Horner après anesthésie péridurale thoracique et analgésie péridurale thoracique continue pour mastectomie a été de 1,4 %. Son mécanisme était compatible avec la propagation céphalique de l'anesthésique local en péridural. Cette étude a été enregistrée sur le site ClinicalTrials.gov sous le numéro: NCT02130739.*

Horner's syndrome is a classic clinical triad of neurological signs that includes ptosis, miosis, and anhidrosis and is accompanied by early conjunctival hyperemia. Though transient Horner's syndrome is thought to be an uncommon complication of epidural anesthesia, its exact incidence is not known. It has been reported as a complication of lumbar or sacral epidural blocks, and most reported cases of Horner's syndrome have been seen in pregnant women receiving lumbar epidural analgesia during labour or for Cesarean delivery.¹⁻³ A few reports have documented Horner's syndrome in both adult and pediatric patients after a thoracic epidural infusion.⁴⁻⁶ The reported incidence of overall neurological complications in patients who receive continuous thoracic epidural analgesia is approximately 3%, but Horner's syndrome was not mentioned as a potential complication.⁷ As it is neither a common nor a severe complication, its occurrence is likely neglected.

Although Horner's syndrome after epidural anesthesia is generally not severe and is self-limiting, it can cause considerable anxiety and patient discomfort, potentially even leading to unnecessary diagnostic investigations. The incidence might be higher in thoracic epidural anesthesia than in lumbar epidural anesthesia because it is thought that the syndrome may be caused by unintentionally high neuraxial spread. Nevertheless, data are lacking regarding the incidence of this syndrome in adults who have undergone thoracic epidural anesthesia. As there are many studies reporting other complications and outcomes after thoracic epidural anesthesia, we chose to focus our study on Horner's syndrome exclusively. Thoracic epidural anesthesia is used widely for control of postoperative pain following modified radical mastectomy;^{8,9} therefore, for this prospective study, we elected to evaluate the incidence of Horner's syndrome in this population.

Methods

This prospective observational study was conducted from September 2010 to December 2013 with institutional review board approval.

Patients scheduled for mastectomy, with or without breast reconstruction, were eligible for the study. A full medical history was taken for each patient with an emphasis on detecting any bleeding disorders as well as anatomic or neurologic abnormalities that might preclude epidural anesthesia. A clinical examination was performed and coagulation parameters were measured. We excluded patients who had more than one abnormal preoperative coagulation parameter, clinical signs of potential bleeding disorders (e.g., bruising, petechiae or ecchymosis), or anatomic or neurological abnormalities (e.g., significant scoliosis or kyphosis, radiculopathy, or ptosis). The patients were recruited the day before surgery and informed consent was obtained. Predefined drop-out criteria included unsuccessful catheter placement (e.g., inability to have the catheter inserted at two vertebral levels), unsuccessful epidural anesthesia (no verified sensory block), dural puncture, or intravascular catheterization (e.g., cerebrospinal fluid [CSF] or blood aspirated through either the catheter or the needle, respectively).

The patients were premedicated with glycopyrrolate 0.2 mg *im* one hour before surgery. After routine monitoring and with the patient in the sitting position, an epidural puncture was performed at the T3-T5 level using a 17G Tuohy needle (Portex Ltd., Hythe, Kent, UK) via a midline approach with local infiltration anesthesia (1% lidocaine). The epidural space was identified with the loss-of-resistance technique using a 10 mL glass syringe filled with saline. A Portex[®] epidural catheter (Portex Ltd., Hythe, Kent, UK), a closed-end catheter with three side holes and an outer catheter diameter of 0.9 mm, was carefully inserted 10 cm into the epidural space. The catheter was gently aspirated for blood or CSF, and 1% lidocaine 3 mL with epinephrine 15 µg (1:200,000) was then injected. Following the injection, each patient was observed for 40 sec to exclude intradural or intravascular placement. Six anesthesiologists with more than three years' experience each performed the thoracic epidural catheterization under the direct supervision of one anesthesiologist with more than 20 years' experience. Thoracic epidural catheterization was omitted when attempts to insert the catheter were unsuccessful at two vertebral levels or when the patient refused during the procedure. When the patient was placed in the supine position, epidural anesthesia was initiated with a bolus of 0.375% or 0.5% ropivacaine 15 mL injected slowly. After confirming that the block was sufficient for the operation

(T1-T6), the patients were given moderate to deep sedation with propofol ($50\text{--}200\text{ }\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ *iv*) along with oxygen via a regular mask. The radial artery was also cannulated for blood pressure monitoring and arterial blood gas analyses. Intraoperatively, additional doses of 0.375% or 0.5% ropivacaine 5–6 mL were given through the catheter at two-hour intervals.

The epidural catheters were left in place postoperatively for continuous thoracic epidural analgesia with a continuous infusion of 0.15% ropivacaine $2\text{ mL}\cdot\text{hr}^{-1}$ with fentanyl $8\text{ }\mu\text{g}\cdot\text{hr}^{-1}$. Independent anesthesiologists checked for signs of Horner's syndrome (e.g., back pain, radiating symptoms [segmental pain or paresthesia corresponding to a dermatome of an epidural block spinal root], numbness, or muscle weakness) one and two hours and one, two, and three days postoperatively. Horner's syndrome was diagnosed by the occurrence of ptosis, miosis, or hyperemia (compared with the preoperative state and the contralateral side), with or without anhydrosis. When Horner's syndrome was suspected, a second experienced anesthesiologist confirmed the diagnosis, and the onset time, patient position, and ambulation were recorded. If the patients consented, a fluoroscopic examination of the spinal column was performed within five minutes of a 10 mL radiocontrast injection through the epidural catheter.

Any postoperative neurological complications related to epidural catheterization were recorded. Headache, postoperative nausea and vomiting (PONV), pruritus, and dizziness were also reported. In patients with any postoperative radicular-type pain at a level adjacent to the catheter insertion site, the epidural catheter was either withdrawn 1–2 cm or removed. The anesthesiologists increased the infusion rate when the analgesia was insufficient and decreased the rate or drug concentration when the patients complained of numbness, motor weakness, or dizziness. Any abnormal findings were recorded. With any positive neurological finding, a full neurological examination was performed by a consultant neurologist.

Data are presented as the absolute number and percentage (95% confidence interval [CI]). The statistical analyses were performed using SPSS® 12.0 (SPSS, Chicago, IL, USA), and the 95% CI was calculated by the Wald method.

Results

There were 633 eligible patients scheduled for mastectomy with or without breast reconstruction (Fig. 1). After exclusion, thoracic epidural anesthesia was offered to 527 patients. Seventy-seven of these patients did not consent to thoracic epidural catheter insertion and were excluded from

Fig. 1 Flow diagram

further study; therefore, 450 patients were enrolled in the study. The patients' ages ranged from 29 to 76 yr (median 50.5 yr; 95% CI 48.4 to 52.7), and all patients were female. The catheter was inserted at the T3-T4 level in 66% of patients and at the T4-T5 level in the remainder. Five patients complained of back discomfort during the epidural puncture or catheterization. The pain disappeared in two patients immediately after the procedure; however, we could not proceed with the procedure in the other three patients. Unsuccessful catheter placement (impossible to insert a catheter at two vertebral levels), unsuccessful epidural anesthesia (no verified sensory block), and dural puncture occurred in three (0.6%; 95% CI 0.0 to 1.6), two (0.4%; 95% CI 0.0 to 1.1), and two (0.4%; 95% CI 0.0 to 1.1) cases, respectively, and blood was present in the needle in one patient (0.2%; 95% CI 0.0 to 0.7). Therefore, we used intravenous instead of epidural analgesia in 11

Table 1 Clinical characteristics of patients with Horner's syndrome

Feature	Patient					
	1	2	3	4	5	6
Age (yr)	62	31	36	38	70	58
Breast operation side	right	left	left	left	right	left
Operation duration (min)	315	550	380	285	320	240
Thoracic level of catheter insertion	T3-4	T3-4	T3-4	T4-5	T4-5	T3-4
Position during surgery	supine	supine	supine	supine	supine	supine
Ambulation after surgery	yes	no	no	no	no	yes
Position when syndrome occurred	supine	supine	supine	supine	supine	supine
Catheter length inserted in the epidural space (cm)	10	10	10	8	10	10
Epidural anesthetic solutions	1	1	2	3	2	1
Onset time after surgery	POD 2	1.5 hr	0.5 hr	1 hr	POD 1	POD1
Time until signs disappeared (min)	30	60	60	180	40	30

Epidural anesthetic solutions: (1) 0.375% ropivacaine 15 mL bolus, 5 mL/2 hr infusion; (2) 0.375% ropivacaine 15 mL bolus, 6 mL/2 hr infusion; (3) 0.5% ropivacaine 15 mL bolus, 5 mL/2 hr infusion; POD = postoperative day

patients and performed successful epidural anesthesia in 439 patients (Fig. 1). The anesthesia and surgery were uneventful, and the patients were returned to the ward via the recovery room in stable condition with adequate analgesia.

Six of 439 patients acquired Horner's syndrome, for an incidence of 1.4% (95% CI 0.5 to 2.5). The onset time of the syndrome ranged from in the recovery room to the second postoperative day. All patients were in the supine position for a period of time before the syndrome occurred. In all six patients, all signs of Horner's syndrome resolved gradually and spontaneously within 30 to 180 min after the epidural infusion was stopped, at which point the patients were given intravenous ketorolac or fentanyl for pain control (Table 1). There were no residual signs or symptoms when the patients were examined after removing the epidural catheter. All six patients had unilateral ptosis and miosis with or without ocular

hyperemia. One patient complained of ipsilateral facial palsy; one patient had motor weakness of her ipsilateral arm, and three patients had paresthesias of their arms (ipsilateral arm in one patient and both arms in the other two patients) (Table 2). With permission from one patient with right-sided Horner's syndrome, we obtained a chest radiograph by injecting radiocontrast through the epidural catheter. The radiograph confirmed the spread of the drug into the epidural space and nerve root. The contrast spread asymmetrically to the first thoracic spinal nerve root on the left side and to the fifth cervical spinal nerve root on the right (Fig. 2).

Postoperative back pain, radiating symptoms (segmental pain or paresthesias corresponding to a dermatome of an epidural block spinal root), numbness, or muscle weakness presented in three (0.6%; 95% CI 0.0 to 1.6), 12 (2.7%; 95% CI 1.4 to 4.6), four (0.9%; 95% CI 0.2 to 1.8), and three (0.6%; 95% CI 0.0 to 1.6) patients, respectively. In

Table 2 Findings in patients with Horner's syndrome

Symptoms	Patient					
	1	2	3	4	5	6
Triad of Horner's syndrome	+	+	+	+	+	+
Side of Horner's syndrome	right	right	right	left	left	left
Ocular hyperemia	—	+	+	+	—	+
Upper extremity motor	intact	weakness	intact	intact	intact	intact
Upper extremity sensory	decreased	decreased	intact	intact	intact	intact
Upper extremity paresthesias	—	cold & tingling	heating	tingling	—	—
Other symptoms	right facial palsy	—	—	eye swelling	—	—
Other side effects	—	dizziness, nausea	—	—	—	—

Fig. 2 Anteroposterior (A) and oblique (B) fluoroscopic examinations of one patient with Horner's syndrome after injecting radiocontrast into the epidural catheter. The cervicothoracic spinal column shows contrast (arrows) in the epidural space and nerve roots. It spread to the first thoracic spinal nerve root on the left side and to the fifth cervical spinal nerve root on the right (the patient had unilateral Horner's syndrome on her right side)

all, three patients complained of headache (0.6%; 95% CI 0.0 to 1.6); 17 complained of PONV (3.9%; 95% CI 2.1 to 5.7); 5 complained of pruritus (1.1%; 95% CI 0.2 to 2.3), and 3 complained of dizziness (0.6%; 95% CI 0.0 to 1.6). Among these patients, 18 patients refused continued epidural infusions, and in the others, the symptoms always stopped shortly after either the epidural catheter was withdrawn or the epidural infusion was reduced. None of these problems required further treatment or had any long-lasting sequelae. No symptoms or signs suggesting epidural hematoma or meningeal inflammation were recognized. The epidural catheter was removed unintentionally in one patient, and two patients asked to have the epidural infusion stopped without giving specific reasons. The epidural infusion was discontinued in 21 patients within three days following the surgery.

Discussion

Six (1.4%) of 439 patients acquired acute transient unilateral Horner's syndrome following thoracic epidural anesthesia and continuous postoperative thoracic epidural analgesia for mastectomy. In all six patients, the signs of Horner's syndrome resolved completely and spontaneously

within three hours of stopping the epidural infusions. The incidence of the other complications related to epidural anesthesia were comparable with previous reports,⁷ and no permanent complication required further treatment in any patient during our study.

Most cases of Horner's syndrome after epidural block have been reported in pregnant women who received lumbar epidural anesthesia. Other studies have not identified Horner's syndrome as a complication of epidural anesthesia.^{10,11} In a 2010 report, Rabinovich *et al.*¹² assumed a 0.13% incidence of Horner's syndrome among 4,598 parturient women who received epidural anesthesia; however, since this was a case series report, this result could have been due to underreporting. In a prospective study conducted in 1983, Clayton *et al.*¹ reported an incidence of 1.33% among 150 labour patients. In our study, the 1.4% incidence of Horner's syndrome was comparable with their results, although, for anatomical reasons, we would have expected a higher incidence in thoracic epidural anesthesia than in lumbar epidural anesthesia. Epidural venous engorgement and elevated epidural pressure observed during pregnancy decrease the volume of epidural space and promote the upward spread of anesthetic solutions. Therefore, neuraxial block is relatively high in pregnant women, which might explain the similar incidence of Horner's syndrome following lumbar epidural anesthesia among labour patients. In addition, an increase in the likelihood of an unintentionally high neuraxial block could explain the relatively high incidence (2.6%) of Horner's syndrome in pediatric patients who receive thoracic epidural analgesia for control of postoperative pain.¹³

Horner's syndrome occurs when conduction in the sympathetic preganglionic B fibres is interrupted in the region of the C8-T2 roots innervating the eyes and face. Hence, the mechanism explaining the occurrence of Horner's syndrome after epidural anesthesia is the cephalic spread of the anesthetic along the epidural space. Gravity and posture can also affect the occurrence. In all our cases, the Horner's syndrome developed after the patient had been in a supine position for a sustained period of time. It is possible that subdural anesthesia could be the reason for an unintentionally high neuraxial block and Horner's syndrome. Nevertheless, there is no other evidence of subdural anesthesia in our reported cases, and the radiological finding in one patient confirmed that the drug had spread into the epidural space to the cervical level.

Horner's syndrome after thoracic epidural analgesia is not a severe complication and is self-limiting; however, it occurs unexpectedly and could cause considerable anxiety, especially if the patient is not given an immediate explanation. In addition, Horner's syndrome is an

indicator that the local anesthesia has spread to a high and unintended neuraxial level.² Therefore, although Horner's syndrome is not a severe complication itself, its significance should not be underestimated. The possibility of its occurrence after epidural anesthesia should be considered before any inappropriate investigations are initiated due to the misdiagnosis of a serious neurological complication such as stroke.

There were several limitations to this study. The surgery and level of epidural catheterization were well confined to an upper thoracic epidural level. In addition, all patients were female; therefore, caution should be exercised in extending this result to a fuller range of thoracic epidural anesthesia or to the male population. Nevertheless, most cases of Horner's syndrome are reported in parturient patients, so the sex limitation makes it easy to compare with lumbar cases.

In summary, there was a 1.4% incidence of Horner's syndrome following thoracic epidural anesthesia and continuous thoracic epidural analgesia for mastectomy. This result is similar to the 1.33% incidence of Horner's syndrome after lumbar epidural block reported for labouring patients.¹ The Horner's syndrome resolved completely and spontaneously in all patients within three hours. Based on the clinical course and radiological findings, we conclude that the mechanism of Horner's syndrome following thoracic epidural anesthesia and analgesia is cephalic spread of local anesthetic.

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Conflicts of interest There are no conflicts of interest.

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