pH Adjustment of mepivacaine decreases the incidence of tourniquet pain during axillary brachial plexus anaesthesia

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The effect of pH adjustment of mepivacaine on the incidence of tourniquet pain during axillary brachial plexus anaesthesia was studied. Thirty-nine patients scheduled for hand surgery, during which use of pneumatic tourniquet for longer than 60 min was planned, were randomized into two groups. Both received axillary brachial plexus block with 40 ml, 1.4% mepivacaine, 1:200,000 epinephrine. The study group had 4 ml sodium bicarbonate (1 mEq·ml⁻¹) added (final pH 7.31), and the control group had 4 ml saline added (final pH 5.6). The incidence of tourniquet pain was determined from cases for which tourniquet inflation lasted longer than 60 min. Tourniquet pain was defined as poorly localized and distinct from an inadequate axillary block by a blinded observer. More tourniquet pain occurred in the control group. The authors conclude that alkalization of mepivacaine for axillary brachial plexus anaesthesia may be indicated in cases where use of pneumatic tourniquet for long periods is planned.

Ce travail étudie les effets de l'ajustement du pH de la mepivacaine sur l'incidence des douleurs causées par le garrot pendant l'anesthésie du plexus brachial par voie axillaire. Trente-neuf patients programmés pour une chirurgie de la main au cours de laquelle un garrot gonflé pourrait être en place pour plus de soixante minutes, sont répartis au hasard entre deux

groupes. Les patients des deux groupes reçoivent un block axillaire réalisé avec 40 ml de mepivacaine 1,4% adrénalinée à 1:200,000. Pour le groupe d'étude, on ajoute à cette solution du bicarbonate de soude 4 ml (1 mEq·ml⁻¹) pour obtenir un pH de 7,31; pour le groupe contrôle, du soluté physiologique 4 ml pour un pH de 5,6. L'incidence des douleurs causées par le garrot est déterminée dans les cas où l'insufflation du garrot dure plus de 60 min. Un observateur neutre définit la douleur du garrot par une douleur mal localisée et distincte de celle d'un block sensoriel incomplet. La douleur du garrot est plus intense dans le groupe contrôle. Les auteurs concluent que l'alcalinisation de la mepivacaine pour le block axillaire pourrait être indiquée lorsqu'on prévoit des durées d'insufflation de garrot dépassant soixante minutes.

Key words

ANAESTHETIC TECHNIQUES: regional, axillary;
ANAESTHETICS, LOCAL: mepivacaine;
EQUIPMENT: tourniquets.

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Accepted for publication 10th October, 1992.

The use of pneumatic tourniquets to provide a bloodless field for upper extremity surgery is common. As with lower extremity use, the duration of use of arm tourniquets is limited by surgeons based on the potential for injury to underlying nerves, blood vessels, and muscle.¹⁻³ However, even within safe intervals, use of a pneumatic tourniquet can be associated with severe pain, refractory to treatment, during otherwise satisfactory regional anaesthesia. Tourniquet pain is known to occur during spinal,⁵⁻¹⁰ epidural,¹¹ and regional anaesthesia of the upper extremity.^{5,12} It occurs despite sensory and motor block adequate to allow skin incision, tissue dissection, and bone manipulation.⁶ The incidence of tourniquet pain is higher during lower extremity surgery than during upper extremity procedures.⁴ Nevertheless, upper extremity surgery with the use of pneumatic tourniquet under brachial plexus anaesthesia can be complicated by a poorly localized pain which is often refractory to treatment.

The incidence of tourniquet pain has been shown to be influenced by the regional anaesthetic technique and by the composition of the local anaesthetic solution. Spi-

nal anaesthesia is superior to epidural anaesthesia.¹¹ Bupivacaine is superior to tetracaine for spinal anaesthesia,⁹ and plain bupivacaine⁷ but not plain tetracaine¹³ is superior to the same solution made hyperbaric with the addition of glucose. Spinal anaesthesia is improved by the addition of epinephrine,* morphine,¹⁴ and clonidine.¹⁵

Alkalinization of mepivacaine has been shown to influence the behaviour of the agent in a variety of regional anaesthetic techniques.¹⁶⁻¹⁸ Recently, we demonstrated a decreased incidence of tourniquet pain during mepivacaine epidural anaesthesia with the alkalinized solution compared with mepivacaine without pH adjustment.¹⁹ The present study was designed to determine whether a similar decrease could be demonstrated during axillary brachial plexus anaesthesia for hand surgery.

Methods

After Institutional Review Board approval, written informed consent was obtained from 39 healthy patients scheduled for hand surgery during which pneumatic tourniquet use for greater than 60 min was anticipated and who had agreed to axillary brachial plexus anaesthesia. A standard adult pneumatic tourniquet was used, calibrated and inflated to 250 mmHg. All patients received axillary block, using a transarterial technique with injection posterior to the artery of 40 ml of 1.4% mepivacaine, 1:200,000 epinephrine. They were randomized into two groups by random card draw. The study group had 4 ml sodium bicarbonate (1 mEq · ml⁻¹, final pH 7.31) added to the solution prior to injection. The control group had the addition of 4 ml, preservative-free saline (final pH 5.6). The quality of the motor and sensory blocks was determined prior to incision, and partial or failed blocks were excluded from the study. Tourniquet pain was defined as a poorly localized upper extremity pain not associated with an inadequate, partial, or regressing axillary block; it was determined by an observer unaware of group assignment. Careful assessment of sensory and motor block was used to rule out block regression. Only non-narcotic sedation was used. If tourniquet pain was identified, treatment with fentanyl was initiated. General anaesthesia was employed if agitation prevented completion of surgery.

Data collected included sex, age, weight, duration of tourniquet inflation, incidence of tourniquet pain, length of tourniquet inflation at first detection of tourniquet

TABLE Results

	Study	Control	P
Sex (M/F)	7/12	11/9	NS
Age (yr, mean/SEM)	53.1 (9.8)	43.9 (6.8)	NS
Weight (kg, mean/SEM)	72.1 (6.0)	71.2 (5.3)	NS
Duration of tourniquet inflation (min, mean/SEM)	104 (9.3)	115 (10.6)	NS
Time at tourniquet pain (min, mean/SEM)	120 (8.6)	91.6 (12)	0.001†
Number with tourniquet pain	2	9	<0.05*
Number requiring general anaesthesia	0	3	0.001†

*Fisher's exact *P*-value.

†Wilcoxon Rank Sum *P*-value.

pain, and use of general anaesthesia for refractory pain. Demographics were compared with Student's *t* test and incidence of tourniquet pain with Fisher's exact test. Significance was considered to be *P* < 0.05.

Results

All blocks resulted in complete anaesthesia and motor block prior to incision. There were no intraoperative block failures. The pH of the plain solution was 5.56–5.60, saline added was 5.58–5.61, and bicarbonate was 7.30–7.34 in three determinations. The study group had more women than men and an older average age, although these differences were not statistically significant. The duration of tourniquet inflation was not different. The time at which tourniquet pain occurred was later in the study group. The incidence of tourniquet pain was higher in the control group, as was the number of patients who required general anaesthesia (Table).

Discussion

The results of this study further confirm the different incidence of tourniquet pain during various regional anaesthetic techniques. It is likely that those techniques which have a lower incidence of tourniquet pain must be more effective at interrupting whatever nociceptive cycle is involved in the aetiology of tourniquet pain.

Unlike the sensory and motor pathways which are involved in somatic blockade or surgical anaesthesia without the use of a pneumatic tourniquet, the pathway associated with tourniquet pain remains obscure. On a basic level, the pain mechanisms postulated by Melzack and Wall²⁰ could apply if larger fibres in the central axis were postulated to inhibit the central effect of the small a-delta and c-fibres which are thought to carry nociceptive tourniquet impulses. If the progression of the block occurred such that the larger fibres remained blocked and the smaller fibres (a-delta, c) became unblocked, a no-

*Gielen MJM, Meulman H, Van Beem H, Bridenbaugh PO. Does the addition of epinephrine to hyperbaric bupivacaine 0.5% in spinal anesthesia decrease the incidence of tourniquet pain (abstr). Proceedings of European Society of Regional Anaesthesia 1986, F3.

ciceptive impulse could be conducted. This is a plausible theory since conduction in a-delta and c-fibres has been shown to be increased by repetitive stimulation.¹⁹⁻²¹ The repetitive stimulus may be the persistent inflation of the pneumatic tourniquet.

Another theory relates to the idea that within an area of surgical anaesthesia, there may be differential degrees of blockade depending on nerve fibre types. Rocco *et al.*²² evaluated the level of blockade during spinal anaesthesia and compared the response to pinprick with that to light touch. There was no correlation between the level of anaesthesia to pinprick and onset of tourniquet pain of the lower extremity, but there was a good correlation between onset of tourniquet pain and a decreasing level of anaesthesia to light touch. They then postulated that these zones of differential blockade would be magnified more during regression of the block and that this magnification would correlate with the incidence of tourniquet pain being greater after 60–90 min of inflation. It may be that after prolonged inflation of the tourniquet, nerve fibres normally involved in conducting only light touch (a-beta) could become nociceptive in the presence of repetitive stimulus.²³ Chabel²⁴ provided support to this theory with an animal experiment that demonstrated activity in nerve fibres after tourniquet inflation which was not present prior to inflation, although it was not clear whether conduction followed somatic or autonomic pathways.

Some support for these theories of tourniquet pain can be derived from clinical experiments that delineate the different incidences of tourniquet pain based on anaesthetic technique. Concepcion *et al.*⁹ postulated that the advantage of bupivacaine over tetracaine was related to the known superiority of bupivacaine for prolonged blockade of the slow conductance c-fibres. Differential sensitivity of tetracaine and bupivacaine in c-fibres was demonstrated *in vitro* by Gissen,²⁵ further supporting this idea. In the experimental preparation, tetracaine blocked small fibres (c) became active sooner than fibres blocked with bupivacaine. Frequency-dependent block *in vitro* is also less effective with tetracaine than with bupivacaine.⁸ With the tourniquet being postulated at the repetitive stimulus, an enhancement of frequency-dependent block would probably lead to more effective blockade of tourniquet pain.

Differential blockade and differential sensitivity of nerve fibres may also explain why the results of this study of mepivacaine and upper extremity tourniquet pain, as well as previous work¹⁹ demonstrate that pH-adjusted mepivacaine decreases the incidence of tourniquet pain. Alkalinization alters the clinical behaviour of mepivacaine. Several studies have shown a decrease in latency to onset of blockade.^{16,18} Candido *et al.*¹⁷ demonstrated

improved duration of anaesthesia, which could be postulated to be related to improved diffusion into larger nerve fibres. This was confirmed by McMorland *et al.*^{26,27} using bupivacaine, who noted prolonged duration of epidural analgesia and anaesthesia with bupivacaine. The influence of alkalinization of local anaesthesia is thought to occur secondary to the considerable increase of the non-ionized form in the solution prior to injection. Also, the greatly increased concentration of carbon dioxide in the solution when exposed to the nerve cell membrane rapidly diffuses inside the cell. This rapid diffusion decreases the intracellular pH which further increases the concentration gradient of the non-ionized form of the local anaesthetic molecule into the cell. The actual PCO₂ of the solution influences this effect.²⁸ Enhanced diffusion may prevent dilution of the effective concentration of the local anaesthetic by mixing with extracellular fluid. This increase in relative concentration of the local anaesthetic may be involved in the differentially increased effectiveness of the alkalinized solution at providing the kind of blockade which later is more effective in preventing tourniquet pain. Another possibility is that frequency-dependent block may be facilitated by the increased concentration of the agent effectively delivered to the nerve fibres.

In summary, the incidence of tourniquet pain during upper extremity surgery using axillary brachial plexus anaesthesia decreases when mepivacaine is alkalinized with bicarbonate. Because the incidence of tourniquet pain becomes high during upper extremity surgery when inflation with pneumatic tourniquet exceeds 60 min, pH-adjusted mepivacaine may be indicated in these cases.

References

- 1 Heppenstall RB, Balderson R, Goodwin C. Pathyophysiological effects distal to a tourniquet in the dog. *J Trauma* 1979; 19: 234–8.
- 2 Rorabeck CH, Kennedy JC. Tourniquet-induced nerve ischemia complicating knee ligament surgery. *Am J Sports Med* 1980; 8: 98–102.
- 3 Flatt AE. Tourniquet time in hand surgery. *Arch Surg* 1972; 104: 190–2.
- 4 Gielen MJM, Stienstra R. Tourniquet hypertension and its prevention: a review. *Reg Anesth* 1991; 16: 191–4.
- 5 Valli H, Rosenberg PH, Kyttä J, Nurminen M. Arterial hypertension associated with the use of a tourniquet with either general or regional anaesthesia. *Acta Anaesthesiol Scand* 1987; 31: 279–83.
- 6 Ebert LD, Deas TC. Cause of tourniquet pain from a pneumatic tourniquet during spinal anesthesia. *Anesthesiology* 1962; 23: 287–90.
- 7 Bridenbaugh PO, Hagenouw RRPW, Gielen MJM, Edström HH. Addition of glucose to bupivacaine in spinal

- anesthesia increases incidence of tourniquet pain. *Anesth Analg* 1986; 65: 1181-5.
- 8 *Stewart A, Lambert DH, Concepcion MA, et al.* Decreased incidence of tourniquet pain during spinal anesthesia with bupivacaine. A possible explanation. *Anesth Analg* 1988; 67: 833-7.
 - 9 *Concepcion MA, Lambert DH, Welsh KA, Covino BG.* Tourniquet pain during spinal anesthesia: a comparison of pain solutions of tetracaine and bupivacaine. *Anesth Analg* 1988; 67: 833-7.
 - 10 *Rocco AG, Concepcion M, Sheskey MC, et al.* A double-blind evaluation of intrathecal bupivacaine without glucose and a standard solution of hyperbaric tetracaine. *Reg Anesth* 1984; 9: 1-7.
 - 11 *Pitkanen MJ, Tuominen MK, Rosenberg PH.* Bupivacaine spinal anesthesia compared with etidocaine epidural anesthesia for orthopedic surgery in young and old patients. *Reg Anesth* 1985; 10: 62-7.
 - 12 *Farah RS, Thomas PS.* Sympathetic blockade and tourniquet pain in surgery of the upper extremity. *Anesth Analg* 1987; 66: 1033-5.
 - 13 *Bonnet F, Zozime JP, Marcandoro J, Buisson VB, Touboul C, Saada M.* Tourniquet pain during spinal anesthesia. Hyperbaric versus isobaric tetracaine. *Reg Anesth* 1988; 13: 29-33.
 - 14 *Tuominen M, Valli H, Kalso E, Rosenberg PH.* Efficacy of 0.3 mg morphine intrathecally in preventing tourniquet pain during spinal anaesthesia with hyperbaric bupivacaine. *Acta Anaesthesiol Scand* 1988; 32: 113-6.
 - 15 *Bonnet F, Diallo A, Saada M, Belon M, Guilbaud M, Boico O.* Prevention of tourniquet pain by spinal isobaric bupivacaine with clonidine. *Br J Anaesth* 1989; 63: 93-6.
 - 16 *Capogna G, Celleno D, Tagariello V.* The effect of pH adjustment of 2% mepivacaine on epidural anesthesia. *Reg Anesth* 1989; 14: 121-3.
 - 17 *Candido KD, Roza SM, Vasireddy AR.* pH adjusted mepivacaine for lower extremity conduction anesthesia. *Reg Anesth* 1989; 14: A68.
 - 18 *Tetzlaff JE, Yoon HJ, O'Hara J, Reaney J, Stein D, Grimes-Rice M.* Alkalinization of mepivacaine accelerates onset of interscaline block for shoulder surgery. *Reg Anesth* 1990; 15: 242-4.
 - 19 *Tetzlaff JE, Yoon HJ, Baird B, Walsh M, Hondorp G.* Alkalinization of mepivacaine for epidural anaesthesia decreases the incidence of tourniquet pain. *Can J Anaesth* 1991; 38: A61.
 - 20 *Melzack R, Wall PD.* Pain mechanisms: a new theory. *Science* 1965; 150: 971-9.
 - 21 *Strichartz G, Zimmerman M.* An explanation for pain originating from tourniquets during regional anesthesia. *Reg Anesth* 1984; 9: 44-5.
 - 22 *Rocco AG, Raymond SA, Murray E, Dhingra U, Freiburger D.* Differential spread of blockade of touch, cold, and pinprick during spinal anesthesia. *Anesth Analg* 1985; 64: 917-23.
 - 23 *Campbell JN, Raja SN, Meyer RA, Mackimmon SE.* Myelinated afferents signal the hyperalgesia associated with nerve injury. *Pain* 1988; 32: 89-4.
 - 24 *Chabel C, Russell LC, Lee R.* Tourniquet-induced limb ischemia: a neurophysiologic animal model. *Anesthesiology* 1990; 72: 1038-44.
 - 25 *Gissen AJ, Covino BG, Gregus J.* Differential sensitivities of mammalian nerve fibers to local anesthetic agents. *Anesthesiology* 1980; 53: 467-74.
 - 26 *McMorland GH, Douglas MJ, Jeffery WK, et al.* Effect of pH-adjustment of bupivacaine on onset and duration of epidural analgesia in parturients. *Can Anaesth Soc J* 1986; 33: 537-41.
 - 27 *McMorland GH, Douglas MJ, Axelson JE.* The effect of pH-adjustment of bupivacaine on onset and duration of epidural anaesthesia for Caesarean section. *Can J Anaesth* 1988; 35: 457-61.
 - 28 *Ackerman WE, Juneja MM, Denson DD, et al.* The effect of pH and PCO₂ on epidural analgesia with 2% 2-chloroprocaine. *Anesth Analg* 1989; 68: 593-8.