

Does the addition of morphine to brachial plexus block improve analgesia after shoulder surgery ?

N. FLORY, E. VAN-GESSEL, F. DONALD, P. HOFFMEYER AND Z. GAMULIN

Summary

We have studied 40 patients undergoing elective shoulder surgery for chronically painful conditions. Patients were allocated randomly to two groups and received interscalene brachial plexus block with 0.5% bupivacaine and adrenaline 1/200 000 40 ml either alone or with the addition of morphine 5 mg. All patients also received a general anaesthetic. The quality of the block, analgesic requirements and any complications or side effects were noted in the intraoperative period and during the 48 h after operation. No significant difference was seen in quality of analgesia or patient satisfaction between the two groups. (*Br. J. Anaesth.* 1995; 75: 23–26)

Key words

Analgesics opioid, morphine. Anaesthetic techniques, regional, brachial plexus. Surgery, orthopaedic.

Numerous studies have investigated nociception and the action of morphine derivatives at peripheral opioid receptors. While it is true that our knowledge of the physiology of these receptors has been advanced greatly by animal studies [1–11], few controlled clinical trials have been reported. They are difficult to compare as they involve a diversity of methodologies, anatomical substrates and types of pain. Perineural injection of morphine has been used for postoperative analgesia after elective surgery involving the foot [12, 13], knee [14] and forearm or hand [15, 16], and injection of morphine around free nerve endings has been evaluated in the context of arthroscopic surgery to the knee [17, 18]. In none of these studies was the type of pain (i.e. acute or chronic), or the presence or absence of an inflammatory reaction specified. This is important as animal studies have shown that the presence of inflammation favours the expression of peripheral opioid receptors [4, 9, 11].

We have performed a double-blind, randomized trial in patients with chronic shoulder pain for which surgical treatment was necessary. By adding morphine 5 mg to the solution used for interscalene brachial plexus block, we assessed the peripheral effect of this opioid on postoperative analgesia.

Patients and methods

The study was approved by the hospital Ethics Committee and 40 patients of both sexes were recruited after obtaining informed consent. All were

undergoing elective shoulder surgery; 35 for suture of the rotator cuff, four for humeral prosthesis insertion and one for osteosynthesis of the shoulder. They were randomized to one of two groups: placebo and morphine. Exclusion criteria were: ASA III, inability to understand the requirements of the protocol for reasons of language or intellect, proposed minor surgery and pain of less than 2 weeks' duration.

Patients received midazolam 7.5 mg orally as premedication. In the anaesthetic room standard monitoring of vital signs was instituted (ECG, non-invasive measurement of arterial blood pressure with a humeral cuff and pulse oximetry). A 17-gauge venous cannula was placed in the non-operated arm.

Interscalene brachial plexus block was carried out with the patient awake and positioned according to the method described by Winnie and Collins [19]. We used a 23-gauge short-bevel pole needle, connected to a nerve stimulator which was set to deliver impulses of 0.2–5 mA (frequency 1 Hz, 50–500 μ s duration). The needle was considered to be placed correctly when contraction of either the biceps or muscle groups in the forearm was seen in response to stimuli of approximately 0.4 mA. The needle was then held immobile and, after aspiration to exclude intravascular placement, the local anaesthetic mixture was injected. All patients received an injection of 0.5% bupivacaine with adrenaline 1/200 000 40 ml followed by either morphine 5 mg made up to 5 ml with 0.9% NaCl or 0.9% NaCl 5 ml alone. The treatment choice was made in a double-blind, randomized fashion.

The quality of block was assessed every 5 min for 15 min after injection of local anaesthetic. This evaluation took the form of testing shoulder pain on passive movement and motor force of the upper limb involved. The block was described as complete if the patient was unable to move his shoulder and experienced no pain on passive movement after 15 min, partial if motor force and pain were diminished but not absent totally, doubtful if one or other variable was diminished, and non-existent if there was no change in either value. General anaesthesia was then induced in all patients using a standard procedure: after preoxygenation for 3 min,

NICOLAS FLORY, MD, ELISABETH VAN-GESSEL, MD, FIONA DONALD, MB, CHB, FRCA, ZDRAVKO GAMULIN, MD, PD (Department of Anaesthesia); PIERRE HOFFMEYER, MD, PD (Department of Orthopaedic Surgery); University Hospital of Geneva, 24, rue Micheli-du-Crest, 1211 Geneva 14, Switzerland. Accepted for publication: February 27, 1995.

fentanyl 0.1–0.15 mg was injected followed by sodium thiopentone of 3–5 mg/kg body weight. Neuromuscular block was achieved with vecuronium 0.1 mg/kg body weight and the trachea intubated. Anaesthesia was maintained with 0.6–0.8% iso-flurane.

During surgery, heart rate, peripheral oxygen saturation (Sa_{O_2}), fractional inspired oxygen concentration ($F_{I_{O_2}}$) and fractional expired carbon dioxide concentration ($F_{E'_{CO_2}}$) were measured continuously and arterial pressure was measured every 5 min. The anaesthetist assessed the quality of analgesia and was free to give supplementary doses of fentanyl if deemed necessary. If the total dose of fentanyl received during anaesthesia was greater than 0.15 mg, the block was considered to be a failure. At the end of operation the patient was taken to the recovery room where assessment of the block was carried out as in the preoperative period and any undesirable effects were noted. Analgesic requirements were evaluated using a visual analogue scale (VAS). Postoperative analgesics consisting of diclofenac 75 mg i.m., morphine 6–10 mg s.c., or both, were given in response to a VAS score of greater than 3. Assessments were made every hour for the first 6 h and 4-hourly thereafter, and continued until 48 h after the start of anaesthesia. Patient satisfaction was measured also.

Data are presented as mean (SD) or median (range). Continuous variables were compared with the unpaired Student's *t* test and ordinal data were analysed using the Mann-Whitney *U* test or chi-square test as required. *P* less than 0.05 was considered significant.

Results

Data were collected over a period of 11 months. There were no significant differences in age, body weight or sex distribution between the two groups (table 1). All interscalene brachial plexus blocks were carried out under the supervision of the same anaesthetist. Table 2 shows the results of the preoperative and immediate postoperative evaluation of the blocks. After operation only 35 of the 40 patients were assessed as five were too sedated. There were no significant differences between the two groups.

Mean duration of surgery and haemodynamic variables at the moment of skin incision are shown in table 3. There were no significant differences between the two groups. No block was considered to have failed in the intraoperative period as no patient received more than fentanyl 0.15 mg.

Shortly after arriving in the recovery room, seven patients complained of pain at the operative site

Table 1 Patient characteristics (mean (range or SD) or number). MAP = Mean arterial pressure. No significant differences between groups

	Placebo group (<i>n</i> = 20)	Morphine group (<i>n</i> = 20)
Age (yr)	52 (21–82)	51 (23–70)
Weight (kg)	72 (17)	73 (12)
Sex (M/F)	12/8	9/11
ASA I/II	4/16	7/13
MAP (mm Hg)	98(14)	96(11)

Table 2 Characteristics of interscalene block before induction and after surgery (*n* = 20 in each group). No significant differences

	Placebo group	Morphine group
Preoperative		
Complete	3	6
Partial	17	13
Doubtful	0	1
No block	0	0
Postoperative		
Complete	13	9
Partial	6	6
Doubtful	0	0
No block	0	1

Table 3 Preoperative variables (mean (SD)) (*n* = 20 in each group). MAP = Mean arterial pressure

	Placebo group	Morphine group
Duration of surgery (min)	81 (31)	78 (16)
MAP at incision (mm Hg)	81 (13)	74 (31)
Heart rate at incision (beat min ⁻¹)	68 (12)	70 (12)

Table 4 Postoperative analgesic data (mean (SD) or range) over 48 h (*n* = 20 in each group)

	Placebo group	Morphine group
VAS score of initial pain (scale 0–10)	5 (3–10)	5 (3–8)
Time of first analgesic intervention (min)	742 (356)	772 (425)
Total number of analgesic interventions/patient	5.2 (2.8)	5.0 (2.7)
Total dose of morphine (mg)	17 (19)	17 (17)
Total dose of diclofenac (mg)	193 (80)	184 (106)

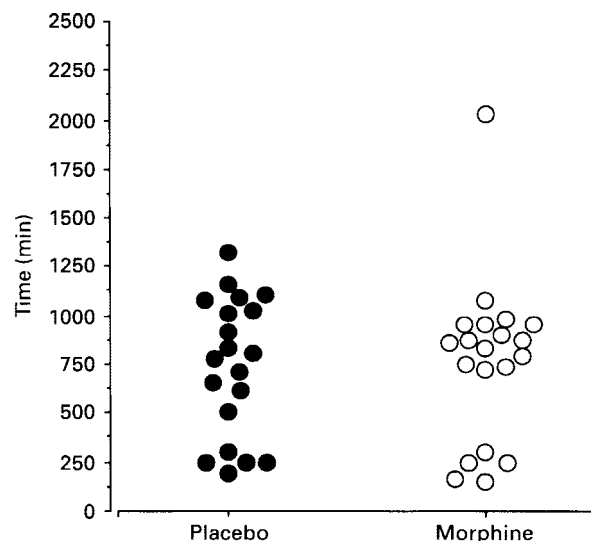


Figure 1 Time from end of operation to the first administration of analgesic in the placebo and morphine groups.

(four in the placebo and three in the morphine group). Table 4 and figure 1 show that there was very little difference between the two groups as to the

time at which the first analgesics were given. The same was true for the intensity of the first pain and the number and total doses of analgesics given. Individual analysis of analgesic requirements over 48 h failed to reveal any significant difference also.

We observed clinically relevant diaphragmatic paralysis in three (7.5 %) of our patients and in one case the patient became dyspnoeic and required oxygen by mask. Two (5 %) patients developed Horner's syndrome which lasted less than 24 h. We saw no cases of dysphonia as a result of recurrent laryngeal nerve paresis. The most common undesirable effects were nausea and vomiting. This occurred in 15 (38 %) patients (five in the placebo, 10 in the morphine group). Three (7.5 %) patients, all in the placebo group, complained of thoracic pruritis, and one (5 %) patient in each group required catheterization because of acute urinary retention.

Discussion

The results of our study suggest that the addition of morphine 5 mg to interscalene brachial plexus block does not improve the quality of intraoperative analgesia, prolong the effect of the block or decrease the requirements for analgesia in the first 48 h after operation.

It has been suggested that the action of opioids injected into the perineural sheath may be central rather than peripheral as a result of transport into the extradural and subarachnoid spaces either by diffusion or by centripetal axonal transport. This is theoretically possible as the perineural sheath is anatomically an extension of the prevertebral fascia. Such transport would thus be easiest for those agents injected closest to the spinal cord. In the case of opioids it would then become possible to induce analgesia via the mu, kappa and delta receptors found in the dorsal horn of the spinal cord. This theory has been invoked to explain how analgesia lasting 36 h was reported after interscalene injection of morphine 5 mg for a patient suffering from chronic pain [20]. However, Dahl and colleagues [14], who compared the effect of morphine injected extradurally with that injected periferorally, concluded that if centripetal axonal transport existed it was not clinically significant. Daugaard, Dahl and Christensen [21] have confirmed that morphine concentrations in cerebrospinal fluid are similar after periferoral or i.m. injection.

Animal studies have highlighted the role of inflammation in the expression of peripheral antinociceptive opioid receptors. Not only are the receptors more active, but certain types may be more frequent according to the type of inflammatory process present. In humans, the peripheral action of opioids has been studied largely in the context of postoperative pain and none of these studies has mentioned the presence or absence of inflammatory phenomena. Only one study has examined the effect of perineural injection of morphine in chronic pain. In this double-blind study, Mays, Lipman and Schnapp [22] reported improved analgesia after morphine 6 mg.

If the above theories are true we would have

expected to see improved postoperative analgesia in our study as all of our patients suffered from chronic pain which was, for the majority, inflammatory in nature and the opioid was injected at a site close to the central nervous system. This was not the case. One possible explanation for this is that the use of a long-acting local anaesthetic agent may have masked the effect of morphine.

It is also possible that opioids have differing effects at peripheral sites as it is known that there are differences in their affinities for the receptor. Fentanyl and morphine have similar affinities for mu receptors but fentanyl and pethidine have much greater affinity for delta and kappa receptors [23]. Gobeaux and colleagues have published two studies involving the use of axillary brachial plexus block with the addition of an opioid. In the first [24], fentanyl 0.1 mg was added to adrenalized lignocaine and a significant reduction in time to onset of the block was achieved, although its duration was not prolonged. In the second [25], the use of pethidine 100 mg resulted in prolongation of the block but no change in onset time. However, Racz and colleagues [15] added morphine 5 mg to axillary brachial plexus block with adrenalized lignocaine and observed no effect. In none of these studies was the nature of the surgery or the type of pain specified. Another factor which should perhaps be taken into consideration is the much greater lipid solubility of fentanyl and pethidine compared with morphine. This may allow greater distribution at the site of action as afferent nociceptive fibres are surrounded by a layer of myelin which presents a significant obstacle to water soluble agents. However, it should be noted that the doses of opioid used by Gobeaux and colleagues were twice those used by Racz and colleagues and ourselves when expressed in terms of potency.

In the literature, success rates for interscalene brachial plexus block range from 82 to 98 % [26]. We had no failures in a group of 40 patients. The principal morbidity associated with this type of block is a 100 % incidence of ipsilateral hemidiaphragmatic paralysis [27, 28] and our finding of clinically evident paralysis in 7.5 % of patients seems acceptable. We are in agreement with Urmeý, Tatts and Sharrock [27] who described diaphragmatic paralysis as an expected sequelae of the block rather than a complication.

Further work is needed to define the role of peripherally acting opioids in this situation. What is clear from our study is that interscalene brachial plexus block with 0.5 % bupivacaine and adrenaline 40 ml gives satisfactory postoperative analgesia for a mean of 11.2 h. Major shoulder surgery can be very painful and the use of such a block remains a valid anaesthetic technique.

References

1. Stein C, Millan MJ, Shippenberg TS, Herz A. Peripheral effect of fentanyl upon nociception in inflamed tissue of the rat. *Neuroscience Letters* 1988; **84**: 225-228.
2. Laduron PM. Axonal transport of opiate receptors in capsaicin sensitive neurones. *Brain Research* 1984; **294**: 157-160.

3. Young WS, Wamsley JK, Zarbin MA, Kuhar MJ. Opioid receptors undergo axonal flow. *Science* 1980; **210**: 76–77.
4. Stein C, Hassan AHS, Przewlocki R, Gramsch C, Peter K, Herz A. Opioids from immunocytes interact with receptors on sensory nerves to inhibit nociception in inflammation. *Proceedings of the National Academy of Sciences USA* 1990; **87**: 5935–5939.
5. Russel NJW, Schaible HG, Schmidt RF. Opiates inhibit the discharges of fine afferent units from inflamed knee joint of the cat. *Neuroscience Letters* 1987; **76**: 107–112.
6. Frank GB. Stereospecific opioid drug receptors on excitable cell membranes. *Canadian Journal of Physiology and Pharmacology* 1985; **63**: 1023–1032.
7. Lembeck F, Donnerer J. Opioid control of the function of primary afferent substance P fibres. *European Journal of Pharmacology* 1985; **114**: 241–246.
8. Ferreira SH, Nakamura M. Prostaglandin hyperalgesia: The peripheral analgesic activity of morphine, enkephalins and opioid antagonists. *Prostaglandins* 1979; **18**: 191–200.
9. Stein C, Millan MJ, Yassouridis A, Herz A. Antinociceptive effects of mu and kappa agonists in inflammation are enhanced by a peripheral opioid receptor-specific mechanism. *European Journal of Pharmacology* 1988; **155**: 255–264.
10. Levine JD, Taiwo YO. Involvement of the mu-opiate receptor in peripheral analgesia. *Neuroscience* 1989; **32**: 571–575.
11. Parsons CG, Czlonkowski A. Peripheral opioid receptors mediating antinociception in inflammation. Activation by endogenous opioids and role of the pituitary-adrenal axis. *Pain* 1990; **41**, 81–93.
12. Bullingham RES, McQuay HJ, Moore RA. Studies on the peripheral action of opioids in postoperative pain in man. *Acta Anaesthesiologica Belgica* 1984; **35**: 285–290.
13. Bullingham R, O'Sullivan G, McQuay HJ, Poppleton P, Marney R, Evans P, Moore M. Perineural injection of morphine fails to relieve postoperative pain in humans. *Anesthesia and Analgesia* 1983; **62**: 164–167.
14. Dahl JB, Daugaard JJ, Kristoffersen E, Johannsen HV, Dahl JA. Perineural morphine: a comparison with epidural morphine. *Anaesthesia* 1988; **43**: 463–465.
15. Racz H, Gunning K, Della Senta D, Forster A. Evaluation of the effect of perineural morphine on the quality of postoperative analgesia after axillary plexus block: a randomized double-blind study. *Anesthesia and Analgesia* 1991; **72**: 769–772.
16. Viel EJ, Eledjam JJ, De La Coussaye JE, D'Athis F. Brachial plexus block with opioids for postoperative pain relief: comparison between buprenorphine and morphine. *Regional Anesthesia* 1989; **14**: 274–278.
17. Stein C, Comisel K, Haimerl E, Yassouridis A, Lehrberger K, Herz A, Peter K. Analgesic effect of intraarticular morphine after arthroscopic knee surgery. *New England Journal of Medicine* 1991; **325**: 1123–1126.
18. Khoury GF, Chen ACN, Garland DE, Stein C. Intraarticular morphine, bupivacaine, and morphine/bupivacaine for pain control after knee videoarthroscopy. *Anesthesiology* 1992; **77**: 263–266.
19. Winnie AP, Collins VJ. The subclavian perivascular technique of brachial plexus anesthesia. *Anesthesiology* 1964; **25**: 353–363.
20. Sanchez R, Nielsen H, Heslet L, Iversen AD. Neuronal blockade with morphine. *Anaesthesia* 1984; **39**: 788–789.
21. Daugaard JJ, Dahl JB, Christensen CB. Concentrations of morphine in the cerebrospinal fluid after femoral perineural morphine administration. *Anesthesia and Analgesia* 1989; **68**: 413.
22. Mays KS, Lipman JJ, Schnapp M. Local analgesia without anesthesia using peripheral perineural morphine injections. *Anesthesia and Analgesia* 1987; **66**: 417–420.
23. Paterson SJ, Robson LE, Kosterlitz HW. Classification of opioid receptors. *Medical Bulletin* 1983; **39**: 31–36.
24. Gobeaux D, Landais A, Bexon G, Cazaban J, Levron JG. Adjonction de fentanyl à la lidocaïne adrénalinée pour le blocage du plexus brachial. *Cahiers d'Anesthesiologie* 1987; **35**: 195–199.
25. Gobeaux D, Landais A. Utilisation de deux morphiniques dans les blocs du plexus brachial. *Cahiers d'Anesthesiologie* 1988; **36**: 437–440.
26. Conn RA, Cofield RH, Byer DE, Linstromberg J.W. Interscalene block anesthesia for shoulder surgery. *Clinical Orthopaedics and Related Research* 1987; **216**: 94–98.
27. Urmey WF, Talts KH, Sharrock NE. One hundred percent incidence of hemidiaphragmatic paresis associated with interscalene brachial plexus anesthesia as diagnosed by ultrasonography. *Anesthesia and Analgesia* 1991; **72**: 498–503.
28. Urmey WF, Gloeggler PJ. Pulmonary function changes during interscalene brachial plexus block: effects of decreasing local anesthetic injection volume. *Regional Anesthesia* 1993; **18**: 244–249.