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ASPECTS OF TREATMENT*

Post-thoracotomy pain relief: combined use of cryoprobe and morphine infusion techniques

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Summary

In a reported study we found that freezing of the intercostal nerves under direct vision at thoracotomy provided better postoperative analgesia than im morphine on demand. Infusions of morphine were also more effective than when used by the intramuscular route. The benefit on the eighth postoperative day was greatest following the use of the cryoprobe. Further studies were carried out to evaluate the benefit of combining 'cryoprobe' analgesia with infusions of morphine. The combined use of morphine infusion and a cryoprobe did not produce greater postoperative pain relief than the use of the cryoprobe alone with im morphine on demand.

Introduction

In a published study from this department *(1)* cryoanalgesia was compared with morphine infusion and with a 'control' group for post-thoracotomy pain relief. Patients were allocated randomly to one of three groups: in each, conduction in the affected intercostal nerves was blocked with bupivacaine or frozen under direct vision at the end of the operation. The first analgesia given on demand consisted of the slow intravenous injection of morphine until either pain was relieved or 20 mg had been given. The subsequent analgesia was as follows:

Group	*Intercostal nerve block*	*First 24 h postoperation*
Control	Bupivacaine	Im morphine on request
Infusion	Bupivacaine	Morphine infusion, supplemented on request
Cryoprobe	Freezing	Im morphine on request

After 24 h patients were given intramuscular morphine or oral dihydrocodeine depending on the nurse's assessment of pain severity. After 48 h only oral dihydrocodeine was available but the amounts used were not recorded.

It was shown that during the first 48 h after the operation there was a clear benefit in pain relief with both the *cryoprobe* and *infusions* when compared with the *control* series in whom the beneficial effects of bupivacaine were trivial. There also seemed to be a possible difference in pain relief between the cryoprobe and infusion groups but the statistical tests did not show a significant advantage of one over the other. At the eighth day after operation there was no difference between the degree of pain in the control and infusion groups but the cryoprobe group of patients had lower average pain scores at rest, although the difference was not significant.

We report here an extension of the study, the objective of which was to assess any benefit of combining morphine infusion with cryoanalgesia when compared with either treatment alone. We also aimed at determining if the apparent benefit of cryoanalgesia late in the postoperative course represented a true benefit or if it was simply an artifact of sampling variation.

More patients were needed for both these purposes. However, for ethical reasons we discontinued the control group since we had shown that this treatment was inferior to the other two. As will be seen later, for practical reasons, we include the findings in the published study with the second part (Table I).

TABLE I *Number of patients in total study*

	Controls	*Infusion*	*Cryoprobe*	*Infusion plus cryoprobe*
Initial study	15	15	15	—
Extension	—	8	8	23
Total cases	15	23	23	23
Combined groups	38		46	

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The Editor would welcome any comments on this paper by readers

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Patients and methods

The patients, aged 25–70 yr, and conforming to grades 1–3 of physical fitness *(2)*, were divided into three groups, after informed consent was obtained. The methods and techniques of measurement were identical to those previously reported *(1)*. In brief, patients scheduled for thoracotomy on a routine thoracic operating list were given a sedative premedication and a balanced anaesthetic technique was used, which included a weight-related dose of morphine. At the end of surgery, five or six intercostal nerves were frozen for 60 s with a cryoprobe (Spembly Ltd, Andover, Hants) (*cryoprobe* and *cryoprobe plus infusion* groups) or anaesthetised with 0.5% bupivacaine (*infusion* group).

In the recovery ward analgesia when required was initially provided by titration of intravenous morphine until pain was relieved or 20 mg given. Thereafter in the *cryoprobe* group morphine was given intramuscularly on demand using a simple weight-related dosage scale. In the *infusion* and *cryoprobe plus infusion* groups analgesia thereafter was provided by morphine delivered by a constant infusion pump. The initial rate of delivery was determined in relation to the patient's weight and age (40–59 kg, morphine 1 mg h^{-1}; 60–79 kg, morphine 1.25 mg h^{-1}; 80–99 kg, morphine 1.5 mg h^{-1}: the dose was reduced by 25% for patients over 60 years of age). The rate was increased if the patient requested more analgesia, or decreased if the nurse thought the patient was overdrowsy. If the nurse thought analgesia was *very* inadequate she could give morphine 5 mg intramuscularly. The infusions were stopped at noon on the first postoperative day and analgesia thereafter was given by the intramuscular route on request.

This trial involved the same investigator, anaesthetic technique and postoperative environment as already reported so the results available from the 15 infusion group and 15 cryoprobe group patients involved in the first randomised controlled trial *(2)* are included in the analyses. A further 8 infusion group patients, 8 cryoprobe group patients and 23 cryoprobe plus infusion group patients were involved in the continued study (Table I), the treatments of these 39 patients being allocated at random. Prior to the final analysis, it was shown that the findings with the first 15 and subsequent 8 patients in the appropriate groups did not differ significantly.

MEASUREMENTS

Severity of pain at rest and on movement was graded by each patient on 10 cm visual analogue scales *(3)* on seven occasions during the first 24 h after operation and on the second and eighth postoperative days, when peak expiratory flow rate (PFR) was also measured. The eighth day was chosen as some patients would have been discharged after this. Furthermore, it was felt that this was a reasonable time to assess the long-term effects of the cryoprobe since the effects of the early large dose of morphine would have worn off and patients would not be requiring potent analgesia.

Chest physiotherapy was applied on four occasions during the first 24 h after operation, at which time the PFR was tested and the pain experienced during physiotherapy was graded by patients on visual analogue scales. The physiotherapist also graded an impression of the patient's attempts at coughing (5 = none, 4 = some, 3 = fair, 2 = good, 1 = very good).

STATISTICAL METHODS

The three study groups were tested for comparability of age, height and weight using one-way analysis of variance and for comparability of sex distribution by the chi-squared test for contingency tables.

All visual analogue scores were subjected to an arc sine transformation because the finite limits of the visual analogue scale constrained the distribution of scores *(4)*. Mean visual analogue scores are presented graphically for the sake of comparison with other studies but statistical results apply to transformed values.

Repeated measures analyses of variance were used to compare transformed values obtained for pain at rest and pain on moving at the seven different times between 3 h postoperatively and 12 noon on the second postoperative day (inclusive) and to compare transformed values obtained for pain of physiotherapy and untransformed values of PFR (expressed as a percentage of preoperative values) obtained at the four physiotherapy sessions.

The transformed values for pain at rest and pain on moving and the untransformed values for percentage PFR obtained on the eighth day from all 46 patients who had cryoanalgesia and all 38 patients who had bupivacaine intercostal nerve blocks at the time of operation were compared using independent sample *t*-tests.

The opinions of the physiotherapists are presented in simple tabular form only.

Results

Table II shows the physical characteristics of the 23 patients in each group. There was no evidence of significant differences in mean age or height or in the sex distribution in the three groups. However, there was a statistically significant difference in mean weight ($F2,66 = 3.48$; $P = 0.04$).

Analysis of transformed scores obtained between 3 h after recovery and 12 noon on the second postoperative day showed that there were no significant differences between groups with respect to pain at rest ($F2,66 = 0.251$; $P = 0.78$) (Fig. 1), pain on movement ($F2,66 = 1.13$; $P = 0.33$) (Fig. 2) or pain of physiotherapy ($F2,66 = 1.28$; $P = 0{\cdot}28$) (Fig. 3).

Transformed scores for pain at rest and pain on moving on the eighth day showed that the group who had cryoanalgesia had significantly less pain at rest than the non-cryoanalgesia group ($P = 0.06$) though there were no significant differences when comparing pain on movement (Table III).

Analysis of percentage PFR values measured during the first 24 h showed no significant differences between groups ($F2,66 = 1.89$; $P = 0.16$) (Table III). Percentage PFR values on the eighth day did not show any difference between the cryoanalgesia and non-cryoanalgesia groups (Fig. 2).

The number of times coughing was rated as good or very good was highest in the cryoprobe plus infusion group and lowest in the cryoprobe group (Table IV). Morphine dosage was similar in the two groups receiving morphine infusions but lower in the cryoprobe group (Table II). Respiratory rate, heart rate and blood pressure were similar in all groups.

TABLE II *Physical characteristics of patients, requirements for morphine and PFR values*

	Cryoprobe (n = 23)	*Infusion (n = 23)*	*Cryoprobe + infusion (n = 23)*
Mean age (yr) Range	54 (35–70)	55 (31–70)	55 (25–69)
Mean weight (kg) Range	67 (54–82)	63 (46–85)	70 (47–80)
Mean height (cm) Range	171 (150–183)	168 (157–183)	172 (157–185)
Sex (M:F)	16:7	15:8	19:4
Mean total morphine dosage (mg) in first 24 h after operation (SED = 2.5)	21.0	29.1	30.7
Mean PFR values (%) during first 24 h (SED = 3.5)	44.9	51.1	50.2

SED = Standard error of the difference between two means.

TABLE III *Pain scores and PFR values on the eighth day (mean ± SE)*

	All cryoprobe cases (n = 46)	*All non-cryoprobe cases (n = 38)*	*t*
Transformed resting pain scores (radians)	0.326 ± 0.031	0.443 ± 0.053	1.91 ($P = 0.06$)
Transformed moving pain scores (radians)	0.523 ± 0.032	0.604 ± 0.057	1.26 ($P = 0.21$)
PFR values %	66.0 ± 2.2	71.2 ± 2.8	1.50 ($P = 0.14$)

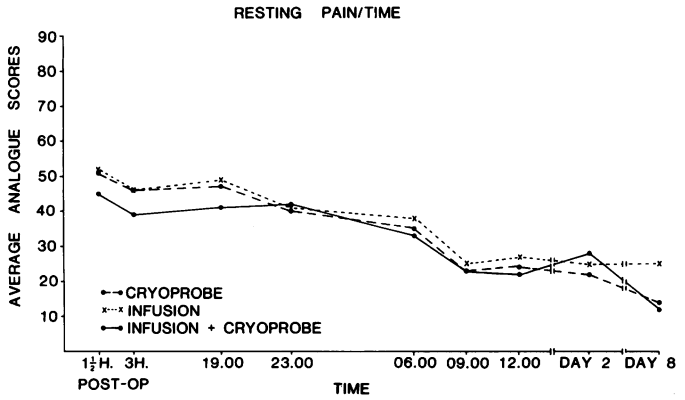

FIG. 1 Changes in average pain scores when resting during the first 24 h.

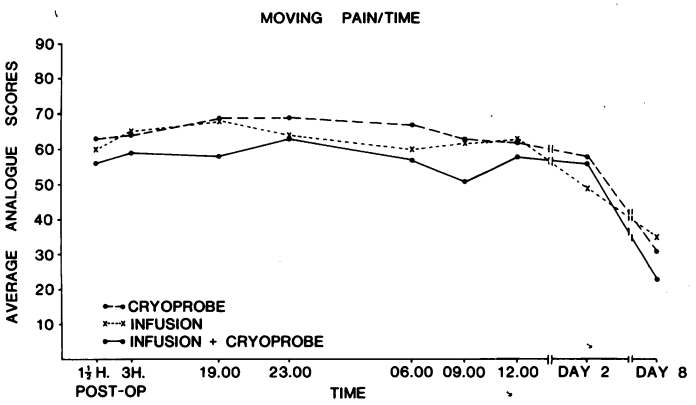

FIG. 2 Changes in average pain scores when moving during the first 24 h.

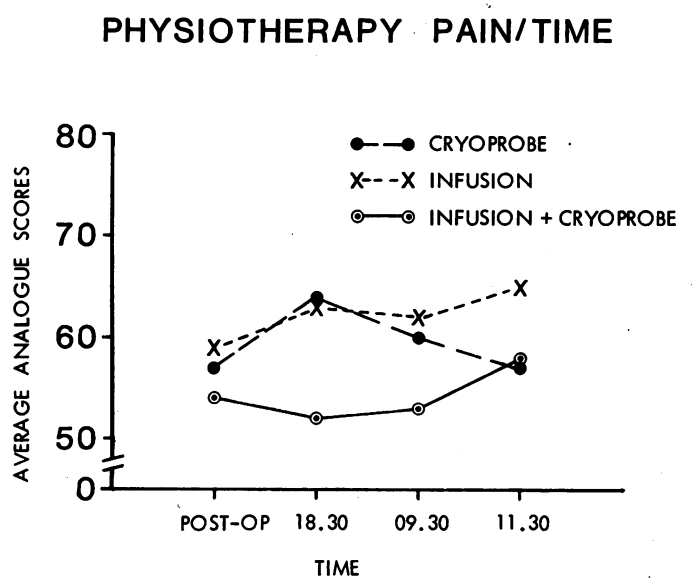

FIG. 3 Changes in average pain scores during physiotherapy during the first 24 h.

TABLE IV *Number of coughing attempts rates as 'good' or 'very good' by the physiotherapists*

	Physiotherapy grades better than 3		
	Cryoprobe (n = 23)	*Infusion (n = 23)*	*Cryoprobe + infusion (n = 23)*
Postoperation	4	8	9
18.30	5	5	8
09.30	6	6	8
11.30	8	10	10
Total	23	29	35

Nurses found the morphine infusions easy to manage and there were no further problems after those reported in the first trial *(1)*. None of the cryoprobe plus infusion group patients required an extra injection of intramuscular morphine whereas five patients in the infusion group were judged to require one. This coincided with the bupivacaine block wearing off during the early afternoon, producing an increase in pain, which could not be relieved simply by increasing the infusion rate.

Discussion

This study may be criticised on the grounds that mean weights in the three groups differed slightly (Table II). While this may be an artifact of sampling variation, it could not affect our conclusions. The weights of the patients do not affect the efficacy of the cryoprobe, and within the range of variation found here, opioids are not normally given on a weight-related basis.

It was disappointing to find that combining the use of cryoanalgesia with morphine infusions did not provide any measurable improvement in analgesia when compared with either technique used alone. The only pointer to any degree of improved analgesia came from a comparison of physiotherapists' opinions, but it would be invalid to draw conclusions from this on its own. We have shown *(1)* that giving morphine by infusion to thoracotomy patients, who had not had cryoanalgesia, provided superior analgesia compared with giving morphine intramuscularly, without requiring an increased dose of the drug. Rutter and colleagues *(5)* have shown similarly good results with morphine infusions given to patients after upper abdominal surgery using a relatively low dosage level and Catling and colleagues *(6)* have also shown similar improvements in analgesia with papaveretum infusions again given to patients after upper abdominal surgery, but using a much higher dosage level.

In contrast Ellis and colleagues *(7)* failed to demonstrate improved analgesia in a group of patients who had undergone upper and lower abdominal surgery when comparing intramuscular morphine administration with pethidine given on demand intravenously and Robinson and colleagues *(8)* did not find significatnly improved analgesia when comparing im pethidine with pethidine given on demand iv to patients in labour. These findings taken in conjunction with the findings reported in this paper suggest that opioid infusions can provide measurably superior analgesia when given to patients after operations which cause

particularly severe postoperative pain but no improved analgesia can be demonstrated, as judged from patients' reports of pain, when the stimulus is generally less severe, such as after lower abdominal surgery.

PFR is not now accepted as an objective measurement of pain. However, it has been suggested as a test of the ability to carry out a simple coordinated task in the postoperative period, poor performance being an indication of a poorly responsive patient *(9)*. To this extent there was no suggestion of patients who had morphine infusions being less responsive than patients who had intramuscular morphine. A further factor in this trial was the possibility that intercostal muscle paralysis due to cryoprobe freezing of nerves might adversely affect respiratory ability *(10)*. On the eighth day, when postoperative drowsiness would no longer be a feature, no significant difference was found in the PFR values when comparing cryoprobe with non-cryoprobe cases.

The finding that pain at rest on the eighth day is significantly lower in cryoprobe patients when compared with non-cryoprobe patients emphasises that the value of cryoanalgesia is still significant beyond the initial postoperative period. This, and the fact that the cryoprobe procedure generally involves only 10 to 15 min extra time for each thoracotomy, has led to the technique being used routinely for post-thoracotomy pain relief in the Royal Victoria Hospital, Belfast.

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Introductory Discourse on the Studies required for the Medical Profession

Extracts from an address to the students of the medical school of St George's Hospital by Sir Benjamin Brodie on 1st October 1838.

. . . There are some studies peculiar to the medical profession to which, if you would do justice to the public, and obtain honour for yourselves, you must be specially devoted: which you must prosecute, not carelessly and as a matter of form, but with zeal and unremitting diligence, through the whole period of what is called your education.

You will perceive what are the three principal divisions of the course of education in which you are now engaged. The first comprehends the science of Anatomy or Physiology; the second that of Pathology, or the science of disease; and in the third division we find whatever relates to Medical and Surgical treatment.

The Studies which will occupy the principal part of your time are those of Anatomy, and of Hospital Practice, and you cannot doubt as to which of these has the claim of precedency. I will not say that a student who attends the wards of the hospital in the beginning of his education, may not thence obtain some sort of useful practical knowledge; but it is plain that he can profit little by it compared with one whose mind has been prepared by a previous diligent attendance on the anatomical lectures and dissecting room. The attendance of anatomical lectures is necessary for your initiation into the study of Anatomy. They give you a general view of what you have to learn, and are, at the same time, the source where you will derive your principal instruction in Physiology. For Anatomy and Physiology are one science, and to teach them separately is about as absurd, as it would be to divide Astronomy into two sciences, the one teaching the figure and size of the heavenly bodies, and the other their motions. But to be a good anatomist the student must labour in the dissecting room: he must unravel the structures of the human body with his own hands, and examine everything for himself. The impressions which dissection leaves upon his mind are not only accurate, but they will be lasting; if he trusts to those which he receives for the discourses and exhibitions in the lecture room, he will find them to be evanescent.

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