SELECTIVE HYPOPHYSECTOMY FOR METASTATIC PAIN
A review of ethyl alcohol ablation of the anterior pituitary in a Regional Pain Relief Unit

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SUMMARY
Selective adenohypophysectomy, by the injection of up to 1 ml of absolute alcohol to the pituitary gland, was used to produce pain relief in 25 patients suffering from metastatic cancer. Thirty-five treatments were given and good analgesia was obtained in 74%. The median duration of pain relief was 6–7 weeks, although some treatments produced relief for up to 20 months. The procedure was most successful in relieving bone pain in patients with advanced carcinoma of the breast or prostate. The use of a fine-gauge needle for the intranasal trans-sphenoidal approach to the gland and the injection of alcohol to the anterior part (pars distalis) of the gland reduced the frequency of the major complications diabetes insipidus (17%) and prolonged visual disturbance (3%).

The method of pituitary destruction by absolute alcohol in the treatment of painful metastases from hormone-dependent cancers was developed by Moricca (1970, 1973, 1974a, b) after earlier workers had described various hormone-subtraction therapies as partially successful in controlling (but not providing analgesia for) the growth of the tumours. The purpose of the present study was to assess retrospectively the efficacy and problems of the technique as used in the Oxford Regional Pain Relief Unit in the 3 years since its introduction.

PATIENTS
Twenty-five patients with metastasizing cancers have undergone the technique of alcohol hypophysectomy at the Unit since the first procedure was performed in December 1977. Thirteen were women with primary carcinoma of breast and nine were men with primary prostatic tumours. There was also one man with primary carcinoma of bronchus, one with primary teratoma of testis, and one woman with a primary carcinoma of the sigmoid colon.

Thirty-five hypophysectomies were performed. Two patients had the procedure repeated, one received three injections and two received a total of four. The mean age of patients at the time of treatment was 59.8 yr (range 29–77 yr), although patients with prostatic cancer were slightly older (mean 67.7 yr).

Patients were considered for hypophysectomy if they met certain criteria: they suffered from bone pain and had obvious skeletal deposits, had previously shown evidence of a symptomatic response to hormone therapy, had a reasonable prognosis in terms of anticipated survival and had a long interval from the diagnosis of the primary tumour to the development of pain.

In any individual, the evaluation of these criteria was inevitably subjective, and part of the purpose of the study was to assess retrospectively how far these requirements had been met. The time and indications for referral to the unit also varied. This was inevitable in a regional unit taking patients from hospitals and general practitioners.

METHOD
Light general anaesthesia was always administered to the patients before hypophysectomy. The vocal cords were sprayed with lignocaine before endotracheal intubation so that the anaesthetic might be maintained solely with nitrous oxide and oxygen during the critical period towards the end of the procedure when the alcohol was injected. The throat was packed with ribbon gauze and both nostrils were prepared with 25% cocaine paste to produce local anaesthesia and vasoconstriction.

A single 16-gauge needle with introducer was passed through one nostril to enter the pituitary fossa via the transphenoidal route, as described by Moricca (1977). Bi-plane image
intensification was used to monitor the needle’s progress, and the introducer was positioned so that it was just within the bony margins of the anterior part of the pituitary fossa. A 20-gauge needle was then passed through the introducer so that it entered 2–3 mm into the substance of the gland (pars distalis). An injection of iophendylate 0.1 ml (Myodil, Glaxo) was used to confirm the position of the needle in the body of the gland. Absolute alcohol 0.8–1.0 ml was instilled to the pituitary fossa, in 0.1-ml increments over 10–15 min, and at this stage the general anaesthetic was lightened so that any movements or dilatation of the pupils could be detected.

The patients stayed in hospital for at least 48 h following the procedure, to determine the efficacy in terms of pain relief (patient’s evaluation), requirements for analgesic drugs, and to monitor the development of complications such as diabetes insipidus. Replacement steroid therapy was instituted routinely, in the form of cortisone acetate 25 mg twice daily, to those patients not already receiving corticosteroids. Patients have then been reviewed at 6-weekly intervals.

The success of the procedure was determined by the patients’ subjective evaluation of pain relief and by their requirement for analgesics. Patients who obtained good relief had either no pain or slight pain after treatment, required only mild analgesics for symptom control or had a significant reduction (>50%) in their narcotic analgesic consumption. Those patients who were considered to have a poor result from the procedure had little in the way of pain relief and had no change in their analgesic requirements.

RESULTS AND COMPLICATIONS
Good analgesia was obtained following 74% of hypophysectomies performed (table I). In those patients suffering from carcinoma of the breast the results were better (79%). The three injections carried out on patients with bronchial, colonic or testicular tumours were unsuccessful in producing analgesia. The hormone-insensitive tumours have been withdrawn from the statistics and no more hypophysectomies are planned for similar patients in future.

Figure 1 shows the duration of analgesia obtained following hypophysectomy. It proved difficult to assess completely as a number of patients who were pain-free on discharge died (Nos 6, 8, 13, 23, 24) or failed to attend the follow-up appointments (Nos 2, 3, 5, 10). Median duration of pain relief was 6–7 weeks. Thirteen of the 31 (42%) hypophysectomies completed on the patients with breast or prostatic tumours still produced analgesia at 6 weeks. Two patients (Nos 14, 25) are still being followed up, having obtained adequate analgesia from their most recent hypophysectomy.

Table II shows the complications, arbitrarily divided into major and minor complications. Only one procedure had to be abandoned, because of a major haemorrhage, but this produced no permanent disturbance and the patient underwent two further successful hypophysectomies. The frequency of headache (17% of all attempts) and nausea (9%) was relatively small. The frequency of diabetes insipidus was 17% (six treatments) and these were mainly among the early treatments in the series. Only four patients required vigorous anti-diuretic hormone therapy.

Histological examination of the pituitary gland was possible in three patients (Nos 4, 11, 17). In two, there was minimal evidence of gland destruction and in the one patient where the damage was obvious (No. 11) no relief of pain had been obtained from the procedure.

DISCUSSION
In 1953 Luft and Olivecrona described surgical ablation of the pituitary gland in the treatment of metastases from hormone-dependent tumours, with a view to reducing the spread of the disease rather than specifically for analgesia. Since then Moricca (1970, 1973, 1974a,b) has devised a method of ablation using alcohol instilled directly to the pituitary. This method has a number of advantages as a simple, safe and inexpensive procedure, which can, if necessary, be repeated a number of times without requiring specialist neurosurgery and a long stay in hospital. The

<table>
<thead>
<tr>
<th>Primary tumour</th>
<th>Good analgesia</th>
<th>Poor analgesia</th>
</tr>
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<tbody>
<tr>
<td>breast</td>
<td>19 (79%)</td>
<td>4</td>
</tr>
<tr>
<td>prostate</td>
<td>12 (75%)</td>
<td>3</td>
</tr>
<tr>
<td>testis</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>colon</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>bronchus</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>
HYPOPHYSECTOMY FOR PAIN

Table II. Complications produced in 35 attempted hypophysectomies

<table>
<thead>
<tr>
<th>Complications</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major</td>
<td></td>
</tr>
<tr>
<td>Major bleed (abandoned procedure)</td>
<td>1</td>
</tr>
<tr>
<td>Loss of visual field</td>
<td>1</td>
</tr>
<tr>
<td>Diabetes insipidus</td>
<td>6 (17%)</td>
</tr>
<tr>
<td>Myxoedema</td>
<td>1</td>
</tr>
<tr>
<td>Minor</td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>6 (17%)</td>
</tr>
<tr>
<td>Vomiting/nausea</td>
<td>3 (9%)</td>
</tr>
<tr>
<td>Temporary pupil change</td>
<td>3 (9%)</td>
</tr>
<tr>
<td>Leak of c.s.f.</td>
<td>2 (6%)</td>
</tr>
<tr>
<td>Epistaxis</td>
<td>1</td>
</tr>
</tbody>
</table>

Fig. 1. Patients, primary tumours and durations of analgesia for 35 treatments in 25 patients.

The technique as practised in the Oxford Regional Pain Relief Unit at Abingdon is carried out with a single injection, applicable to an analgesic method performed by anaesthetists.

The aim of the technique reported by previous workers (Corssen et al., 1977; Moricca, 1977; Lipton, 1978; Lipton et al., 1978) has been total pituitary ablation, and the volumes of absolute alcohol used have generally been larger than those in the present series. Corssen and others (1977) described 1–2 ml, Moricca (1977) used 0.6–2.0 ml and Lipton (1978) 1 ml. Our own aim has been selective anterior hypophysectomy, using absolute alcohol 0.8–1.0 ml with the needle tip just within the body of the adenohypophysis. Consequently, our frequency of diabetes insipidus is lower (17%) than those quoted by Moricca (“very frequent”) and Lipton (“most, but rarely extreme”), and our figures improved as the number increased. The most distressing complication for patients was the development of visual disturbance. This occurred infrequently but, in retrospect, was found to have resulted when there was failure of the needle to enter the substance of the adenohypophysis or where the rate of alcohol injection had been too rapid.

Our success in terms of analgesia is comparable to that of other series using alcohol ablation of the pituitary. Seventy-four percent had significant pain relief, with 48% of the treatments that provided analgesia for breast or prostatic cancers lasting at least 6 weeks. Corssen and others (1977) described complete relief in 54% of 24 patients,
plus some analgesia in a further 42%. Lipton and others (1978) described complete relief from 41% of 155 injections with a median duration of 4 months of analgesia from the successful injections. Our series includes good relief in 80% of 31 injections, with a median duration of 2 months from the 17 successful injections that have been followed up beyond 2 weeks.

Our success rate is also comparable to that of other workers using different methods of hypophysectomy. Gye and others (1979) used cryohypophysectomy in 22 patients with metastatic breast cancer and obtained pain relief for 3 months in 55% of the cases.

The mechanism of pain relief following hypophysectomy remains uncertain, but it has been suggested that part of the effect may be a result of the spread of alcohol via the pituitary stalk into the hypothalamus, thereby directly causing fixation with alcohol, or indirectly causing thrombosis and infarction (Miles and Lipton, 1976; Moricca, 1977; Yanagida et al., 1979; Williams et al., 1980). Although we have no clear evidence to confirm this hypothesis, a number of points are in its favour. At the time of injection contrast was seen to track up the pituitary stalk in most of hypophysectomy procedures; the destruction of the pituitary gland assessed by measurement of pituitary hormone production could not be related to the frequency and degree of analgesia (authors' personal observation) and two patients who had complete relief of symptoms had little evidence of adenohypophyseal destruction postmortem.

We consider that the technique described above, of selective adenohypophysectomy with a small volume of absolute alcohol, is a valuable method of providing analgesia in patients with terminal cancer in whom the tumour is demonstrably hormone-sensitive, and where bony metastases are causing unbearable pain. It is a relatively quick and simple method involving as little confinement to hospital, discomfort and surgical intervention as possible in patients with limited life expectancy.

REFERENCES


HYPOPHYSECTOMIE SELECTIVE POUR LES DOULEURS METASTATIQUES

Résumé

On a utilisé l'adénohypophysectomie sélective par l'injection d'alcool absolu (jusqu'à 1 ml) dans la glande pituitaire, pour soulager la douleur de 25 patients souffrant d'un cancer métastatique. On a administré trente-cinq traitements et obtenu une bonne analgésie dans 74% des cas. La durée moyenne du soulagement de la douleur a été de 6 à 7 semaines, bien que dans certains cas on ait obtenu un soulagement pendant une période allant jusqu'à 20 mois. Ce procédé a été particulièrement efficace pour le soulagement de la douleur dans les os chez les patients atteints d'un carcinome avancé du sein ou de la prostate. L'usage d'une aiguille de petit calibre pour l'injection intranasale transphénoidale de la glande et l'injection d'alcool dans la partie antérieure de la glande (pars distalis) a réduit la fréquence des principales complications: diabète insipide (17%) et perturbations visuelles prolongées (3%).
SELEKTIVE HYPHYPHENEXTIRPATION GEGEN METASTATISCHE SCHMERZEN

Ein Überblick über die Äthylalkohol-Ablation der vorderen Hypophyse bei einer regionalen Schmerzendlösungsklinik

ZUSAMMENFASSUNG


HIPOFISECTOMIA SELECTIVA PARA EL DOLOR METASTATICO

Revisión del ablación de la pituitaria anterior mediante alcohol etílico en una unidad local de mitigación del dolor

SUMARIO

Se usó adenohipofisectomia selectiva para producir la mitigación del dolor en 25 pacientes que sufrían de cáncer metastático, efectuándose esto mediante la inyección de hasta 1 ml de alcohol anhidro dentro de la glándula pituitaria. Se administraron treinta y cinco tratamientos y se obtuvo una buena analgesia en el 74%. La duración media de la mitigación de dolor fue de 6 a 7 semanas, aunque algunos tratamientos produjeron mitigación por periodos que llegaron a los 20 meses. El procedimiento alcanzó su máximo éxito en la mitigación del dolor de huesos en aquellos pacientes con carcinoma avanzado del pecho o de la próstata. El uso de una aguja fina para el recorrido transfenoidal del curso intranasal, hasta llegar a la glándula, y la inyección del alcohol en la parte anterior (pars distalis) de la glándula, redujo la frecuencia de las principales complicaciones de la diabetes insipidus (17%) y de la perturbación visual de gran duración (3%).