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Recent Advances in Local Analgesia in Dental Surgery (*Summary*)

Dr Goldman described the results of a well-designed double-blind trial comparing lignocaine, now regarded as a standard analgesic, with a newer compound, prilocaine; 67 dental surgeons and over 12,000 cases were involved. It was shown that 3% prilocaine with adrenaline 1 : 300,000 was as effective but shorter acting than 2% lignocaine with adrenaline 1 : 80,000; initial pain was less with prilocaine and onset of anæsthesia was as quick as with lignocaine.

An early analysis of some of the results of this trial has been published by Goldman & Gray (1963, *Brit. dent. J.* **115**, 59).

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Clinical Experience with Prilocaine

From time to time our attention is drawn to the hazards of local anæsthesia. In 1956 Edwards *et al.* reported on 1,000 deaths associated with anæsthesia, of which 7 occurred in patients receiving local anæsthesia (0·7%); 4 of them received surface anæsthesia, 2 caudal and one intravenous. In 1963 Clifton & Hotten reported on 162 deaths, 52 of which were due to anæsthesia; 2 of them could be attributed to local anæsthetic overdosage.

Some years ago I studied 14,000 coroner's post-mortems over the periods 1943–4, 1949–50 and 1955–56. The post-mortems carried out in each of these periods averaged 4,700. Of these, an average of 270 autopsies were performed on cases arising in association with surgery. Approximately 110 deaths occurred in each two-year period in which anæsthesia was held to be contributory. There were 6 deaths in 1943–4, 7 in 1949–50 and 3 in 1955–6 associated with local anæsthesia, excluding spinal and epidural anæsthesia. Sensitivity to cocaine accounted for 3 deaths in 1943–4, 2 in 1949–50 and one in 1955–6.

Dinnick (1964) reported on a further 600 deaths associated with anæsthesia and gave details of 25 deaths occurring during or shortly after bronchoscopy. He also mentioned a patient weighing 8 stone (50·5 kg) who received 4·5 ml of 2% amethocaine and who died from convulsions.

Deacock & Simpson (1964) reported 13 cases of death associated with overdosage of lignocaine, one of which was that of a woman aged 20 who collapsed and died following the topical application of 4% lignocaine to the larynx and tracheobronchial tree, the dose probably exceeding 12 ml. They stressed once again that the maximum permissible dosage for a fit adult is 200 mg of lignocaine plain, or 500 mg if adrenaline is added. Toxic effects are likely to occur only when levels of lignocaine in the blood reach 5 μg/ml in the conscious subject and 10 μg/ml under general anæsthesia.

One problem of a topical anæsthetic is to obtain adequate analgesia without exceeding the maximum safe dose; whereas a skilled and experienced operator can do it with small volumes, the inexperienced operator frequently uses large volumes. The recommended maximum dosage is shown in Table 1.

Table 1
Recommended maximum dosage of local anæsthetic agents

Agent	*Concentration (g/100 ml)*	*Recommended maximum volume for a fit 70 kg individual (ml)*
Cocaine	10	1–2
	5	4
Lignocaine	4	5
Cinchocaine	2	2
Amethocaine	2	2
	0·5	8
Prilocaine	4	10

Åström & Persson (1961) have studied the absorption of various local anæsthetic agents after intratracheal injection in the rabbit. The very rapid rate of absorption of amethocaine is illustrated by the fact that LD 50 is nearly equal for the intravenous and intratracheal routes. On the other hand lignocaine and prilocaine were only about one-quarter to one-fifth as toxic by the intratracheal as by the intravenous route. Cocaine occupied an intermediate place between amethocaine and lignocaine when applied to the tracheal mucosa.

Englesson *et al.* (1964) have studied the difference in tolerance to intravenous lignocaine and prilocaine in man and have shown that a 70 kg fit adult will tolerate 400 mg of prilocaine without any untoward side-effects. On the basis of these and other studies, prilocaine is said to be at least 40% less toxic than lignocaine.

As a clinical anæsthetist I am naturally interested in the development of any drug which promises to bring greater safety to patients and yet, at the same time, to be as effective as or an improvement upon an already established agent. For this reason, safety, I wanted to find out whether prilocaine, which is certainly less toxic than drugs previously employed, was of value in clinical practice; for, if both increased safety and

efficiency were present, a considerable advance would have been achieved.

I shall discuss two groups of procedures: (1) Patients undergoing diagnostic bronchoscopy under topical anæsthesia with 4% prilocaine as the agent. (2) Patients undergoing obstetric procedures in which 0·5% prilocaine without adrenaline has been used in the majority of cases.

In order that the information obtained during this study could be processed and statistically analysed, forms were drawn up with the help of Dr Peter Frisch, based on those developed by Dr Victor Goldman for the study of dental anæsthesia, but I must stress that this information has not yet been statistically handled and that the data presented here should be regarded as a preliminary report.

Bronchoscopy

Topical analgesia was produced in 161 consecutive cases using 4% prilocaine for bronchoscopy in the conscious subject. There were 151 men and 10 women; 27 cases were aged 40–49, 66 were 50–59, 43 were 60–69 and 12 were 70–79. Some of the patients were cachectic and the quantity of solution used was adjusted according to their clinical status and weight.

Premedication: All patients received a standard premedication of Omnopon 20 mg intramuscularly, given one hour before, and an amethocaine lozenge to suck (65 mg) thirty minutes before.

Method of administration: There were four administrators in this series, who were instructed not to exceed 10 ml of 4% prilocaine in 70 kg individuals. In 87 of the cases the application was solely by means of a spray applied to the mouth, pharynx, larynx and trachea; in 74 cases the spray was combined with the application of swabs, soaked in a known quantity of the solution to each pyriform fossa.

Method of assessment: Three grades of assessment were used: (1) Satisfactory, enabling bronchoscopy to be carried out with the normal amount of ease expected of this procedure under local analgesia. (2) Partially satisfactory. (3) Failure. These findings were based on the unanimous opinion of both the administrator and the operator.

Results: A satisfactory result was obtained in 151 cases (94%); there was one complete failure in a patient with secretions; there were 9 partially satisfactory cases (6%).

In a small series of patients blood was taken at two-minute intervals, following the administration of topical prilocaine, for twenty minutes; all the blood levels were well below 1 μg/ml, 0·36 being the highest level recorded (colorimetric method: Woods *et al.* 1951). Englesson *et al.* (1964) had maximum plasma levels of 1·7±0·3 (SE mean) within five minutes in cases receiving 400 mg intravenously.

Conclusions: This was not a controlled trial and the results are open to all the criticisms that a trial of this nature may have levelled against it. The results, however, show that 4% prilocaine, in quantities up to 10 ml, is a satisfactory analgesic agent for the procedure of bronchoscopy, at the same time offering the patient a wider margin of safety than other agents at present available. Investigations are now proceeding into the use of 2% and 3% prilocaine for topical anæsthesia.

Obstetrics

There were approximately 50 operators, comprising housemen and undergraduates. The total number of obstetric cases was 388, of which 80 were pudendal block alone, 32 were pudendal block combined with infiltration, and 276 were infiltration alone.

Infiltration: The total of 276 consisted of 155 tears, 188 episiotomies and 3 forceps deliveries. The forms for 54 cases were incomplete; an analysis of the 222 complete forms is shown in Table 2.

Table 2

Results in 323 obstetric cases

	No. of cases treated by		
	Infiltration alone	*Pudendal block alone*	*Infiltration and pudendal block*
Total completed forms	222	69	32
Age group (years)			
15–19	24	8	2
20–39	196	60	30
40–49	2	1	
Solution used			
0·5% with adrenaline	6		
0·5% with no adrenaline	213	69	32
1·0% with adrenaline	3		
Quantity used (ml)			
5–10	16	1	
10–15	59	1	
15–25	105	1	
25–35	17	2	
35–50	14	9	4
50–65	7 (all 0·5% without adrenaline)	26	14
65–80	3 (all 0·5% without adrenaline)	17	13
over 80	1 (all 0·5% without adrenaline)	12	1
Onset of analgesia (min)			
< 1	56	45	5
1– 2	126	12	14
2– 4	26	11	12
4– 5	9	1	1
5–10	4		
over 10	1		
Duration (min)			
30	100	24	10
60	95	33	12
90	7	2	2
120	8	3	3
180	2	1	
over 3 hours	10	6	5

A satisfactory result was obtained in 182 cases (82%), a partial result in 37 cases (17%) and a failure in 3 cases. It is possible that, when the results are analysed, failure and success may be related to the skill of the operator.

Pudendal block: Of the total of 80 cases so far analysed, incomplete forms numbered 11. The analyses of the 69 complete forms is shown in Table 2.

Of the 80 cases, low forceps accounted for 48, mid forceps for 5, low forceps+episiotomy 10, episiotomy alone 9, extraction+episiotomy 2, extraction alone 1, mid forceps+episiotomy 1, others 4.

A satisfactory result was obtained in 62 of the 69 cases (90%), a partial result in 5 (7%), and a failure in 2 (3%).

Infiltration and pudendal block: Of the total of 32 cases, low forceps+episiotomy accounted for 13 cases, low forceps alone for 12 cases, mid forceps 3, extraction+episiotomy 1, episiotomy alone 1, extraction alone 1, mid forceps+episiotomy 1.

The results, which are analysed in Table 2, were satisfactory in 26 cases (90%) and partial in 3 (10%); there were no failures.

Discussion

A total of 270 completely satisfactory results were obtained in 314 obstetric patients receiving 0·5% prilocaine without adrenaline; this represented 86% of the total. It is possible that the failure rate was associated with lack of skill in the administrator; this will be cleared up when the forms are subjected to statistical analysis.

The highest success rate was with pudendal block alone (90%), which was not increased by combining pudendal block with infiltration. Total failures were 1·6%. The most frequent range of quantity was 50–65 ml for pudendal blocks with and without infiltration. As would be expected, infiltration demanded a smaller quantity, averaging 15–25 ml.

Analgesia appeared to begin in less than one minute with pudendal block; this may be linked with the skill of the operator. With infiltration alone it began within one to two minutes.

Other factors such as side-effects and the effects on the child have been studied and, as soon as the forms have been processed, the data will be available.

In conclusion, so far as bronchoscopy with prilocaine is concerned, it is my opinion that a significant advance has occurred, but before it is possible to come to any conclusion regarding the role of prilocaine in obstetrics further investigation and more complete statistical analyses must be carried out.

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Toxicity and Clinical Use of Prilocaine

It has been shown both in animal and human studies that, weight for weight, prilocaine is less toxic to the central nervous system than lignocaine (Englesson *et al.* 1964). As the general toxicity of a local anæsthetic drug is related to the level reached in the blood following absorption from the site of injection, we have measured the plasma levels of both lignocaine and prilocaine under identical conditions.

All the patients underwent major gynæcological surgery and received either epidural or intercostal nerve block. The number of cases in each group are shown in Table 1.

Table 1
Epidural or intercostal nerve block in gynæcological surgery

Site	*Drug*	*Concentration*	*Dose (mg)*	*No. of cases*
Epidural	Lignocaine	2%	400	15
Epidural	Prilocaine	2%	400	13
Intercostal	Lignocaine	2%	400	11
Intercostal	Prilocaine	2%	400	13
Intercostal	Lignocaine	1%	400	10
Intercostal	Prilocaine	1%	400	0

By taking blood samples 5, 10, 15, 20, 30 and 60 minutes after the injection, the rise and fall of the plasma concentration could be followed in each patient. To allow comparison between groups of patients the means at each time interval have been plotted (Fig 1); all series showed that prilocaine gave lower plasma levels than lignocaine and these differences were statistically significant. When comparing the plasma levels reached by different drugs, some caution is necessary before conclusions are drawn regarding toxicity: low levels with some drugs may be associated with toxic effects and could indicate that accumulation was occurring in the central nervous system. The