INTRA VENOUS REGIONAL ANALGESIA*

AN ASSESSMENT OF THE PROCEDURE FOR THE SURGERY OF HAND INFECTIONS

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‘Vein anaesthesia’, using procaine, was first described by Bier in 1908 and 1910. He cannulated an exposed vein in an isolated limb segment and washed out the veins afterwards to remove the procaine. This was followed by a number of papers, including those of Morrison, who modified the technique by injecting the veins distal to a single tourniquet, and Adams, who reviewed the subject.

Our interest in intravenous regional analgesia was aroused by Holmes’ description of the procedure. The procedure appeared to afford effective analgesia of rapid onset, together with a bloodless field.

At first we used the procedure in traumatic cases, but found the axillary brachial block more useful in these cases. We found the technique well suited to the management of hand infections because of its quickness and the short duration of the surgery of hand infections.

Several recent papers have been published, but they have included few cases of hand infections. A comparison of some of these reports is given in Table I. Our experience with the procedure in the surgery of 1,000 hand infections is presented, and a modification is suggested in order to minimize complications and ensure effectiveness.

MATERIAL

 Patients admitted to the Ernest Oppenheimer Hospital are drawn from a population of 50,000 adult male African mine workers, in whom major illness and disability have been excluded by pre-employment clinical and X-ray examination. Workers’ ages range between 18 and 60 years, but the majority are in the 20-30 year age-group.

Hand infections occur commonly in our population and most cases requiring surgical treatment were operated upon under intravenous regional analgesia. We collected 1,000 cases between February 1964 and May 1965. These were all inpatients and all cases were operated upon in our aseptic theatre, where monitoring and resuscitation equipment is available.

METHOD

Most of our patients received 100 mg. of pethidine intramuscularly, 1 hour before operation. In the theatre, a sphygmomanometer cuff was applied to the affected arm and a Gordh needle was introduced into a distal forearm vein. The recumbent patient elevated his arm to empty the veins. The cuff was then rapidly inflated to a pressure above his systolic


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TABLE I. COMPARISON OF CASE REPORTS

<table>
<thead>
<tr>
<th>Year</th>
<th>Authors</th>
<th>Analgesic</th>
<th>No. of cases (arm and leg)</th>
<th>Toxic effects</th>
<th>Remarks on method</th>
</tr>
</thead>
<tbody>
<tr>
<td>1908</td>
<td>Bier</td>
<td>Procaine</td>
<td>244</td>
<td>5</td>
<td>(slight)</td>
</tr>
<tr>
<td>1910</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Effective safe method</td>
</tr>
<tr>
<td>1931</td>
<td>Morrison</td>
<td>Procaine</td>
<td>30</td>
<td>2</td>
<td>(transient)</td>
</tr>
<tr>
<td>1963</td>
<td>Holmes</td>
<td>Lignocaine</td>
<td>56</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>1964</td>
<td>Bell et al.</td>
<td>Lignocaine</td>
<td>514</td>
<td>11</td>
<td>Effective and 'relatively harmless'</td>
</tr>
<tr>
<td>1965</td>
<td></td>
<td></td>
<td>64</td>
<td>1</td>
<td>Low toxicity Adequate analgesia 97%</td>
</tr>
<tr>
<td>1966</td>
<td>Cox</td>
<td>Lignocaine</td>
<td>47</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>1965</td>
<td>Adams et al.</td>
<td>Lignocaine</td>
<td>36</td>
<td>0</td>
<td>Grattifying feasibility, simplicity, effectiveness and lack of side-effects</td>
</tr>
<tr>
<td>1965</td>
<td>Kennedy et al.</td>
<td>Lignocaine</td>
<td>77</td>
<td>23</td>
<td>(including 1 cardiac arrest)</td>
</tr>
<tr>
<td>1965</td>
<td>Sorbie and Chacha</td>
<td>Lignocaine</td>
<td>128</td>
<td>15</td>
<td>Valuable. Effective and safe</td>
</tr>
<tr>
<td>1965</td>
<td>Monty and Deller</td>
<td>Lignocaine</td>
<td>134</td>
<td>0</td>
<td>Convenient, simple, safe, efficient</td>
</tr>
<tr>
<td>1965</td>
<td>Present</td>
<td>Lignocaine</td>
<td>1,000</td>
<td>10</td>
<td>Effective and safe, in our population</td>
</tr>
</tbody>
</table>
decrease the volume of solution needed to produce analgesia. In our cases this was contraindicated by the presence of infection.

To minimize discomfort from the tourniquet for long operations, Holmes\(^1\) described a 2-cuff technique. Hoyle\(^2\) has described a convenient double cuff. Our surgical procedures were short; few lasted longer than 10 minutes and our cases tolerated a single cuff well.

Bell and his co-workers\(^3\) recommended a 20-minute tourniquet time before injection of the anaesthetic solution, thereby reducing the amount of anaesthetic required, but we feel that one of the main features of the technique, namely its quickness, is then lost.

To produce uniform analgesia, the cuff should be applied well above the median cubital veins in the cubital fossa and the Gordh needle should be inserted as far distally as possible.

Skin blotches and weals. Apart from the blotchy appearance which the skin takes on after injection of the local anaesthetic, as described by Holmes,\(^4\) we have also noted skin weals, maximal in the cubital fossa in a number of patients, especially when a large volume is injected. The patients had no untoward reaction on release of the tourniquet, therefore this does not appear to be significant.

**Contraindications**

In our experience contraindications to the use of the technique are:

1. Pre-existing venous thrombosis of the arm.
2. Bilateral hand infections (where the dose required to do both sides would exceed the safe maximal dose).
3. Extensive oedema, making it impossible to find a vein.

**Anaesthetic Solution**

We used a solution of lignocaine in 988 cases and mepivacaine in 12 cases. Reports of methaemoglobinemia with prilocaine\(^5\) are not encouraging but 2-chlorprocaine\(^6\) appears to be of low toxicity and we intend investigating the use of this analgesic in future.

**RESULTS**

The results of our 1,000 cases are divided into 5 unequal groups according to the type and dilution of local analgesic used (Table II). Maximum safe doses of lignocaine, with\(^7\) and without\(^8\) a vasopressor, have been suggested. We were prepared to encounter side-effects and we gave doses of up to 700 mg. Many of our cases received more than 200 mg. All our patients had painful lesions and we continued injecting analgesic solution in 10 ml. increments until the patient was pain free. Results were recorded as 'successful' or 'failed', according to whether or not discomfort was experienced during the subsequent surgical procedure.

**Group I**

We used 1% lignocaine in our first 132 cases, because of the alleged inefficacy of local analgesics in the presence of infection.\(^9\) We realized later that this was not necessary.

In this group analgesia was successful in 128 cases and failed in 4. Doses of 300 - 700 mg. were administered. Six cases developed signs of cortical stimulation; 4 of these became euphoric, excited and began twitching. We called this state a 'pre-seizure'. These cases were controlled with small intravenous doses of thiopentone or methohexitone. Two cases progressed to grand mal seizures. No prolonged effects were noted. We abandoned the use of 1% lignocaine because of the high incidence of side-effects (4.5%).

**Group II**

In our second group we used lignocaine, diluted to 0.5% with distilled water. There are 4 cases in this group. All complained of pain during the injection. Analgesia was successfully produced in 1 case and failed in 3. One case had a seizure. These poor results were probably caused by inadequate diffusion of the hypotonic solution into the extracellular fluid. Most of the injected lignocaine must have remained in the veins and been flushed into the systemic circulation when the cuff was released. We have demonstrated that, besides diffusing poorly, the hypotonic solution causes in vitro haemolysis of fresh blood. It should not be used.

**Group III**

In our third group (803 cases) we used 0.5% lignocaine in isotonic saline. We obtained our best results with this solution. Analgesia was successful in 801 cases and failed in 2. One hypertensive patient had a seizure, which was controlled with methohexitone. Fig. 1 shows the relation of mean dose related to patients' weight and our recommended maximum dose, and Fig. 2 shows the volume distribution in the same group.

![Graph](image-url)

**Group IV**

The sequence of cases in group III was broken by the trial of isotonic 0.5%, mepivacaine, in 12 cases. Successful analgesia resulted in all 12 and no toxic effects were noted, but 0.5% mepivacaine appeared to offer no advantage over 0.5% lignocaine.

**Group V**

In 49 cases we injected 3-3 mg./kg. of 1% lignocaine, followed by a varying volume of normal saline. We hoped that the saline would force the lignocaine peripherally to its site of action and so produce adequate analgesia. This technique was successful in 48 cases and failed in 1. In recent cases, using up to 5 mg./kg. of 0.5% lignocaine, followed by saline when necessary, we have had 100% success. We have encountered no signs of toxicity.

**Associated Pathology**

We also used the technique successfully and without complications in 3 patients with myelogenous leukaemia (1), infectious hepatitis (1) and mumps (1).
DISCUSSION

The pharmacology and toxicology of lignocaine and mepivacaine have been detailed in the literature. Comparative studies have shown that they have equal potency and toxicity. Toxicity increases as the square of their concentration.

Uses of Local Anaesthetic Agents

Intravenous injections of lignocaine have been used without untoward effect in the treatment of cardiac arrhythmias and epilepsy for the relief of pain, and as an adjunct to general anaesthesia, but reports of toxic and fatal reactions following the intravascular absorption of lignocaine present a warning to be remembered.

In 1957 the Scandinavian Pharmacopoeia Council recommended 200 mg. of plain lignocaine and 500 mg. of lignocaine with a vasopressor as safe maximum doses for infiltration analgesia and nerve block. For a 70 kg. man, this is 3 mg./kg. of plain lignocaine and 7 mg./kg. with a vasopressor.

Toxicity of Local Analgesics

Sadove et al. suggested that toxicity is dependent upon the weight of drug administered, its concentration and the rate of its administration. Other important factors are its rate of metabolism and individual idiosyncrasy to it.

Toxic effects of local analgesics can be divided into central and peripheral effects. Cortical stimulation is followed by medullary depression, with resultant cardiovascular and respiratory depression. Large doses of local analgesic depress the myocardium directly.

Steinhaus suggested that the minimum dose of lignocaine producing cortical stimulation is 20 - 50% of the minimum lethal dose and that there is a reasonable safety margin. Deacock and Simpson have discussed the effects and management of mild and severe lignocaine intoxication.

In our cases we frequently observed drowsiness and euphoria. We regarded this as an extension of the pharmacological action of lignocaine. Eight of our cases showed signs of cortical stimulation, which were controlled by small doses of intravenous barbiturate (Table III). All 8 cases had received more than 5 mg./kg. of lignocaine. We did not encounter significant cardiovascular or respiratory depression.

Local Complications

Monty and Deller reported 3 cases of superficial venous thrombosis at the site of injection from lignocaine-containing chlor- cresol. We observed superficial venous thrombosis in 2 patients.

The first patient developed a thrombosis of his superficial forearm veins 3 weeks after surgery to a deep palmar abscess. We are of the opinion that this was caused by the inflammatory process, rather than the technique.

The second patient developed a thrombosis in a vein which was ligated at operation, and in this case the added effects of venous stasis owing to ligation and slight irritation to the vessel wall caused by the injection, were probably responsible.

No other local complications were encountered.

MODE OF PRODUCTION OF ANALGESIA

The Venous Reservoir

In an isolated arm, injected lignocaine is dispersed through the superficial and deep forearm veins until the venous reservoir has been filled. During dispersion the veins become distended with solution, which mixes with the blood remaining in an unexsanguinated arm. This increases the dilution of the lignocaine, lowering its concentration to a level close to its minimum effective concentration.

Venography has shown that venous valves do not impede the retrograde flow of injected solutions. Adams and Albert measured blood volumes of adult's arms and found the average to be 170 ml. Van Niekerk and Coetzee demonstrated that intra-arterial injections of as little as 5 ml. of isotonic 0.5% lignocaine, produced regional analgesia. Much larger volumes are required to produce analgesia by the intravenous route, because of the large size of the venous reservoir which has to be filled.
This is demonstrated by the injection of local anaesthetic with contrast medium into a vein and into an artery, distal to a cuff (Figs. 3a and 3b).

\[ \text{Fig. 3(a)} \quad \text{Fig. 3(b)} \]

**Dispersion and Distribution**

If a large enough volume is injected, lignocaine solution is dispersed, by retrograde flow, to venules and capillaries of all tissues below the cuff, including nerve trunks, their ramifications and endings.

The involvement of major nerve trunks has been demonstrated by the intravenous injection of local analgesic solution into an arm segment, isolated between 2 cuffs. Analgesia was produced between the cuffs and distal to them. The development of analgesia was rapid between the cuffs, but slower distally. This suggests that minor branches and nerve endings are blocked before trunks but that nerves of all sizes are eventually blocked if distribution has been adequate.

**Diffusion**

At capillary level lignocaine rapidly diffuses into extracellular fluid and penetrates nerve coverings. A lignocaine gradient, across the capillary membrane, causes diffusion to occur until intravascular and extravascular concentrations are equal. Dye-diffusion studies in rabbits suggest that a diffusion gradient may persist in an obstructed vein for up to 15 minutes. We believe that inadequate diffusion and poor analgesia result when hypotonic solutions are injected.

**Dissociation**

In the slightly alkaline extraneural fluid, if sufficient buffering capacity is present, lignocaine salt dissociates. (RHN → RN + H⁺). Active base is released and hydrogen ions are removed. At the low tissue pHs associated with infections, higher concentrations of salt are needed to maintain a minimal effective concentration (Cm), because of the lowered buffering capacity of the tissue fluid. With intravenous regional analgesia, nerve fibres not blocked near an infected area will be blocked proximally, where tissue pH is normal. For this reason a low concentration of lignocaine provides satisfactory analgesia.

**Action**

Active lignocaine base penetrates nerve coverings and produces membrane stabilization of individual nerve fibres, preventing their depolarization. (The flow of ions across the nerve membrane is blocked, resting potential, capacitance and membrane resistance are unaltered, but depolarization is prevented and analgesia results.)

In low concentrations local analgesic solutions produce a differential block. Small diameter c (0.5 - 1.0 μm) and Aβ (1 - 4 μm) fibres, transmitting sensations of pain and temperature, are blocked. Usually the larger Aα (13 - 22 μm), Aβ (8 - 13 μm) and Aγ (4 - 8 μm) fibres are not blocked, and touch, proprioception and motor function remain intact.

Nerve block produced by prolonged tourniquet compression blocks large motor fibres first. We believe that the paralysis which develops late during intravenous analgesia, i.e. after the cuff has been inflated for 20 minutes or more, is produced mainly by this mechanism.

We believe that the rapid onset of analgesia results from the dispersal of lignocaine close to its site of action, leaving insignificant barriers to be penetrated before nerve block is produced.

**Release of Cuff**

When the cuff is released, blood flow through the arm is re-established immediately. Lignocaine in the venous reservoir is flushed into the systemic circulation and diffusion gradients are reversed. Lymph flow is re-established and lignocaine in the extracellular fluid is removed via the lymphatics. Lignocaine fixed to the cells of tissues, other than nerves, shows pharmacological inactivity. Because of its fixity it is slowly removed from the arm. There is evidence which suggests that the amount of local tissue fixation increases with increasing tourniquet time, and that smaller amounts of lignocaine remaining in the extracellular fluid are thus available for systemic redistribution if the tourniquet time exceeds 30 minutes. The incidence of toxic effects is therefore lower. The rapid return of sensation suggests that the removal and systemic redistribution of extracellular lignocaine is a rapid process.

**Redistribution**

All tissues rapidly remove lignocaine from the systemic circulation. Lipoid and renal tissue have a high affinity for it.
Lignocaine is rapidly metabolized by the normal liver. Its aromatic ring is oxidized to a phenolic compound, which is conjugated with sulphate and excreted in the urine. A small percentage is excreted unaltered. With impaired liver function the rate of metabolism is slowed.

The ratio between rate of release and rate of metabolism determines whether or not side-effects occur.

When small amounts of lignocaine are injected intravenously, toxic amounts are not taken up by vulnerable tissues. With larger amounts, metabolism may keep pace with release and prevent toxic effects. With massive amounts, when metabolism cannot keep pace with release, vulnerable tissues absorb toxic amounts and disaster may result.

Toxicity

Toxic doses in terms of mg. lignocaine/unit mass of brain or heart cannot be measured, unless a fatal reaction occurs. Attempts have been made to correlate toxic dose with plasma lignocaine levels. (Bromage and Robson suggested that levels of 6-7 mg/l. are safe and that toxic effects occur when plasma levels exceed 10 mg/l. Folds and McNall produced toxic effects within 18 minutes in all 10 of the cases to whom they administered 0.5 mg. lignocaine/kg./minute. When they stopped their infusion, mean plasma levels were 5.29 ± 0.55 mg/l., although 630 mg. might have been administered.)

We feel that the total amount of lignocaine taken up by vulnerable tissues is the deciding factor in the production of side-effects. This amount cannot be deduced from measurement of a single plasma lignocaine level. After release of the cuff, redistribution and uptake are progressive. One of our cases, who had received 450 mg. of lignocaine, had a seizure 10 minutes after the cuff had been released.

Englesson et al. injected 200 mg. ± 3 mg/kg. of lignocaine directly into the systemic circulation. No serious central nervous system or cardiovascular side-effects occurred, although plasma levels of up to 4.4 mg/l. were measured.

Safe Dose

In our cases no significant toxic effects were observed when doses of up to 5 mg./kg. of lignocaine were used, although our tourniquet times were short, so that tissue fixation was not maximal. With increasing doses above 5 mg./kg., side-effects occurred with increasing frequency.

The minimum effective dose of lignocaine should be used for each patient.

If adequate analgesia is not produced by a volume containing up to 5 mg./kg. of isotonic 0.5% lignocaine (i.e. 1 ml./kg.), then we recommend the use of a 'chaser' injection of saline, to fill the venous reservoir and force the lignocaine peripherally. This will produce analgesia without increasing the dose of lignocaine.

Conclusions

The technique of intravenous regional analgesia is simple, quick and effective.

It does not replace any of the established methods of producing regional analgesia in the arm, but it is a useful additional method. It provides good operating conditions for the surgery of hand infections.

In our cases, the procedure proved to be safe with doses of up to 5 mg./kg. of 0.5% lignocaine in isotonic saline, although tourniquet times were short. If this dose is exceeded, systemic side-effects may occur. The occurrence and severity of side-effects depends on the total dose given, its concentration, and the rate of its release from the arm.

The possibility of the occurrence of side-effects limits the performance of the procedure to places where equipment for resuscitation, by intermittent positive-pressure ventilation, intra-venous infusion and vasopressors, is immediately available.

Since the presentation of this paper, we have used up to 5 mg./kg. of 0.5% lignocaine followed by a 'chaser' of saline when necessary, in more than 400 patients, with uniform success and without complications.

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