Topical Anesthesia for Endoscopy; Evaluation of Prilocaine (Citanest), a New Local Anesthetic

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Topical anesthesia represents a commonly used anesthetic technique for a variety of endoscopic procedures. In general, local anesthesia for endoscopy is a safe and effective procedure. However, it has been shown that certain local anesthetics, such as tetracaine, are rapidly absorbed from the mucous membranes of the respiratory tract and can lead to severe toxic effects in man. Thus, it would be desirable to use a local anesthetic topically in the tracheobronchial tree which combines both anesthetic effectiveness and low systemic toxicity in order to avoid any systemic reactions which might occur due to rapid absorption from the mucous membranes of the respiratory tract.

During the past ten years, we have used 1 or 2 per cent lidocaine (Xylocaine) as the local anesthetic agent of choice for endoscopic procedures. Although we have not observed any serious adverse effects with lidocaine, a series of studies was initiated with a new local anesthetic agent, prilocaine (Citanest), whose potency is comparable to that of lidocaine, but whose toxicity is approximately 50 per cent less than that of lidocaine. Although a great number of clinical studies have confirmed the earlier pharmacologic reports that prilocaine is comparable in potency to lidocaine, but considerably less toxic, little data is available on the topical anesthetic efficacy of prilocaine in man. To date, Thornton and Telivuo have published data in a limited number of patients which indicate that prilocaine in a concentration of 4 per cent appears to have a topical anesthetic effect comparable to that of lidocaine.

The present study was initiated in order to determine how 2 and 3 per cent solutions of prilocaine compare in effectiveness with 2 per cent lidocaine for endoscopy. In order to avoid the possibility of bias, the comparison of prilocaine and lidocaine was made by means of a double-blind study. In addition, prilocaine alone was studied in another series in order to determine accurately the onset, duration, and effectiveness of this agent for topical anesthesia.

Method

For the past 13 years, lidocaine (Xylocaine), 1 or 2 per cent, has been used as a local anesthetic in endoscopy. That is, with the exception of when the prilocaine was used in this study. Our technique of anesthesia consists of spraying the oral pharynx and applying pledgets of cotton dipped in anesthetic into each arytenoid. Then the patient inhales the anesthetic, placing this either through the nose or dripping it into the oral pharynx with the body tilted to the right or to the left. Enough of the anesthetic is utilized until the cough reflex has been abolished. This usually consists of approximately 3 or 4 ml of anesthetic being instilled into each bronchial system. When the patient complains of difficulty in swallowing, then we feel that this is the end point and that the anesthesia is complete to proceed with the endoscopy. After the cough reflex has been abolished, the endoscopy procedure can be done, or if a bronchogram is needed, the contrast media is simply dripped into the oral pharynx or through the nose. Again, the patient is tilted to either side for position so desired filling can be obtained.
This procedure has been found to be simple and effective.

The above-mentioned technique has been used exclusively by the senior author. At the Missouri State Sanatorium, a catheter is usually inserted into the trachea and bronchograms performed in this routine manner.

**RESULTS**

A. **Double-Blind Study**

A total of 276 patients were studied in double-blind fashion. Approximately one-third of the patients were treated with 2 per cent lidocaine, while one-third were treated with 2 per cent prilocaine, and the remaining one-third with 3 per cent prilocaine. The results of this study are presented in Table 1. As can be seen, the subjects in the three groups were similar with respect to age, sex distribution, and body weight. The volume of anesthetic employed varied from an average of 16 ml in the 2 per cent lidocaine group to 19.9 ml in the 3 per cent prilocaine group. The onset of anesthetic effect was approximately eight minutes in the three groups with no significant difference between any of the three groups. Duration in this study represents the time between effective anesthesia and the time the patient stated the anesthetic had worn off or that he could swallow normally. As can be seen, no difference existed between the three groups. With respect to effectiveness of anesthesia, no significant difference was observed between the three groups. Lidocaine, however, had a significantly greater effect on abolishment of cough reflex than 2 per cent prilocaine (p = <0.05). No difference was found between lidocaine and 3 per cent prilocaine.

With regard to side effects, no adverse effect of a systemic or local nature were observed that could be directly attributable to the local anesthetic agents employed. One patient complained of nausea, another complained for headache, and one case of tachycardia was observed. However, these probably were all referable to the endo-

<table>
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<tr>
<th>Agent</th>
<th>No. Cases</th>
<th>Age (range)</th>
<th>Sex</th>
<th>Avg Wt (kg)</th>
<th>Avg Anest Vol (ml)</th>
<th>Anesthetic effects</th>
<th>Cough reflex</th>
<th>Anesthesia Duration (min)</th>
<th>Side Effects</th>
<th>Duration</th>
<th>Cyanosis</th>
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<tbody>
<tr>
<td>Lidocaine 2%</td>
<td>97</td>
<td>(39-80)</td>
<td>M:54</td>
<td>18.1</td>
<td>16.0</td>
<td>Adequate 94% (85.4%)</td>
<td>Abolished 79.4% (90.8%)</td>
<td>8.1</td>
<td>None</td>
<td>Trace 1</td>
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<tr>
<td>Prilocaine 2%</td>
<td>95</td>
<td>(10-82)</td>
<td>M:54</td>
<td>14.4</td>
<td>16.6</td>
<td>Adequate 92% (87%)</td>
<td>Abolished 77.4% (83.7%)</td>
<td>8.3</td>
<td>None</td>
<td>Trace 1</td>
<td></td>
</tr>
<tr>
<td>Prilocaine 3%</td>
<td>94</td>
<td>(15-79)</td>
<td>M:58</td>
<td>14.2</td>
<td>19.9</td>
<td>Adequate 90% (96.7%)</td>
<td>Abolished 84.4% (90.9%)</td>
<td>8.1</td>
<td>None</td>
<td>Trace 1</td>
<td></td>
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* + lidocaine vs. prilocaine 2% p < 0.05
  + lidocaine vs. prilocaine 3% p > 0.05
  + prilocaine 2% vs. prilocaine 3% p > 0.05
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scopic procedure rather than the local anesthetic agent. One patient treated with 2 per cent prilocaine did complain of a burning sensation which may be referable to the local anesthetic agent. It has been reported in other studies that in high doses prilocaine can cause a slight degree of methemoglobinemia. Thus, the lips and nail beds of all patients were carefully examined for cyanosis which might be referable to production of methemoglobin. One mild case of cyanosis was observed in a patient treated with 3 per cent prilocaine and two cases of trace cyanosis were observed, one in a patient treated with 2 per cent prilocaine and another in a patient treated with 3 per cent prilocaine. No cyanosis was observed in the lidocaine series.

B. Topical Anesthetic Properties of Prilocaine.

In order to determine more accurately the anesthetic effectiveness of prilocaine, an additional study was carried out in 204 patients to determine such properties as onset of anesthesia, duration of anesthesia, as well as effectiveness of anesthesia. Twenty-one of these patients were treated with 2 per cent prilocaine and the remaining 182 cases were treated with 3 per cent prilocaine. The values are presented in Table 2. As can be seen, the latency of 2 per cent prilocaine in this small series was 13 minutes as compared to 8.6 minutes for the 3 per cent prilocaine. When a larger number of cases were studied with 2 per cent prilocaine in the double blind investigation, no difference in latency was observed between the 2 and 3 per cent solutions. With regard to duration of topical anesthesia, the 2 per cent prilocaine group has an average duration of 40.5 minutes as compared to an average topical anesthetic duration of 51.6 minutes in the 3 per cent prilocaine group. Little difference between 2 and 3 per cent prilocaine was observed with respect to anesthetic effectiveness and the ability to abolish the cough reflex. These results are similar to those obtained in the double blind

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<tbody>
<tr>
<td>Prilocaine 2%</td>
<td>22</td>
<td>63.4 (34-82)</td>
<td>154.3 (110-190)</td>
<td>17.6</td>
<td>Adequate 21* (99.7%)</td>
<td>Abolished 20+ (91.9%)</td>
<td>40.5</td>
<td></td>
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<tr>
<td>Prilocaine 3%</td>
<td>182</td>
<td>56.0 (13-87)</td>
<td>141.8 (90-240)</td>
<td>15.3</td>
<td>Adequate 178 (97.4%)</td>
<td>Abolished 158 (86.5%)</td>
<td>51.6</td>
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* prilocaine 2% vs. prilocaine 3% p = >0.3 (chi-square)
study. Since the anesthetic effectiveness of 2 per cent prilocaine is so high (96 per cent), it is not surprising that increasing the concentration fails to significantly increase the anesthetic effectiveness. No adverse effects were noted in this study despite the use of doses as large as 900 mg of prilocaine.

**Discussion**

The results of this study indicate that both 2 and 3 per cent prilocaine are potent topical anesthetic solutions which can be effectively used for anesthesia prior to endoscopy. No difference could be determined between the effectiveness of these two solutions of prilocaine and that of lidocaine which has served as our standard for topical anesthesia for the past ten years. Three per cent prilocaine may have an advantage in terms of producing a longer duration of anesthetic action. However, since most endoscopy procedures rarely last over 30 minutes, it would appear that the 2 per cent prilocaine solution is adequate for most endoscopy procedures. Since little difference in anesthetic effectiveness was observed between lidocaine and prilocaine, the lower potential systemic toxicity of prilocaine might suggest that this agent is more suitable for use in the tracheobronchial tree. It has been shown by Adriani and Campbell that certain local anesthetic agents, such as tetracaine, are rapidly absorbed from the mucous membranes of the respiratory tract and can lead to adverse systemic effects. Studies by Astrom and Persson in experimental animals have also shown the rapid absorption of tetracaine from the respiratory tract, but these same studies indicate that both lidocaine and prilocaine are not absorbed as rapidly when applied to the mucous membranes of the respiratory tract. Telivuo has carried out measurements of prilocaine and lidocaine blood levels following application of these agents to the respiratory tract and has found a lower blood level concentration for prilocaine as compared to lidocaine. If blood levels of local anesthetics are related to their potential for producing systemic toxicity, this would indicate that prilocaine when used topically for endoscopy does have less of a potential toxicity than lidocaine. The clinical safety of prilocaine has been demonstrated in a number of studies in which single injections of 900 - 1200 mg have been made. The only side effect noted to date with prilocaine is its ability to produce methemoglobinemia when given in large amounts. However, since this condition does not appear to be serious, and since it only occurs when large amounts are administered, this would not appear to be a deterrent to the use of prilocaine for topical anesthesia prior to endoscopy.

These studies also confirm the topical anesthetic effectiveness of prilocaine as reported previously by Thornton and Johnston. However, the studies also indicate that it is not necessary to use a 4 per cent solution of prilocaine as was employed by Thornton and Johnston. The anesthetic effectiveness of 2 per cent prilocaine appears to be equal to that of 3 per cent prilocaine, and therefore would seem to be adequate for most endoscopic procedures.

**Summary**

A clinical study was carried out to evaluate the topical anesthetic effectiveness of a new local anesthetic, prilocaine (Citanest). A double blind comparison of 2 and 3 per cent prilocaine and 2 per cent lidocaine (Xylocaine) was carried out and no statistically significant difference between these agents was observed with regard to topical anesthesia. Lidocaine did have a statistically greater effect on abolishing the cough reflex when compared to 2 per cent prilocaine, but not as compared to 3 per cent prilocaine. A more careful comparison of 2 and 3 per cent prilocaine alone indicates that one can increase the duration of topical anesthesia by increasing the concentration of this agent. However, for practical purpose, 2 per cent prilocaine appears to be adequate for most endoscopy procedures and in this study 2 per cent prilocaine was as effective as 2 per
cent lidocaine as a topical anesthetic for endoscopy.

Acknowledgments: We wish to thank our anesthesiologists, Dr. O. B. Crawford and his partners, for controlling the anesthetic agents and issuing them to us individually, thus insuring the integrity of this study.

We also wish to thank the operating room nurses at St. John’s Hospital and Burge Protestant Hospital, Springfield, Missouri, and the Missouri State Sanatorium, for their cooperation in this study.

Resumen

La efectividad de un nuevo anestésico local, la prilocaina (Citanest) ha sido estudiada mediante la comparación de la prilocaina al 2 y 3% y la lidocaina (xilocaina) al 2%.

No se pudo comprobar diferencia apreciable entre estos dos agentes en cuanto a sus efectos anestésicos tópicos. La lidocaina manifestó una acción estadísticamente significativa; la lidocaina al 3% aumenta la concentración del reflejo tóxico, comparativamente a la prilocaina al 2%, pero no con relación a la misma al 3%.

La comparación cuidadosa de la prilocaina en solución al 2 y 3% indica que la duración del efecto anestésico tópico aumenta con la concentración de este agente. Sin embargo, para los efectos prácticos la prilocaina al 2% parece adecuada para la mayor parte de los procedimientos de endoscopia y en este estudio, la prilocaina al 2% se mostró tan efectiva como la lidocaina a la misma concentración como anestésico tópico para la endoscopia.

Zusammenfassung

Es wurde eine klinische Untersuchung angelöst zwecks Ermittlung des lokal anästhetischen Wertes eines neuen Lokal-Anästhetikums, namentlich Prilocain (Citanest). Ein Vergleich im doppelten Blindversuch von 2% und 3% Prilocain und 2% Lidocain (Xylocain) wurde unternommen, und es fand sich keine statistisch ins Gewicht fallende Differenz zwischen diesen beiden Stoffen im Hinblick auf die lokale Anästhesie. Lidocain hatte einen statistisch größeren Effekt auf die Beseitigung des Hustenreflexes im Vergleich zu einer 2%-igen Prilocain-Lösung, jedoch nicht im Vergleich zu einer 3%-igen Prilocain-Lösung. Ein sorgfältiger Vergleich von 2% und 3% Prilocain allein weist darauf hin, daß man die Dauer der Lokalanästhesie verlängern kann durch Erhöhung der Konzentration dieses Stoffes. Es scheint jedoch für die praktischen Zwecke eine 2%-ige Prilocain-Lösung auszureichen, jedenfalls für die meisten endoskopischen Untersuchungen, und auch bei dieser Untersuchung erwies sich Prilocain in 2%-iger Lösung ebenso wirkungsvoll eine 2%-ige Lidocain-Lösung für die Lokal-Anästhesie zur Endoskopie.

References


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