

# A Comparative Trial of Succinylcholine vs Low Dose Atracurium-Lidocaine Combination for Intubation in Short Outpatient Procedures

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Despite its many disadvantages, succinylcholine is the most commonly used drug for intubation of patients for short out-patient procedure. This double blind trial compared a low dose atracurium/lidocaine combination to succinylcholine for intubation in 40 ASA1 adult patients. Low dose atracurium/lidocaine provided clinical intubating conditions at two minutes and cardiovascular stability equivalent to succinylcholine with significantly less myalgia. Spontaneous respiration was slower after low dose atracurium/lidocaine relative to succinylcholine. Low dose atracurium/lidocaine may provide an acceptable alternative to succinylcholine for intubation in short outpatient procedures.

In most patients, the ease with which tracheal intubation can be achieved depends on the technical proficiency of the anesthetist, the depth of anesthesia and the degree of muscle relaxation. A deficiency in one or two of these factors can usually be compensated by amplification of the remaining factors.<sup>1</sup> Succinylcholine (Sc) is the most commonly used drug for intubation of patients for short outpatient procedures. It has a brief duration of

action of 5 to 10 minutes and intubation can usually be accomplished one minute after its administration.

There are a number of problems associated with the use of Sc. These can be divided into six broad categories:

1. Post operative muscle pain
2. Elevated intraocular and intragastric pressure
3. Cardiac dysrhythmias
4. Prolonged duration of action due to the prolonged presence of a reduced amount or atypical form of pseudocholinesterase.
5. Hyperkalemia
6. Triggering agent for malignant hyperthermia

Succinylcholine induced muscle pain is a common problem in ambulatory surgery patients. Recently it has been reported to occur between 41% and 63% of the time in non-pretreated outpatients.<sup>2,3,4</sup> It occurs more frequently following minor surgery, in women and in bedridden patients.<sup>5</sup> Waters and Mapleson<sup>4</sup> hypothesized that pain is secondary to damage sustained in the muscle by the unsynchronized contraction of adjacent muscle fibers just before the onset of paralysis. Most investigators believe that pre-treatment with a subparalyzing dose of a non-depolarizing muscle relaxant prevents the fasciculation by Sc and thereby decreases the muscle pain.<sup>5</sup>

Sc induced cardiac dysrhythmias are many and varied. These are principally manifested as sinus bradycardias, junctional rhythms and ventricular dysrhythmias ranging from unifocal premature ventricular contractions to ventricular fibrillation. Sinus bradycardia is the most common, occurring most frequently in children. It usually occurs after a second dose of Sc is given approximately five minutes after the first.<sup>6</sup>

Atracurium, a drug recently developed by Stenlake et al.<sup>7</sup> in Glasgow is a competitive non-depolarizing neuro-

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muscular blocking agent. Doses ranging from 0.15 to 0.8 mg/kg have been reported for the use of endotracheal intubation.<sup>8</sup> Atracurium, particularly in high doses, has been associated with histamine release, which can rarely lead to bronchospasm and cardiovascular collapse.<sup>9</sup> Atracurium doses in the order of 0.2 mg/kg have been associated with remarkable cardiovascular stability.<sup>10</sup>

The speed of onset of atracurium depends on the dose used (larger doses having quicker onset), the anesthetic agent used (inhalation agents potentiate atracurium) and the use of the priming principles.<sup>11,12,13</sup> Doses of 0.4 to 0.5 mg/kg (the recommended dose range for intubation)<sup>14</sup> will, in most instances, show complete neuromuscular blockade within two minutes.<sup>12,14</sup> Higher doses of 0.9 mg/kg have not been shown to increase the speed of onset.<sup>14</sup> A lower dose of 0.2 mg/kg provides adequate skeletal relaxation<sup>15</sup> but is considerably slower in onset,<sup>12</sup> and is associated with slight laryngeal movement, and mild coughing in response to intubation.<sup>16</sup>

The duration of action of atracurium is also dose dependent with a higher dose having a considerably longer duration of action. This is a disadvantage in short outpatient procedures due to the prolonged absence of spontaneous respiration. When 0.3 mg/kg of atracurium is used, spontaneous respiration can return in 24 minutes.<sup>17</sup>

Intravenous lidocaine in dosages of 1.5 mg/kg given two minutes prior to intubation has been shown to suppress the cough reflex, prevent a rise in blood pressure and heart rate associated with intubation, decrease the MAC of halothane 10–28%, decrease the incidence of arrhythmias associated with intubation, and to possibly suppress the rise in intracerebral pressure associated with intubation.<sup>18–21</sup> Lidocaine has also been shown to reduce both the incidence and severity of post-operative myalgias by 50%.<sup>3</sup>

This study compared the intubating conditions in patients given a combination of lidocaine (1.5 mg/kg) and atracurium (0.2 mg/kg) to those observed in patients receiving succinylcholine (1.0 mg/kg) for short outpatient procedures. It was hypothesized that lidocaine and atracurium combination would provide cardiovascular stability, less post-operative muscle pain, a short absence of spontaneous respiration and an acceptably short duration of action when compared to succinylcholine.

## MATERIALS AND METHODS

Forty adult (ASA I) patients who had requested general anesthesia for the surgical removal of their impacted third molar teeth were asked to participate in this study. An informed written consent was obtained prior to surgery. The patients were randomly allocated to one of two groups, an atracurium–lidocaine (A/L) group and a succi-

nylcholine (Sc) group. All procedures had an expected surgical time of at least 30 minutes but not more than two hours. The patients were placed in a semisupine position and ECG and pulse oximeter monitors were applied. An automatic blood pressure cuff was placed on the right arm and an intravenous infusion was started on the left.

The Puritan-Bennett/Datex Neuromuscular Transmitter monitor 221 (NMT 221; Puritan-Bennett, Wilmington, Massachusetts) was applied to the right hand and arm of each subject. Silver chloride electrodes were placed over the hypothenar aspect of the right hand. The systolic, diastolic and mean arterial blood pressures were continuously monitored and recorded at one minute intervals for the first ten minutes of the procedure and thereafter at every three minutes. The ECG was continuously monitored during the entire procedure, and was recorded on paper from the start of intubation, and up until two minutes following the completion of intubation.

Neuromuscular blockade was assessed by using the NMT monitor. The stimulator delivers a train-of-four (T1/T4 ratio) 0.1 ms square wave impulses over the ulnar nerve at 0.5 Hz and repeats every 20 seconds. The 20 second time interval between trains avoids any potentiating effect of neuromuscular transmission and the first twitch response of every train-of-four is considered a true single twitch. The signals obtained were amplified, filtered, rectified, and electronically integrated (EMG). The resulting value of single twitch height (STH) was expressed as a percentage of the base line relaxant free twitch amplitude. It was then presented on a digital display and recorded by a plotter.

Patients were administered intravenously 100 mcg of fentanyl in two increments while breathing 100% oxygen. After 2 minutes methohexital (2 mg/kg) was infused intravenously to induce anesthesia. Additional doses of methohexital (25% of the initial dose) were given if required to obtain loss of eyelid reflex. A series of three baseline T1/T4 ratio responses were then obtained after the NMT monitor calibration mode was completed. A priming dose of atracurium (0.05 mg/kg) for the A/L group or saline for the Sc group was then administered.

Ventilation with 2% halothane, 50% N<sub>2</sub>O and 50% O<sub>2</sub> was assisted as necessary to maintain the end tidal CO<sub>2</sub> between 35 and 45 mmHg as measured on a capnograph. At three minutes following the priming dose, the remaining dose of atracurium (0.15 mg/kg) followed by lidocaine (1.5 mg/kg) or Sc (1 mg/kg) followed by saline were given and an additional dose of methohexital (0.5 mg/kg) was administered. At 2 minutes a direct laryngoscopy and nasotracheal intubation was initiated and the quality of intubation conditions recorded by the same anesthetist. The blinded anesthetist was not present in the room during the administration of the muscle relaxant drugs so that he could not be influenced by the presence

of fasciculation or movement. Assessment of the intubation conditions were made with four category scales:

Ease of oral opening: 1—could not open the mouth sufficiently; 2—oral opening just adequate for intubation; 3—easy oral opening and essentially ideal for intubation.

Ease of vocal cord visualization: 1—could not see the cords at all; 2—half or less of the vocal cords were visible; 3—all of the vocal cords were visible.

Movement of the vocal cords: 1—vocal cords closed tightly; 2—vocal cords partly relaxed; 3—vocal cords fully relaxed.

Movement in intubation; 1—generalized muscular movement and/or marked coughing; 2—mild coughing; 3—patient completely relaxed, no coughing.

Following intubation, the patient was manually ventilated with 1% halothane, 70% nitrous oxide and 30% oxygen and adjustments were made to approximate normal blood pressure for each patient. The end tidal carbon dioxide was continuously monitored and ventilation adjusted to maintain approximately 50 mm Hg until spontaneous ventilation occurred. The time at which patients did so was noted and the STH and T1/T4 ratio at that time, were recorded.

At the completion of surgery the assessment of neuromuscular blockade was continued. If there was 100% recovery of STH and T1/T4 ratio, the patient was given 100% oxygen and extubated. If 100% recovery had not occurred the neuromuscular blockade was reversed using edrophonium (0.5 mg/kg) and atropine (0.6 mg) prior to extubation with 100% oxygen. Patients were transferred to recovery room and when stable, discharged to an escort. Patients were given a questionnaire concerning postoperative muscle pain and stiffness and were requested to complete this approximately 48 hours after surgery. They were asked to record on the second day after their operation, whether they had muscle discomfort (none [1], mild [2], moderate [3] or severe [4]) stiffness and/or tenderness. They were asked to record their answers for three areas of anatomy; their arms or shoulders, chest or back, or in their stomach or legs. At the usual one week postoperative surgical visit, patients returned their completed questionnaire and were asked to complete another one to evaluate muscle pain and stiffness after one week.

Demographic data was tested with an unpaired Student's t-test. ECG recordings were examined blindly. The number of episodes of ventricular ectopy and other changes from normal sinus rhythm were recorded. The changes in heart rate between the two groups were addressed separately. Any treatment to correct a rhythm abnormality was noted. Ventricular ectopy was assessed by counting the number of individual occurrences of each episode. Ventricular irritability and rhythm were evaluated statistically using the unpaired Student's t-test to deter-

mine any significant differences between the groups. Changes in systolic and mean arterial pressure during intubation were also evaluated using the unpaired Student's t-test. The intubation variables were tested non parametrically using the Mann-Whitney Wilcoxon test. The speed of onset for the two neuromuscular blocking agents was determined by the mean time taken to achieve maximum blockade of STH and T1/T4 ratio. The times to initiation of spontaneous respiration, return of 100% STH and T1/T4 ratio, the percentage of neuromuscular blockade at intubation and the initiation of spontaneous respiration were compared using the unpaired Student's t-test. Postoperative muscular pain was evaluated in three anatomic areas (shoulder and arms, chest and back, abdomen and legs) and the scores of the two drug groups compared using a nonparametric Mann-Whitney Wilcoxon test.

## RESULTS

There were 21 patients (13 female) in the Sc group and 19 patients (12 female) in the A/L group. Their mean ages were 22.0 yrs (range 18–30) for the Sc group and 22.9 yrs (range 18–38). Their mean weights were 65.4 kg (S.D. = 13.1) for the Sc group and 65.4 kg (S.D. = 15.6). None of these values were statistically different.

The results for the neuromuscular blockade are shown in Table 1. The A/L group showed a significant delay in the onset of maximal NMB ( $p < 0.001$ ). Duration of action of atracurium was also significantly longer as measured by STH and T1/T4 ratio ( $p < 0.001$ ). One patient in the Sc group required a second dose of succinylcholine due to the ineffective action and laryngospasm during attempted intubation following the first dose. This patient's data is not included in the respiratory time, duration times, or STH at return of spontaneous respiration. The time taken to achieve spontaneous respiration was significantly longer in the A/L group ( $p < 0.001$ ). The STH at intubation was significantly ( $p < 0.001$ ) lower for Sc group. There was no dose effect correlation for either group, nor was there any significant correlation between intubation conditions and the degree NMB (using a Pearson correlation coefficient). There was a significant difference ( $p < 0.05$ ) between the two groups as to the degree of maximum NMB. 71.4% of the Sc group reached completed neuromuscular blockade as opposed to only 15.1% of the A/L group.

The degree of NMB (STH) at the return of spontaneous respiration was not significantly different between the two groups. Eight patients in the A/L group required reversal of the NMB because the operation was completed prior to the return of 100% of pretreatment STH or T1/T4 ratio. Two patients within this group did have a 100% STH return but not a 100% T1/T4 ratio.

**Table 1.** Summary of neuromuscular blockade data (mean  $\pm$  standard deviation).

	<i>Succinylcholine</i>	<i>Atracurium/Lidocaine</i>	
Onset time (secs)	88.6 $\pm$ 52.0	462.1 $\pm$ 141.6	p < 0.001
Time until spontaneous ventilation (mins)	7.6 $\pm$ 2.1 <sup>a</sup>	12.2 $\pm$ 4.2	p < 0.001
Time for 100% recovery of STH (mins)	12.1 $\pm$ 4.6 <sup>a</sup>	37.7 $\pm$ 9.2 <sup>b</sup>	p < 0.001
Duration for 100% recovery of T1/T4 (mins)	12.1 $\pm$ 4.6 <sup>a</sup>	48.9 $\pm$ 9.6 <sup>c</sup>	p < 0.001 (3) n = 11
STH at intubation (% of control STH)	10.2 $\pm$ 25.0 (range 0–90)	63.4 $\pm$ 23.4 (range 12–100)	p < 0.001
STH at maximum blockade (% of control STH)	5.7 $\pm$ 19.2 (range 0–87.5)	19.5 $\pm$ 16.1 (range 0–57.8)	p < 0.005
STH at spontaneous respiration (% of control STH)	34.5 $\pm$ 35.7 <sup>a</sup>	24.3 $\pm$ 15.4	N.S.
STH at reversal (% of control STH)	N/A	83.6 $\pm$ 19.2 <sup>d</sup>	
T1/T4 at intubation	N/A	55.2 $\pm$ 22.1	
T1/T4 at maximum blockade	N/A	16.6 $\pm$ 17.1	
T1/T4 at respiration	N/A	22.7 $\pm$ 19.1	
T1/T4 at reversal	N/A	55.4 $\pm$ 14.0 <sup>d</sup>	

<sup>a</sup> N = 20, one patient in the succinylcholine group required a second dose of the drug due to laryngeal spasm during attempted intubation.

<sup>b</sup> N = 13, six patients had not recovered 100% STH at the time of reversal in the A/L group.

<sup>c</sup> N = 11, eight patients had not recovered 100% T1/T4 at the time of reversal in the A/L group.

<sup>d</sup> N = 8, eight patients in the A/L group required reversal of NMB.

There were no significant differences in preintubation systolic blood pressure, preintubation pulse rate, postintubation mean arterial pressure or postintubation pulse rate between the two groups (Table 2). The A/L group did have a significantly ( $p < 0.05$ ) lower pre-intubation mean arterial pressure. There was no significant differences in the increase in pulse rates associated with intubation.

Analysis of the ECG data showed that two patients in the Sc group and one in the A/L group had episodes of ventricular ectopy during the intubation. On all occasions these were less than five ectopic beats per patient. Three patients in the A/L group and one in the Sc group had loss of p waves during intubation. These irregularities were of longer durations, in one case, lasting up to 100 beats in the A/L group.

There were no differences in intubation conditions or in the number of attempts at intubation required between the groups (Table 3). Muscle stiffness and tenderness was greater in the Sc group at two days (Table 4). This was

significant for the arm or shoulder and chest or back. At one week nearly all muscular symptoms had resolved and there were no differences between the two groups.

## DISCUSSION

A combination of lidocaine and atracurium was evaluated to overcome some of the deficiencies of the use of a single low dose of atracurium, thereby decreasing coughing, bucking and movement during intubation, by increasing the depth of anesthesia and decreasing the tracheal irritation. The use of a combination drug therapy when compared to a single drug therapy complicates interpretations as either low dose atracurium or lidocaine by themselves could have produced the results independently. However, the use of lidocaine in the succinylcholine group would not have alleviated most of the inherent problems associated with the use of the succinylcholine except probably

**Table 2.** Cardiovascular effects (mean  $\pm$  standard deviation)

	<i>Succinylcholine</i>	<i>Atracurium/Lidocaine</i>	
Systolic blood pressure Pre-intubation	100.2 $\pm$ 15.9	92.5 $\pm$ 16.2	NS
Systolic blood pressure Post intubation	120.0 $\pm$ 19.1	109.7 $\pm$ 17.8	NS
Mean arterial pressure Pre-intubation	78.0 $\pm$ 13.5	68.4 $\pm$ 9.7	p < 0.05
Pulse rate Pre-intubation	74.9 $\pm$ 13.1	72.2 $\pm$ 11.9	NS
Pulse rate Post-intubation	83.1 $\pm$ 11.7	87.1 $\pm$ 15.7	NS

**Table 3.** Intubation conditions (mean  $\pm$  standard conditions).

	Succinylcholine	Atracurium/Lidocaine	
Ease of oral opening	2.89 $\pm$ 0.32	2.79 $\pm$ 0.42	NS
Ease of vocal cord visualization	2.90 $\pm$ 0.44	3.00 $\pm$ 0.00	NS
Movement of vocal cords	2.86 $\pm$ 0.48	2.89 $\pm$ 0.32	NS
Bodily movement on intubation	2.81 $\pm$ 0.51	2.74 $\pm$ 0.45	NS
Number of attempts at intubation	1.1 $\pm$ 0.4	1.1 $\pm$ 0.3	NS

reducing the incidence and severity of post-operative myalgia.

The mean time to maximal NMB (using STH) for atracurium (0.2 mg/kg) was approximately 7.7 minutes. This time was similar to that reported by Ramsey et al.<sup>11</sup> of 7.7 minutes when using nitrous oxide and enflurane and that of 7.1 minutes when used without any inhalation agent.<sup>14</sup> The effect of a priming dose was not assessed in this paper.

It is well recognized that inhalation agents potentiate the intensity of NMB, prolong the duration of the block and may increase the speed of blockade in neuromuscular blockade produced by atracurium.<sup>11,22</sup> The degree of maximal NMB (STH) for atracurium in the study was 19.5% of initial twitch height. This was not as great as that reported by Ramsey et al.<sup>11</sup> of 6.7% who used halothane anesthesia and that of Stirt et al.<sup>22</sup> of 3% using enflurane. However, the value was close to that of 19% reported by Payne and Hughes<sup>12</sup> and 26% reported by Hughes and Payne<sup>14</sup> using balanced anesthesia. In the format of the present study, stabilization of halothane anesthesia would not have occurred in contrast to the cases of Ramsey et al.<sup>11</sup> and Stirt et al.<sup>22</sup> Thus, as was demonstrated by this study, the degree of NMB would be expected to be close to that seen with balanced anesthesia. The degree of mean maximal NMB (STH) for succinylcholine in this study was 5.7% of the initial twitch height. Gergis et al.<sup>1</sup> reported a similar height of 6.6% and Stirt et al.<sup>8</sup> reported a mean value of 2% for ten patients.

With doses of 0.3 mg/kg of atracurium, Astley et al.<sup>17</sup> reported that spontaneous respiration returned within

24.0 minutes. In the present study with doses of 0.2 mg/kg spontaneous respiration returned at a mean of 12.2 minutes. Astley et al.<sup>17</sup> demonstrated that the return of spontaneous respiration does not imply a return of full neuromuscular function. This study confirms those results by demonstrating a greater than 65% block of STH at the return of spontaneous respiration for both succinylcholine and the A/L groups. Following the use of 1 mg/kg of succinylcholine spontaneous respiration usually returns at around 6.0 minutes<sup>23</sup> although this is influenced by the type of induction agent used. The present study had a similar value of 7.6 minutes for the return of spontaneous respiration in this group.

Intubating conditions depend not only on the depth of neuromuscular blockade, but also on the depth of anesthesia and anatomical factors as well. Intubating conditions between the two groups were indistinguishable. In only one patient did a laryngospasm occur during intubation and this occurred in the Sc group and required a second dose of Sc to control the situation. Low dose atracurium has been purported to enable adequate skeletal relaxation but is associated with a high incidence of coughing and bucking during intubation.<sup>15,16</sup> Intravenous lidocaine is widely recognized to increase the depth of anesthesia, reduce the cardiovascular response and to depress the cough reflex associated with intubation.<sup>18,19,21</sup> It appears in this study that adequate skeletal relaxation was obtained for intubation by the depth of anesthesia and the use of low dose atracurium. The cough reflex was probably suppressed by the use of intravenous lidocaine and an adequate depth of anesthesia. This combination

**Table 4.** Muscular stiffness and tenderness 48 hours postoperatively.

	Succinylcholine	Atracurium/Lidocaine	
2 days			
Arms or shoulders	1.57 $\pm$ 0.68	1.11 $\pm$ 0.32	p < 0.05
Chest or back	1.67 $\pm$ 0.73	1.11 $\pm$ 0.46	p < 0.01
Stomach or legs	1.29 $\pm$ 0.56	1.11 $\pm$ 0.32	NS
7 days			
Arms or shoulders	1.05 $\pm$ 0.22	1.00 $\pm$ 0.00	NS
Chest or back	1.05 $\pm$ 0.22	1.00 $\pm$ 0.00	NS
Stomach or legs	1.00 $\pm$ 0.00	1.00 $\pm$ 0.00	NS

(A/L) lead to intubation conditions comparable to those produced by Sc.

The incidence of Sc induced muscle pain of 47% in the present study is in agreement with previous work.<sup>3,4</sup> As expected the incidence of postoperative myalgia was very low in the A/L group. Lidocaine, when used intravenously has been shown to have a protective effect against postoperative myalgia<sup>3,24</sup> and therefore comparison of the studies which only used atracurium was not possible. By one week nearly all myalgia had resolved.

In conclusion, the A/L combination provided equal clinical intubating conditions when compared with the Sc group at two minutes. Cardiovascular stability was comparable between the two groups. Although the duration of NMB was longer, the return of ventilatory efforts by the patient was on average only five minutes later than the Sc group. Postoperative myalgia was significantly greater in the Sc group. It appears that low dose atracurium with lidocaine may provide an acceptable alternative for intubation with respect of ease of intubation, cardiovascular stability and myalgia, as compared to succinylcholine for short outpatient procedures.

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