Atracurium besylate is rapidly inactivated at physiological pH and temperature by Hofmann elimination and by ester hydrolysis independent of the serum pseudocholinesterase activity (Stenlake, 1979; Hughes and Chapple, 1981; Payne and Hughes, 1981; Katz et al., 1982). In contrast, suxamethonium is rapidly hydrolysed by the serum pseudocholinesterase (Kalow, 1959).

In vitro experiments have shown that the half-life for the degradation of atracurium is unchanged whether incubated in plasma of patients with normal or abnormal cholinesterase, while the half-life of suxamethonium is markedly prolonged when incubated in plasma having abnormal cholinesterase (Merrett, Thompson and Webb, 1983).

We have investigated the serum pseudocholinesterase activity in 17 pregnant women undergoing Caesarean section under general anaesthesia, and compared the enzyme activity with the duration of neuromuscular blockade achieved by suxamethonium 1.5 mg kg$^{-1}$ v. atracurium 0.25 mg kg$^{-1}$.

PATIENTS AND METHODS

The mean age was 27 ± 4.8 (SD) yr, and mean body weight 56.5 ± 25.8 kg.

Serum pseudocholinesterase activity

Serum pseudocholinesterase activity was measured spectrophotometrically in all patients, using propionylthiocholine (PTC) or suxamethonium as substrate. Dibucaine and fluoride numbers were also determined with PTC as a substrate (Evans and Wroe, 1978).

SUMMARY

Serum pseudocholinesterase activity in pregnant women was assayed spectrophotometrically using either propionylthiocholine or suxamethonium as substrate. All patients had a normal phenotype as indicated by normal dibucaine and fluoride numbers. However, the mean cholinesterase activity was lower than in the general population. There was a negative correlation between cholinesterase activity and the duration of neuromuscular blockade following suxamethonium, but no correlation was observed between the cholinesterase activity and the duration of block following atracurium.

Neuromuscular transmission

Neuromuscular transmission was assessed clinically with a battery-operated Myotest Mk 2 nerve stimulator. The ulnar nerve was stimulated supramaximally at the wrist every 10 s, while the contraction response of the fingers was observed (Viby-Mogensen, 1982). The duration of complete neuromuscular blockade following suxamethonium and atracurium was computed as the time between the onset of complete block until the onset of muscle contraction.

Anaesthesia technique

All patients were premedicated with glycopyrrolate 0.4 mg i.m. 40 min before surgery. Anaesthesia was induced with thiopentone 3 mg kg$^{-1}$ i.v. followed by suxamethonium 1.5 mg kg$^{-1}$ i.v. The trachea was intubated. Ventilation was controlled using 60% nitrous oxide in oxygen. When the twitch response started to recover after the suxamethonium block, an initial bolus of atracurium 0.25 mg kg$^{-1}$ was injected i.v. The duration of complete neuromuscular blockade following suxamethonium 1.5 mg kg$^{-1}$ and atracurium...
0.25 mg kg\(^{-1}\) was recorded. Neuromuscular blockade was maintained as required by injecting one-fifth of the original dose of atracurium (0.05 mg kg\(^{-1}\)); the number of supplementary doses and the intervals between them were recorded. At the end of surgery, the neuromuscular blockade was antagonized with a mixture of neostigmine and atropine.

**RESULTS**

**Serum pseudocholinesterase activity**

The serum pseudocholinesterase activity, as determined by using PTC or suxamethonium as substrates, showed marked linear correlation \((r = 0.95)\) (fig. 1). The mean serum pseudocholinesterase activity with PTC as a substrate was 3.42 ± (SD) 0.66 u. ml\(^{-1}\) (control 4.1 ± 1.4 u. ml\(^{-1}\)); with suxamethonium as a substrate it was 45.6 ± 11.2 u. litre\(^{-1}\) (control 58.2 ± 14.2 u. litre\(^{-1}\)). These values were significantly lower than the control values in our population \((P < 0.01)\). All patients had a normal phenotype \([E,u E,u]\) as indicated by their dibucaine \((87.8 ± 2.8)\) and fluoride \((81.5 ± 6.1)\) numbers.

**Neuromuscular blockade**

**Suxamethonium.** Suxamethonium 1.5 mg kg\(^{-1}\) produced complete neuromuscular block for 6.2 ± 2.9 min. There was a significant correlation \((P < 0.001)\) between the duration of neuromuscular blockade and the plasma pseudocholinesterase activity as determined by using either PTC or suxamethonium as substrate (fig. 2).

**Atracurium.** The initial bolus of atracurium 0.25 mg kg\(^{-1}\) produced complete neuromuscular block for 27.7 ± 10.9 min. There was no significant correlation between the plasma cholinesterase activity determined by using PTC or suxamethonium as substrate and the duration of action of atracurium (fig. 3).

Table 1 shows the intervals between the initial bolus and the subsequent supplementary doses of atracurium. The mean number of supplementary doses required to maintain blockade throughout surgery was 1.85 ± 1.3. No cumulative effect followed repeated doses.

The injection of the initial bolus of atracurium was followed by short-lasting palmar flush in five patients and by a generalized rash in one. No bronchospasm or significant cardiovascular change followed either the initial or the subsequent doses of atracurium in any patient. At the end of surgery, which lasted 28.3 ± 2.5 min, the neuromuscular blockade could be adequately antagonized by a mixture of neostigmine 0.025 mg kg\(^{-1}\) and atropine 0.01 mg kg\(^{-1}\).

Seven babies were delivered during suxamethonium block before the administration of atracurium, and 10 were delivered following atracurium injection. The Apgar scores of all newborns ranged between 7–9 at 1 min, and 8–10 at 5 min.

**Table 1.** Time intervals (mean ± SD) between the initial bolus of atracurium and subsequent supplementary doses. No cumulative effect was observed following repeated doses

<table>
<thead>
<tr>
<th></th>
<th>Initial atracurium to 1st maintenance</th>
<th>1st to 2nd maintenance</th>
<th>2nd to 3rd maintenance</th>
<th>3rd to 4th maintenance</th>
<th>4th to 5th maintenance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time (min)</td>
<td>27.7 ± 10.9</td>
<td>12.5 ± 5.9</td>
<td>13.2 ± 4.8</td>
<td>13.1 ± 4.8</td>
<td>13.2 ± 4.7</td>
</tr>
<tr>
<td>n</td>
<td>17</td>
<td>17</td>
<td>14</td>
<td>7</td>
<td>4</td>
</tr>
</tbody>
</table>
**DISCUSSION**

This report confirms previous investigations showing that atracurium can be used safely in patients undergoing Caesarean section (Flynn, Frank and Hughes, 1984). There were no adverse effects in either the mother or the newborn. It also confirms that the plasma pseudocholinesterase is decreased during pregnancy (Shnider, 1985). This decrease has been observed even in early pregnancy (Howard, East and Chaney, 1978), and in gestational trophoblastic disease (Davies, Carmichael and Dymond, 1983).

In all patients the serum pseudocholinesterase was the usual [E1u E1u] phenotype as indicated by normal dibucaine and fluoride numbers. The rapid rate of suxamethonium hydrolysis by the genotypically normal pseudocholinesterase is such that only a small fraction of the original dose actually reaches the neuromuscular junction (Kalow, 1959). Our report shows a negative corre-
lation between the duration of suxamethonium blockade and the pseudocholinesterase activity as assayed with PTC or suxamethonium itself as substrate. Low cholinesterase activity is associated with an increased duration of suxamethonium blockade (Foldes, Rendell-Baker and Birch, 1956; Viby-Mogensen, 1980). However, because of the extremely rapid hydrolysis of suxamethonium by the normal enzyme, a clinically significant prolongation of suxamethonium blockade will only occur in cases of extreme decrease in the normal enzymatic activity, as in organophosphorus poisoning (Baraka, Chaya and Abu Jaude, 1984).

Our technique of assay has shown that the ability of normal cholinesterase to hydrolyse PTC as a substrate correlates well with its ability to hydrolyse suxamethonium ($r = 0.95$). This is different from the genotypically atypical enzyme which hydrolyses suxamethonium at a much slower rate than other substrates. Therefore, assay of pseudocholinesterase activity with suxamethonium itself as a substrate is a better indicator of suxamethonium sensitivity than other substrates such as benzoylcholine (Goedde, Held and Atland, 1968).

Atracurium, in contrast to suxamethonium, is not destroyed by the pseudocholinesterase. This

![Graph](https://example.com/graph.png)

**Fig. 3.** Correlation between serum cholinesterase activity and duration of neuromuscular block by atracurium. With suxamethonium as substrate (top), activity (u. litre$^{-1}$) = 0.288 x duration (min) + 58.3; $r = 0.031$, $n = 17$. With propionylthiocholine as substrate (bottom), activity (u. ml$^{-1}$) = -0.0072 x duration (min) + 3.51; $r = -0.085$, $n = 17$.  

```r
fig_3 <- ggplot(data, aes(x = duration, y = activity)) + geom_point() + geom_smooth(method = "lm") + labs(x = "Atracurium block (min)", y = "Cholinesterase activity with suxamethonium (u litre$^{-1}$) or propionylthiocholine (u ml$^{-1}$)")
```
has been shown in vitro by Merrett, Thompson and Webb (1983), and is confirmed in vivo by the present report, which shows no correlation between the duration of neuromuscular blockade produced by atracurium and the cholinesterase activity. We have shown previously that atracurium blockade is not prolonged in patients inheriting the atypical gene (Baraka and Abu Jaude, 1984), or in patients whose normal pseudocholinesterase activity is quantitatively inhibited by anticholinesterases such as organophosphorus compounds (Baraka, Chaya and Abu Jaude, 1984), or neostigmine and pyridostigmine therapy (Baraka et al., 1981; Baraka and Dajani, 1984).

We conclude that the duration of neuromuscular blockade by atracurium is not related to the pseudocholinesterase activity. The drug can be administered safely to patients with low pseudocholinesterase.

REFERENCES


