Prevention of Succinylcholine-induced Myalgia with Lidocaine Pretreatment

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We studied the effects of 3 mg·kg^{-1} lidocaine iv on the succinylcholine (SCh)-induced myalgia in 94 unpremedicated ambulant patients undergoing dilatation and curettage of the uterus. The post-SCh myalgia was confirmed through interview by telephone. The data were correlated with the degree of fasciculation and changes in the serum electrolytes and creatine kinase (CK) levels following SCh administration. Pretreatment with lidocaine, 3 mg·kg^{-1} iv, significantly reduced the incidence of myalgia from 40.4% of control group to 12.8% of lidocaine-treated group, but not the CK levels. The severity of myalgia was not related to the intensity of fasciculation assessed by visual observation. The pretreatment with lidocaine had no untoward effect on the circulation, although the peak arterial and peak venous lidocaine levels achieved were 29.6 ± 23 μg·ml^{-1} and 10.1 ± 3.3 μg·ml^{-1} respectively. These findings indicated that the pretreatment with lidocaine, 3 mg·kg^{-1} iv, was effective in prevention of SCh-induced myalgia. (Key words: lidocaine pretreatment; post-succinylcholine myalgia)

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Generalized myalgia after succinylcholine (SCh) administration is a frequent complication, and is an important cause of anaesthetic morbidity in outpatient gynaecological surgery. These patients are generally young, healthy, ambulatory and undergoing minor surgery[1,2]. Many methods to attenuate SCh myalgia have been studied, including intravenous (i.v.) lidocaine[3-8]. However, little information is available on the haemodynamic effects and serum lidocaine levels after large doses of i.v. lidocaine ($>$ 2 mg·kg^{-1}). The present study was attempted to investigate the effects of 3 mg·kg^{-1} of lidocaine on the SCh induced fasciculation and myalgia, circulation, serum electrolytes and the creatine kinase levels. The serum lidocaine level was also measured.

Methods

Ninety-four Chinese patients, all ASA physical status I, undergoing elective, outpatient dilatation and curettage of the uterus, were assigned randomly to one of two groups (control or lidocaine group) after institutional approval and patient informed consents were obtained. All patients were unpremedicated and received similar anaesthetic technique by one investigator. The control group was administered fentanyl, 1 μg·kg^{-1}, and 2.5% thiopental sodium, 4 mg·kg^{-1}, i.v. and SCh (David Bull Laboratory), 1 mg·kg^{-1} i.v. 3 min after thiopental. Ventilation was controlled by mask using 70% nitrous oxide and 30% oxygen. The same technique was employed in the lidocaine group except that 1.5% lidocaine hydrochloride (ASTRA), 3 mg·kg^{-1}, was administered i.v. over one minute after thiopental sodium and SCh, 1 mg·kg^{-1}, was administered i.v. 2 min after lidocaine. Fasci-

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Table 1. Serum electrolytes and creatine kinase levels before and after SCh in two groups

	Control	Lidocaine	P Value
Sodium (135–150 mmol/L)			
Pre-induction	141.3 ± 4.70	143.0 ± 2.38	NS
2 minutes	140.8 ± 5.48	142.6 ± 2.50	NS
5 minutes	141.5 ± 5.54	142.7 ± 2.31	NS
10 minutes	141.1 ± 6.16	142.6 ± 2.15	NS
120 minutes	141.7 ± 5.02	143.1 ± 2.40	NS
Potassium (3.30–5.0 mmol/L)			
Pre-induction	4.04 ± 1.27	4.07 ± 0.46	NS
2 minutes	4.21 ± 0.46	4.05 ± 0.42	NS
5 minutes	3.98 ± 0.30	3.97 ± 0.41	NS
10 minutes	4.17 ± 0.84	3.98 ± 0.32	NS
120 minutes	3.91 ± 0.34	3.99 ± 0.55	NS
Total Calcium (2.2–2.6 mmol/L)			
Pre-induction	2.25 ± 0.20	2.22 ± 0.13	NS
2 minutes	2.26 ± 0.20	2.23 ± 0.12	NS
5 minutes	2.23 ± 0.17	2.23 ± 0.13	NS
10 minutes	2.21 ± 10.20	2.23 ± 0.15	NS
120 minutes	2.27 ± 0.24	2.21 ± 0.13	NS
Ionized Calcium (1.13–1.32 mmol/L)			
Pre-induction	1.14 ± 0.11	1.15 ± 0.10	NS
2 minutes	1.13 ± 0.10	1.16 ± 0.08	NS
5 minutes	1.14 ± 0.09	1.16 ± 0.12	NS
10 minutes	1.14 ± 0.11	1.15 ± 0.08	NS
120 minutes	1.16 ± 0.07	1.15 ± 0.06	NS
Phosphate (0.8–1.4 mmol/L)			
Pre-induction	1.22 ± 0.22	1.22 ± 0.15	NS
2 minutes	1.17 ± 0.11	1.19 ± 0.13	NS
5 minutes	1.17 ± 0.11	1.21 ± 0.15	NS
10 minutes	1.17 ± 0.10	1.21 ± 0.15	NS
120 minutes	1.14 ± 0.12	1.19 ± 0.16	NS
Creatine Kinase (20–240 U/L)			
Pre-induction	76.8 ± 38.7	79.7 ± 37.7	NS
2 minutes	86.0 ± 48.8	78.4 ± 38.3	NS
5 minutes	78.4 ± 39.6	75.0 ± 33.9	NS
10 minutes	78.8 ± 36.9	73.9 ± 27.5	NS
120 minutes	132.4 ± 92.3[†*]	124.3 ± 91.1[†*]	NS

Values quoted in paracentesis are normal reference values.

† – significant when compared with pre-induction value.

*$P < 0.001$. NS – not significant.

culations were graded on a score of 0 (no fasciculation) to 3 (whole limb movement) by visual observation.

Venous blood was sampled from all patients through venous cannula placed in the antecubital fossa vein, immediately before induction, and 2, 5, 10 and 120 min after SCh administration. The blood samples were sent immediately to the laboratory for serum sodium, potassium, total calcium, ionized calcium, phosphate and creatine kinase (CK).

Venous and arterial blood was also sampled from six and eleven patients respectively

Fig. 1. Comparison of incidence and severity of myalgia in two groups. Severity of myalgia was graded from 0 to 2 (see text). $P < 0.01$; Fisher's Exact Test.
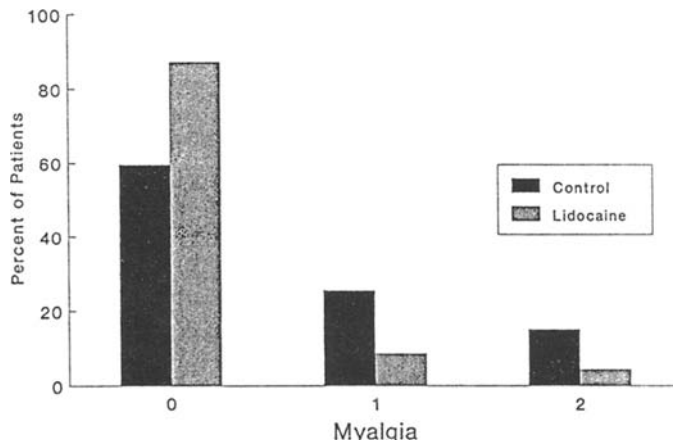
in the lidocaine group 0.5, 1, 2, 3, 4, 5, 10, 15, 20, 30, 60, 90 and 120 min after the administration of lidocaine for serum lidocaine level. After centrifugation, serum lidocaine concentrations were measured twice by enzyme immunoassay (EMIT) technique. Venous blood was also sampled from a group of 15 patients who underwent similar gynaecological procedure but did not receive SCh or lidocaine. They received fentanyl, thiopental, isoflurane, nitrous oxide and oxygen. Blood was sampled at the same time as in the other two groups. Only CK level was measured in these patients.

Blood pressure and heart rate were measured at one minute interval for fifteen minutes by an automatic blood pressure monitor (DINAMAP). ECG (lead II) and pulse oximeter were continuously monitored throughout the procedure, ECG was recorded before and for three minutes after i.v. lidocaine.

On the third postoperative day, postoperative myalgia was evaluated by telephone interviews conducted by an investigator who was not informed of the lidocaine pretreatment. Myalgia was graded according to its severity from 0 to 2 (0; no pain, absence of complaints either spontaneously or on direct questioning, 1; mild to moderate pain, involving one or more than one area of the body, usually elicited on direct questioning but not requiring analgesics, 2; severe pain, generalized, severe in nature, often intolera-

ble and requiring analgesics).

One-way analysis of variance (ANOVA) was used to test the significance of difference among the means of pre-induction and post-SCh electrolytes and CK of the two groups. Mean values between the control and treatment group were analyzed by using unpaired t test. Fisher's Exact Test was used to analyze the relation between myalgia and fasciculation. Statistical significance was accepted at $P < 0.05$. All values are expressed as mean ± SD unless stated otherwise.

Results

The age and weight of control group and lidocaine group were 31.4 ± 8.1 years, 53 ± 6.2 kg and 30.5 ± 6.3 years, 51.2 ± 7.3 kg respectively.

The pre-induction values of electrolytes and CK were all within the normal range. The post-SCh values of electrolytes and CK were not significantly different between the two groups (table 1).

Control Group

The overall incidence of myalgia was 40.4% and the incidence of mild-moderate (grade 1) and severe pain (grade 2) was 25.5% and 15% respectively. The serum electrolytes did not change significantly following SCh i.v. However, CK level increased significantly at 120 min post-SCh (132.4 ± 92.3 $u \cdot l^{-1}$) when compared to pre-induction level $P < 0.001$, table 1). The increase in CK level

Table 2. Relation between fasciculation and myalgia after SCh. See text for grading of fasciculation (0–3) and myalgia (0–2)

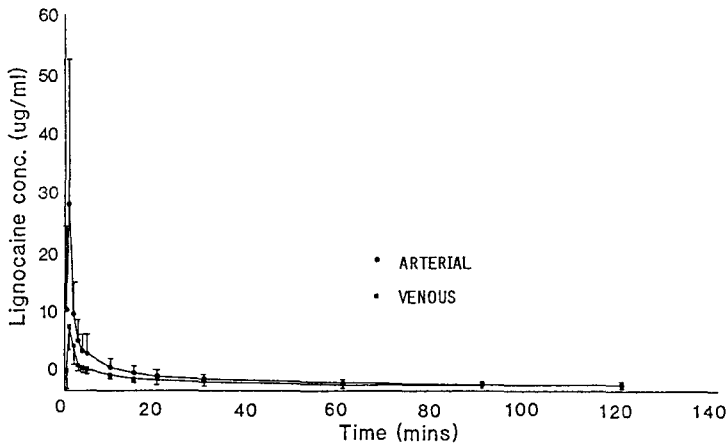| Fasciculation Myalgia	0	1	2	3	Total
0	5 (5.3%)	34 (36.2%)	21 (22.3%)	9 (9.6%)	69 (73.4%)
1	0	10 (10.6%)	6 (6.4%)	0	16 (17%)
2	1 (1.1%)	4 (4.3%)	2 (2.1%)	2 (2.1%)	9 (9.6%)
Total	6 (6.4%)	48 (51.1%)	29 (30.8%)	11 (11.7%)	94 (100%)

$P = 0.45$ (Fisher Exact Text)

Fig. 2. Arterial and venous serum lidocaine levels after 3 mg·kg^{-1}i.v. lidocaine.

was the same in patients with and without myalgia. Six patients had CK level of more than 240 u·l^{-1}.

Lidocaine Group

The overall incidence of myalgia was decreased significantly from 40.4% in the control group to 12.8% and the incidence of mild-moderate (grade 1) from 25.5% to 8.5% and severe pain (grade 2) from 15% to 4.3%. ($P < 0.01$, fig. 1). The serum electrolytes did not change significantly following SCh i.v. However, CK level increased significantly at 120 min post-SCh (124.3 ± 91.1 u·l^{-1}) when compared to pre-induction level ($P < 0.001$, table 1). The increase in CK level was the same in patients with and without myalgia. Four patients had CK level of more than 240

u·l^{-1}.

There was no significant rise in CK level in the 15 patients who did not receive SCh. Their CK level at 120 min post-SCh were 58.2 ± 19.3 u·l^{-1}.

Fasciculation and Myalgia

There was no relationship between intensity of fasciculation and severity of myalgia ($P = 0.45$, table 2).

Serum Lidocaine Level

Peak arterial and venous serum lidocaine level one minute after the administration were 29.6 ± 23 μg·ml^{-1} and 10.1 ± 3.3 μg·ml^{-1} respectively (fig. 2). Both mean arterial and venous serum lidocaine levels dropped to below 5 μg·ml^{-1} after 5 min.

Fig. 3. Changes in systolic, mean and diastolic blood pressure in the lidocaine group. A = pre-induction, B = 1 min after thiopental + fentanyl, C = 1 min after lidocaine (lid), D = 2 min after lid, E = 1 min after SCh, F = 2 min after SCh, G = 3 min after SCh.
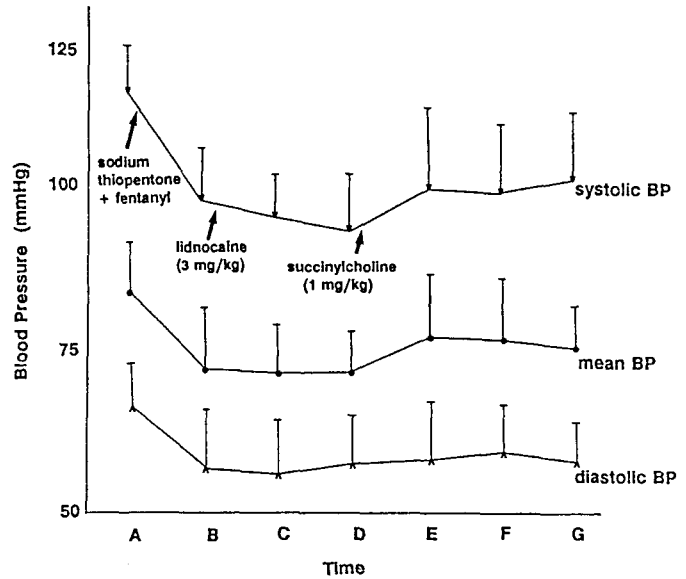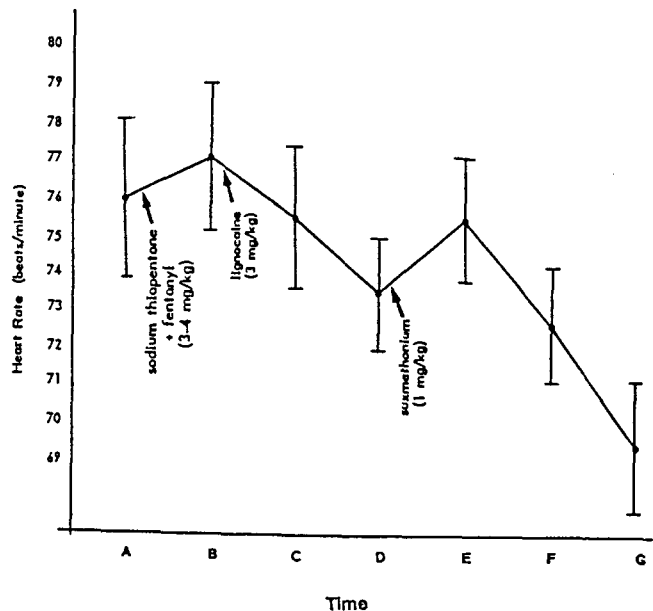
Fig. 4. Changes in heart rate in the lidocaine group. A = pre-induction, B = 1 min after thiopental + fentanyl, C = 1 min after lidocaine (lid) D = 2 min after lid, E = 1 min after SCh, F = 2 min after SCh, G = 3 min after SCh.

Effect on the Circulation

The systolic, mean and diastolic blood pressure decreased significantly ($P < 0.01$) one minute after thiopental and fentanyl induction but did not decrease any further after lidocaine (fig. 3). No significant changes in the heart rate (fig. 4) or ECG were observed.

Discussion

The present study showed that lidocaine pretreatment significantly reduced the incidence of myalgia and had no significant effect on the circulation. However, it did not attenuate SCh-induced fasciculation and the rise in CK levels.

A summary of review of the English literatures on the use of lidocaine pretreatment for SCh-induced myalgia is shown in table 3. Most of the studies showed that lidocaine pretreatment was effective in reducing the

Table 3. Review of literatures on lidocaine pretreatment for SCh-induced myalgia

Induction Agents	Lidocaine (Lid.) dose	Time interval between Lid & SCh	Succinylcholine (SCh.) dose	Patient Characteristics	Reduction in incidence of myalgia	References
–	6 mg·kg^{-1} i.v. × 2–3 mins	immediate	1 mg·kg^{-1}	M + F 7–83 yrs	62% →4%	3
Thiopental	3–4 mg·kg^{-1} i.v.	–	30–50 mg	M + F 6–65 yrs	52% →14%	4
Propanidid	0.75 mg·kg^{-1} i.v.	together	0.35 mg·kg^{-1}	M + F 14–71 yrs	44.5% →16%	5
Thiopental 3–5 mg·kg^{-1}	2 mg·kg^{-1} i.v.	–	1 mg·kg^{-1}	M + F 14–45 yrs	45% →8%	6
Thiopental 3–5 mg·kg^{-1} Fentanyl 1 mg·kg^{-1}	2 mg·kg^{-1} i.v.	–	1.5 mg·kg^{-1}	F	no reduction	7
Thiopental 4 mg·kg^{-1}	1.5 mg·kg^{-1} i.v. × 60–90 s	2–3 mins	1.2 mg·kg^{-1}	F 19–43 yrs	no reduction	8
Thiopental 6 mg·kg^{-1}	90–110 mg throat spray	2–3 mins	1 mg·kg^{-1}	F 19–46 yrs	71.1% →33%	9
Fentanyl 1 mg·kg^{-1} Thiopental 4 mg·kg^{-1}	3 mg·kg^{-1} i.v. × 1 min	2 mins	1 mg·kg^{-1}	F 19–38 yrs	40.4% →12.8%	Current study

incidence of SCh-induced myalgia. However, comparison is difficult due to the differences in the induction agents used, doses of lidocaine and SCh, routes of administration of lidocaine and patient demography. For example, sodium thiopental had been shown to reduce the incidence of myalgia significantly when SCh was administered immediately following thiopental[10]. As the mechanism of SCh-induced myalgia remains uncertain and the mechanism of the protective effect of lidocaine is also unclear. However, lidocaine has been shown to depress neural events at the motor nerve terminal[11].

This study confirmed the finding of previous studies[12–14] that visual intensity of fasciculation was unrelated to severity of myalgia. We also confirmed the finding of a previous study[15] that lidocaine pretreatment (3 mg·kg^{-1}) was ineffective in preventing SCh-induced fasciculation, though, higher dose of lidocaine (6 mg·kg^{-1}) was shown to prevent

SCh-induced fasciculation[15].

We did not find any significant change in serum potassium and total calcium levels following SCh. This is at variance with other findings which indicated[16,17] a slight increase in potassium and a decrease in total calcium. We also did not find any significant change in serum calcium (total and ionized) between those patients with myalgia and those without myalgia, whereas Collier[17] found a significant fall in mean total calcium level in the myalgia group one minute after SCh administration. The differences in the electrolyte changes could be related to the induction agents used and the frequency of blood sampling. Sodium thiopental, which was the induction agent used in this study, had been shown to cause a significant decrease in plasma potassium concentration[18]. This could obscure slight increase in potassium level following SCh in normal patients. Other workers who found a slight increase

in potassium used enflurane[16] or althesin[17] as induction agents. In this study, blood were sampled intermittently as compared to other study[17] where blood was sampled every minute. As a result, a transient rise or fall in the serum electrolytes could therefore be missed.

SCh-induce myalgia has been attributed to damage to skeletal muscle[14,19], supported by a rise in serum myoglobin within 1 h and CK levels 24–48 hrs following SCh administration[20–23]. Besides a rise in CK level following SCh, we showed an early rise in CK levels within 2 hrs after SCh administration. We were not able to monitor the CK levels of our patients beyond 2 hrs after SCh administration, as our patients were discharged home 5–6 hrs after the surgical procedure. The clinical significance of an early rise in CK levels after SCh administration is not known. We also confirmed the finding of previous study[23] that an increase in CK level was not related to the incidence of myalgia. Lidocaine pretreatment also did not prevent the rise in CK level. There is a possibility that the rise in CK level in our patients can be attributed to the dilatation and curettage of the uterus because traces of CK has been found in nearly all the organs in the body including the uterus[24]. However, this possibility may be denied since the CK level did not rise in 15 patients who underwent the same procedure but did not receive SCh.

We measured total serum lidocaine level serially as measurements of serum lidocaine concentration is of potential value to serve as an indicator of risk of systemic toxicity. It is reported, toxic manifestation in the central nervous system were observed when the plasma levels were above 5 $\mu g \cdot ml^{-1}$ in conscious volunteers[25,26]. However, Bromage & Robson[27] have pointed out that general anaesthesia (as used in this study) will obtund the early signs of toxicity of the central nervous system. They considered that, under light general anaesthesia, plasma levels of the order of 10 $\mu g \cdot ml^{-1}$ were necessary before toxic effects, eg. hypotension, could be detected. Although the peak arterial (29.6

± 23 $\mu g \cdot ml^{-1}$) and peak venous (10.1 ± 3.3 $\mu g \cdot ml^{-1}$) lidocaine levels of our patients were higher than the accepted toxic level, we did not observed any significant change in the circulation of our patients following lidocaine. Wikinski et al.[15] also failed to demonstrate any significant change in BP, HR and ECG following 2–6 $mg \cdot kg^{-1}$ lidocaine i.v. whereas Usubiaga et al.[3] noted a downward displacement of the S wave in the ECG of their patients following 6 $mg \cdot kg^{-1}$ lidocaine i.v.

This study confirms clinically that i.v. lidocaine diminishes the incidence and severity of myalgia following SCh. However, the precise mechanism of this phenomenon requires further investigation. The dose of lidocaine used in this study were high from a usual clinical standard, in view of the potentially toxic blood levels achieved, therefore, the effectiveness of lower doses of lidocaine should also be explored.

In summary, SCh-induced myalgia was attenuated to a significant extent by i.v. lidocaine 3 $mg \cdot kg^{-1}$ preceding SCh. However, this dose of lidocaine did not attenuate SCh-induced fasciculation, nor does it attenuate the rise in CK level at 2 hrs after SCh.

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