ASERF Report:

"Effects of facial topical lidocaine application on serum levels of lidocaine and monoethylglycinexylidide"

Introduction:

Topical lidocaine is a commonly used form of anesthesia for a wealth of procedures across a large number of disciplines, including laser treatments. It is considered a safer and more acceptable form of anesthetic compared to hypodermic injections; however there have been reports of fatalities following its application. It is well known that above certain serum lidocaine concentrations patients start to experience effects of toxicity such as light headedness, paraesthesia, nausea and vomiting and this can progress to seizures and cardio-respiratory depression, which ultimately can lead to death. 4% lidocaine cream is significant in that it is currently the highest concentration lidocaine with liposomal delivery available over the counter, and therefore was the drug used in this study.

Lidocaine typically has a half life of around 90-120min in individuals with normal hepatic function. Physiologically lidocaine metabolizes into monoethylglycinexylidide (MEGX), an active metabolite which may be as potent as lidocaine in terms of toxicity. Therefore despite decreasing serum lidocaine levels the additive effect of serum MEGX levels may result in toxicity.

Method:

This study examined blood serum levels of both lidocaine and MEGX after the application of 4% topical lidocaine ointment to the face in 25 healthy volunteers split into 4 groups (A,B,C,D). Group A had 2.5g of LMX-4 applied to the face for one hour without occlusion, group B had 5g applied to the face for 0.5hr without occlusion, group C had 5g applied to the face for 1hr without occlusion and group D had 5g applied to the face with occlusion for one hour. Blood was drawn every 30 minutes for 4 hours, to evaluate serum concentrations.

Results:

Group D had the highest serum levels of lidocaine and MEGX, a three- fold increase compared to group C which had the same dose (5g topical 4% lidocaine) but without occlusion (figure 1). In group D peak serum levels occurred at 90 min for serum lidocaine, which was also the fastest of the 4 groups. Serum MEGX levels peaked much later than serum lidocaine levels at 210 min. Individual serum levels did not exceed 0.6μg/mL. Across the groups there were significant inter individual variation in both lidocaine and MEGX serum levels ($p=0.0162$).

Across all 4 groups serum lidocaine levels peaked and then decreased, by the conclusion of the study at 240 min (table 1). This peak appeared at the earliest time interval in group D where an occlusive dressing was used. This was in contrast to MEGX levels, where there was a continuing increase in MEGX levels in groups A, and B at the 240min. Serum MEGX levels did however, start to decrease in groups C and D after 210 min.

Peak serum levels of lidocaine and MEGX combined in group D approached 0.60μg/mL in one individual, (although the mean serum level for that group was 0.3μg/mL), the therapeutic range for intravenous administration when treating dsyrhythmias is 1.0-5.0μg/mL.

5g applications of 4% lidocaine resulted in higher serum concentration of both lidocaine and MEGX. This was also true when exposure time was increased. When comparing group A to group C, doubling the dose of 4%lidocaine from 2.5g to 5.0g resulted in double the serum levels of MEGX and a 50% increase in the serum lidocaine levels (Mann-Whitney 2 tailed p = 0.0207 with 95% CI).

When comparing groups C and D, the addition of an occlusive dressing resulted in tripling the serum lidocaine levels, and doubling the serum MEGX levels, and this was statistically significant (Mann-Whitney 2 tailed p = 0.0003).

When comparing all 4 groups (figure2) there was significant differences between the combined serum concentrations of lidocaine and MEGX (p=0.0001).

Conclusion:

Topical lidocaine preparations are increasingly being used to provide a patient friendly form of non-invasive analgesia for a multitude of procedures. Some preparations are available over the counter for unsupervised patient use. There have however, been fatalities as a result of this, and our study suggests that this is due to the unpredictability of lidocaine metabolism between individuals. Therefore, a more comprehensive body of toxicity studies needs to be performed before we can categorically state that topical lidocaine is truly safe and the limits to which that safety applies.

Recommendations:

Further studies would be useful to determine the safety profile of the different lidocaine preparations, with particular reference to the over the counter topical anesthesias. We would suggest studies looking at:

1. Effect of surface area in relation to concentration of lidocaine applied with and without occlusive dressings.
2. Comparisons between the different topical anesthetic preparations and their absorption through skin
3. Affect of serum levels of lidocaine when the stratum corneum is disrupted for example following pretreatment of the skin with an ablative laser.

A manuscript has been prepared based on the results detailed above and will be submitted for publication to Aesthetic Surgery Journal.

Figure 1:

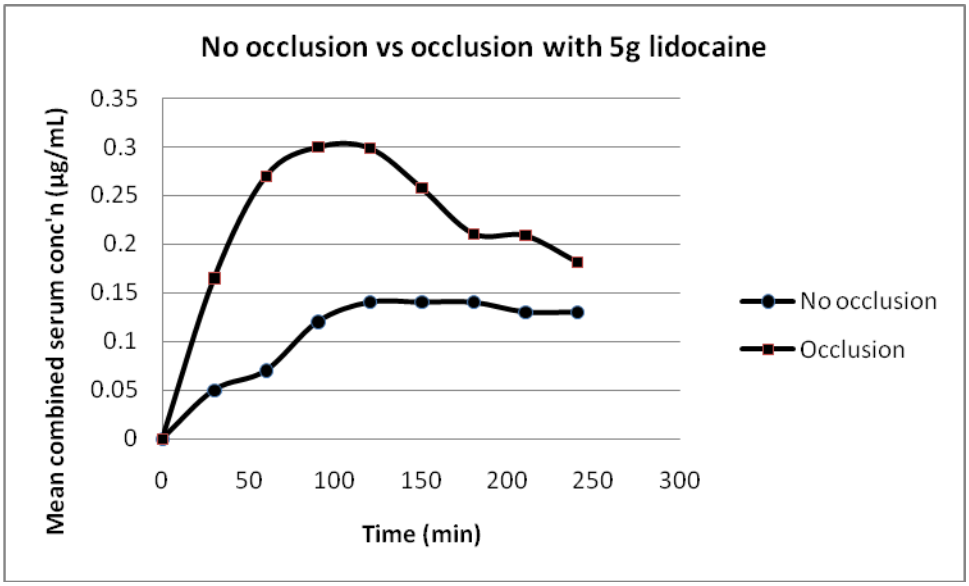
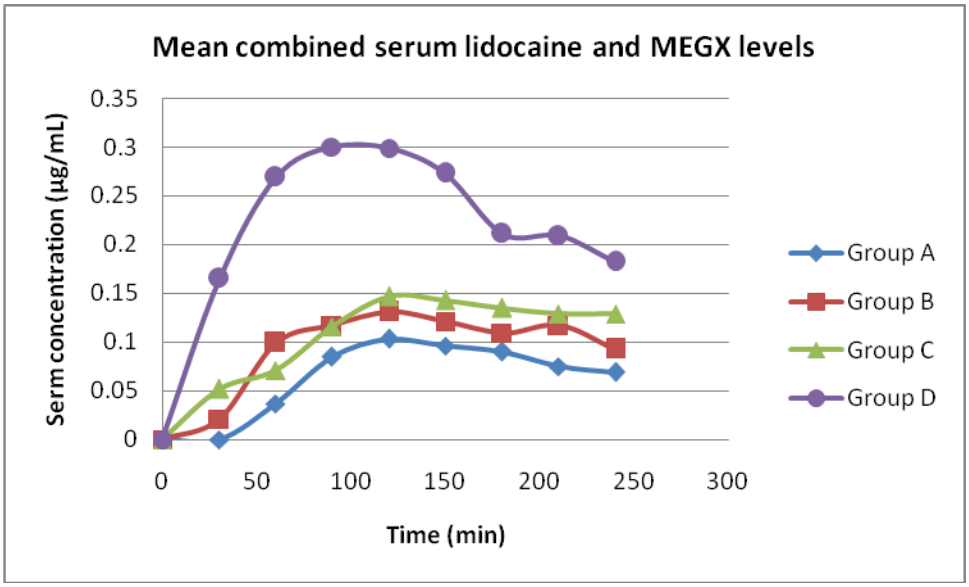


Table 1: Mean Serum Lidocaine and MEGX highest levels versus time

Group	Serum Lidocaine (µg/mL)	Time (Min)	Serum MEGX (µg/mL)	Time (min)
A	0.09	120	0.012	240
B	0.12	120	0.016	240
C	0.13	120	0.012	210
D	0.28	90	0.033	150

Group A – 2.5g topical lidocaine, 1 hr, no occlusion
Group B - 5g topical lidocaine, 0.5hr, no occlusion
Group C – 5g topical lidocaine, 1hr, no occlusion
Group D – 5g topical lidocaine, 1hr, with occlusion

Figure 2:


Mean combined serum lidocaine and MEGX levels
Serm concentration (µg/mL)
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
0
50
100
150
200
250
300
Time (min)
Group A
Group B
Group C
Group D