

The Effect of Premedication with Ketorolac on Pain Relief During Chemical Peeling

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Background : A majority of patients undergoing chemical peeling complain of pain severe enough to disturb the process of the peeling. However, there has been few controlled studies on pain control during chemical peeling.

Objectives : We evaluated the efficacy and safety of pretreatment with intramuscular ketorolac (Tarasyn®, 30mg) and oral diazepam (Valium®, 5mg) in comparison with control and diazepam groups, and compared the sensitivity of pain between two sexes.

Methods : The patients were randomly assigned to one of three groups: control, diazepam, and ketorolac plus diazepam groups. Pain intensity was assessed 5 times at every ten minutes from the beginning of the peeling using visual analog scale (VAS).

Results : At every 10 minutes of pain assessment, ketorolac plus diazepam group recorded the lowest VAS among the three groups. Except at the first 10 minutes, the differences were statistically significant. There was no significant difference in the pain intensity between the sexes at all five times. After application of Jessner's solution, there was significant increase of VAS in all groups.

Conclusion : The ketorolac pretreatment is a safe and effective modality of pain relief prior to chemical peeling without the adverse reactions. (Ann Dermatol 14(1) 18-21, 2002).

Key Words : Chemical peeling, Diazepam, Ketorolac, Pain control

A majority of patients undergoing chemical peeling complain of very severe pain, such as immediate stinging, burning sensation and rebound stinging. It often disturbs the peeling and may persist from a few minutes to a day or more. Unfortunately, the pain is likely to be underestimated and there has been few literature on pain control before chemical peeling.

The present study, a randomized controlled trial, was designed with the following objectives: evaluation of the efficacy and safety of pretreatment with intramuscular ketorolac (Tarasyn®, 30mg) and oral diazepam (Valium®, 5mg) in comparison with

control and diazepam groups, and comparison of the sensitivity of pain between the two genders.

MATERIAL AND METHODS

Patients

Fifty-five patients ranging in age from sixteen to forty-nine years were included in this study. The mean age was 26.8 years and the study groups were similar in age distribution (Table 1). Patients with hepatic or renal disorders, allergies to NSAIDs, a history of drug or alcohol abuse, a history of bleeding diathesis or active peptic ulcer were excluded. Pregnant or lactating women were also excluded. All patients signed an informed consent form.

Study Design

The patients were randomly assigned to one of three groups: non-premedicated control,

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diazepam (Valium® 5mg) alone, and ketorolac (Tarasyn® 30mg) plus diazepam (Valium® 5mg) groups. The assigned medications were administered about 10 minutes before the peeling. Diazepam was administered sublingually and ketorolac, intra-muscularly.

Pain assessment was done by self-rated 10-cm visual analog scale (VAS; 0 = no pain to 10 = intolerable pain). The pain scores were assessed 5 times at every 10 minutes from the beginning of the peels, and also, before and after application of Jessner's solution.

In almost all cases, Jessner's solution was applied on the whole face after 50% trichloroacetic acid (TCA) peeling.

Statistical Analysis

Statistical analysis was performed using SPSS version 9.0 (SPSS Inc.) for Windows (Microsoft Co.). Differences in VAS among the three groups were analyzed using Kruskal-Wallis test, and comparison of VAS between the groups, between the sexes, and between before and after application of Jessner's solution were analyzed by Mann-Whitney U test. P values < 0.05 were considered significant.

RESULTS

There were significant differences in mean pain scores among the groups. At every 10 minutes of pain assessment, ketorolac plus diazepam group recorded the lowest VAS among the three groups. Except VAS at the first 10 minutes, the differences were statistically significant. There were no significant differences in pain intensity between control and diazepam groups (Table 2, Fig. 1).

In comparing the pain intensity between the sexes, there was no significant difference at each time of pain assessment (Table 3).

After application of Jessner's solution, there was significant increase of VAS in all groups (Table 4, Fig. 2), but the degree of increase was not significantly different among the three groups.

Finally, there was no considerable adverse effect or noticeable compromise in the effectiveness of the peels by ketorolac pretreatment compared with previous experience of peels

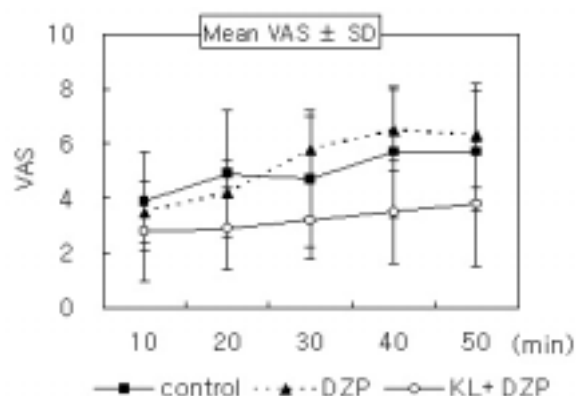


Fig. 1. The comparison of pain intensity among the three groups. Data show mean VAS ± SD. *, $p < 0.05$; DZP, diazepam; KL, ketorolac

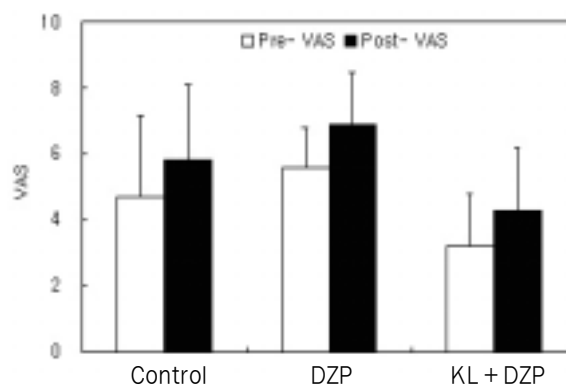


Fig. 2. The comparison of pain intensity between before and after application of Jessner's solution. Data show mean VAS ± SD. DZP, diazepam; KL, ketorolac

done without any pretreatment.

DISCUSSION

The pain developing during medium depth and deep chemical peels is very intense and must be troublesome to both patients and operator. For pain relief, various methods are used including local or general anesthetics, analgesics, sedatives, fans, ice, etc. Unfortunately, there is few literature on pain control before chemical peeling. Taylor¹ investigated the efficacy of EMLA (lidocaine 2.5% and prilocaine 2.5%) after 35% TCA or Baker's peels and found the dramatic pain relief and safety of EMLA. Koppel² et al evaluated the efficacy of EMLA versus ELA-Max (lido-

Table 1. Patient characteristics.

	Number (M/F)	Age (Mean \pm SD(yr))
Control	15(5/10)	26.9 \pm 5.0
DZP	10(2/8)	30.5 \pm 9.7
KL+DZP	30(8/22)	25.5 \pm 6.9
Total	55(15/40)	26.8 \pm 7.2

SD; standard deviation, DZP; diazepam, KL; ketorolac

Table 2. Mean VAS among the groups.

	VAS1	VAS2	VAS3	VAS4	VAS5	VAS total
Control	3.9 \pm 1.8	4.9 \pm 2.3	4.7 \pm 2.5	5.7 \pm 2.4	5.7 \pm 2.2	24.7 \pm 1.0
DZP	3.5 \pm 1.1	4.2 \pm 1.2	5.8 \pm 1.2	6.5 \pm 1.5	6.3 \pm 1.9	26.3 \pm 4.8
KL+DZP	2.8 \pm 1.8	2.9 \pm 1.5	3.2 \pm 1.4	3.5 \pm 1.9	3.8 \pm 2.2	16.2 \pm 6.7
p value	ns*	<0.05	<0.05	<0.05	<0.05	<0.05

ns* , not significant; DZP; diazepam, KL; ketorolac
Data show mean VAS \pm SD.

Table 3. The differences in mean VAS between the sexes

		VAS1	VAS2	VAS3	VAS4	VAS5	VAS total
Control	M	3.2 \pm 1.9	4.8 \pm 2.7	3.4 \pm 2.1	5.0 \pm 1.9	5.2 \pm 1.6	21.6 \pm 9.2
	F	4.2 \pm 1.8	4.9 \pm 2.2	5.3 \pm 2.5	6.0 \pm 2.6	5.9 \pm 2.4	26.3 \pm 10.5
DZP	M	4.0 \pm 1.4	5.0 \pm 0.0	6.5 \pm 2.1	8.0 \pm 0.0	6.5 \pm 2.1	30.0 \pm 1.4
	F	3.4 \pm 1.1	4.0 \pm 1.3	5.6 \pm 1.1	6.1 \pm 1.5	6.3 \pm 2.0	25.4 \pm 5.0
KL+DZP	M	2.6 \pm 1.4	3.5 \pm 1.1	3.4 \pm 1.1	4.1 \pm 1.6	4.1 \pm 1.7	17.8 \pm 4.8
	F	2.9 \pm 2.0	2.6 \pm 1.6	3.2 \pm 1.6	3.2 \pm 1.9	3.7 \pm 2.3	15.6 \pm 7.3
p value		ns*	ns*	ns*	ns*	ns*	ns*

ns* , not significant; DZP, diazepam; KL, ketorolac
Data show mean VAS \pm SD.

caine 4%) before 35% TCA peel, and confirmed their efficacy. Rubin³ reported the efficacy of a topical lidocaine/prilocaine anesthetic gel in relieving the discomfort felt during 35% TCA peels. Although 80% of patients experienced at least a 40% reduction in discomfort when compared to previous 35% TCA peels done without application of anesthetic gel, he found that the skin frosted more slowly, irregularly, and intensely.

In our pain management program, we tried to avoid the unfavorable effects on the peels caused by the preoperative application of

Table 4. The differences in mean VAS between before and after application of Jessner's solution

	Pre-VAS	Post-VAS	p value
Control	4.7 \pm 2.5	5.8 \pm 2.3	<0.05
DZP	5.6 \pm 1.2	6.9 \pm 1.6	<0.05
KL+DZP	3.2 \pm 1.6	4.3 \pm 1.9	<0.05

DZP, diazepam; KL, ketorolac
Data show mean VAS \pm SD.

topical anesthetic creams and the disadvantages such as the need for the careful removal of the cream and the discontinuation of the procedure for about 30 minutes a waiting the onset of the anesthetic effect². And also, our study was aimed to avoid the use of narcotic medications, thereby eliminating many of the deleterious effects associated with the administration of opioids, such as nausea, ileus, urinary retention, excessive sedation, diminished respiratory function, and addiction.

Ketorolac is a new potent nonsteroidal anti-inflammatory drug that exhibits anti-inflam-

matory, analgesic, and antipyretic activity. It inhibits the cyclo-oxygenase enzyme system and hence prostaglandin synthesis. It is mainly indicated for short-term relief of moderate to severe pains. It has no significant effect on the central nervous system and no sedative or anxiolytic properties⁴⁻⁶.

Ketorolac pretreatment has many advantages. It has a rapid onset of about 10 minutes and appears to be as effective as morphine for short-term management of moderate to severe pain⁷. It has no effect on central opioid receptors. Hence, it does not exacerbate opioid-related respiratory depression or sedation⁴⁻⁶. And there is no risk of addiction after repeated usage for subsequent peeling. The intramuscular administration is convenient. It makes the peels more tolerable for the patient and more comfortable for the operator. Its routine use has been associated with significant adverse effects including gastrointestinal bleeding, perioperative bleeding, and acute renal failure, but its occasional and short-term uses do not need to be limited as pretreatment in outpatient one-day operation such as chemical peeling, laser resurfacing, dermabrasion, etc ^{4, 8-10}. Most of these side effects can be avoided through proper patient selection, dosing, and short-term administration. In our study, we also didn't experience any of these.

In the present study, there were significant differences in mean pain scores among the groups. At every 10 minutes of pain assessment, ketorolac plus diazepam group recorded the lowest VAS among the three groups; the differences were statistically significant, except VAS at the first 10 minutes. Our data suggest that ketorolac pretreatment has a significant effect of pain relief during TCA peeling without considerable adverse effect or noticeable compromise in the effectiveness of the peels by ketorolac pretreatment.

In comparing the pain intensity between the sexes, there was no significant difference according to the time sequences, and thus we speculate that the male and the female might have similar pain sensitivity and/or responsiveness to the intervention by ketorolac or diazepam.

As expected, there was significant increase of

VAS in all groups just after application of Jessner's solution, although the degree of increase was not significantly different among the three groups.

In conclusion, the ketorolac pretreatment seems to be safe and effective as a means of pain relief prior to chemical peeling without the adverse reactions.

REFERENCES

1. Taylor MB. EMLA for effective pain relief following chemical peeling. *Dermatol Surg* 1995;21:736-739.
2. Koppel RA, Coleman KM, Colman WP. The efficacy of EMLA versus ELA-Max for pain relief in medium-depth chemical peeling: a clinical and histopathological evaluation. *Dermatol Surg* 2000; 26:61-64.
3. Rubin MG. The efficacy of a topical lidocaine/ prilocaine anesthetic gel in 35% trichloroacetic acid peels. *Dermatol Surg* 1995;21:223-225.
4. Livak KM, McEvoy GK. Ketorolac, an injectable nonnarcotic analgesic. *Clin Pharmacol* 1990;9:921-935.
5. Moote C. Efficacy of nonsteroidal anti-inflammatory drugs in the management of postoperative pain. *Drugs* 1992;44(Suppl5):14-30.
6. Ferreira SH. Peripheral analgesia: mechanism of the analgesic action of aspirin-like drugs and opiate-antagonists. *Br J Clin Pharmacol* 1980;10:237S-245S.
7. Gillies GW, Kenny GN, Bullingham RE, McArdle CS. The morphine-sparing effect of ketorolac tromethamine: a study of a new potential nonsteroidal anti-inflammatory agent after abdominal surgery. *Anesthesia* 1987;42:727-731.
8. Haragsim L, Dalal R, Bagga H, Bastani B. Ketorolac-induced acute renal failure and hyperkalemia: report of three cases. *Am J Kid Dis* 1994;24:578-580.
9. Spoward K, Greer IA, McLaren M, et al. Haemostatic effects of ketorolac with and without concomitant heparin in normal volunteers. *Thrombo Haemost* 1988;60:381-386.
10. Strom BL, Berlin JA, Kinman JL, et al. Parenteral ketorolac and risk of gastrointestinal and operative site bleeding: a postmarketing surveillance study. *JAMA* 1996;275:376-382.