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**DECREASED CENTRAL CORNEAL SENSITIVITY IN THE 50% GALACTOSE-FED RAT MODEL OF DIABETIC OCULAR COMPLICATIONS.**

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**Purpose:** To evaluate corneal sensitivity in 50% galactose-fed rats and explore its potential use in assessing diabetic keratopathy in this animal model.
**Methods:** Weanling male Sprague-Dawley rats were divided into two weight-matched groups and fed Purina laboratory chow (#5001) plus 1) 50% alpha cellulose fiber (controls, n=9); or 2) 50% D-galactose (n=12). Corneal sensitivity measurements were conducted after 12 months on the diets. A Cochet-Bonnet Aesthesiometer (Luneau) was mounted on a micromanipulator such that the end of the filament (0.012 mm diameter) was in the plane of focus of a slit-lamp biomicroscope (AO). The instrument was utilized to determine Corneal touch threshold (CTT). This index of corneal sensitivity was defined as the exerted pressure on the cornea which elicited a blink response to 50% of the stimuli (5/10). Rats were restrained without medication in a specially designed restrainer. Left corneal sensitivity measurements were conducted sequentially at mean pressures of 11, 12, 13, 16 mg/.0113 sq mm (filament lengths of 6, 5.5, 5.0, 4.5, respectively). Right corneal sensitivity measurements were conducted in the reverse order of applied pressures. The filament was applied perpendicularly to the central corneal surface (at pupil) and the first visible bending of the filament as well as blink responses were confirmed by two independent investigators. Fluorescein (0.25%) staining was utilized to examine corneal epithelial integrity following completion of sensitivity measurements on each eye.
**Results:** Paired T-tests comparing left and right corneal sensitivities within groups were not significantly different at any pressure. Corneal sensitivity was significantly decreased ($p<0.0001$) in the galactose-fed rats at all pressures compared to controls. Mean sensitivity of control rats was above CTT at each pressure. Mean corneal sensitivity of the galactose-fed rats was below CTT at each pressure. No clinically significant epithelial defects were noted by fluorescein staining.
**Conclusions:** This study is the first to.demonstrate a decreased central corneal sensitivity in the galactose-fed rat model of diabetic complications. This model could be useful for investigating the pathogenic mechanism(s) involved in decreased corneal sensitivity associated with diabetic keratopathy.

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**CORNEAL SENSITIVITY TO CHEMICAL, MECHANICAL AND THERMAL STIMULI IN HUMANS.**

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***Purpose***: To measure corneal sensitivity to various modalities of stimuli (chemical, mechanical, thermal) in human subjects.
***Methods***: Two tanks containing air and 100% $CO_2$ were connected through a pressure gauge to a set of solenoid 2-way valves. The output of individual valves was connected to independent flow regulators that introduced a pre-established flow of gas in a common outlet. Simultaneous opening of one of the air and one of the $CO_2$ valves produced a gas mixture containing various % of $CO_2$, that was stored in a chamber and expelled at adjustable flows. The gas mixture was carried with a tube to a 3-way solenoid valve, with an output entering a nozzle and the other diverting the gas away from the eye. A Peltier cell placed in the final traject of the gas and connected to a servocontrolled unit permitted to change the temperature of the gas between 5° and 45°C. The nozzle was attached to a slit-lamp positioning device and placed in front of the cornea. Duration of gas pulses and interstimulus intervals could be adjusted by regulating the opening of the 3-way valve.
***Results***: The instrument generated pulses of gas of variable $CO_2$ concentration (30% to 80%, in 2%-3% steps) at a flow below or over mechanical threshold and at low or high temperature. Increasing sensations of irritation were elicited by increasing the concentration of $CO_2$ in the gas mixture. With air at 33° at a flow under mechanical threshold, no sensation was evoked; however, a sensation of irritation was reported when the temperature of the gas was reduced to 10°C.
***Conclusions***: This method permits the stimulation of the cornea with controlled mechanical, chemical and thermal stimuli. Suprathreshold mechanical forces, pH drops and cold air applied to the cornea evoked always a sensation of irritation. Supported by CICYT SAF 93-0267

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**EFFECTS OF MORPHINE ON THE RESPONSE OF PAIN CORNEAL FIBERS TO CHEMICAL AND MECHANICAL STIMULATION**

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***Purpose*** It has been reported that morphine sulphate (MS) reduces corneal sensitivity to mechanical stimulation in human eyes with a corneal abrasion. We explored the effects of morphine on the sensitivity of corneal nociceptive fibers to noxious stimuli.
***Methods*** In anesthetized cats, electrical activity of single corneal sensory units was recorded from ciliary nerve filaments. Polymodal nociceptive fibers were identified by their firing responses to mechanical stimulation with a Cochet-Bonnet esthesiometer and to pH drops elicited by a 30s, 98.5% $CO_2$ jet directed to the cornea. MS was applied topically and the responsiveness to $CO_2$ tested 5, 15, 20, 25, 35, 40, 50, 60 and 65 min afterwards. Increasing concentrations of MS (0.1, 0.2, 0.5, 1 mg/ml) were applied at min.0, 23,38 and 53, respectively.
***Results*** Five min. after MS application (0.1mg/ml), the impulse frequency of the response to $CO_2$ was reduced to 85% of control in 6/10 units and to about 50% 15 min. afterwards. At 65 min., after application of increasing doses of MS, the response was 50% lower than control in 4/6 fibers. Two of these units also exhibited an increased mechanical threshold.
***Conclusions*** The results show that MS decreases chemical and mechanical sensitivity of a part of the polymodal nociceptive units of the cornea. This anesthetic effect may explain the reduction of corneal sensitivity with MS application in human patients.

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**TITLE : COMPARATIVE STUDY OF TOPICAL 0,1% INDOMETHACIN SOLUTION COMPARED TO 0,1% DICLOFENAC AND PLACEBO AFTER EXCIMER LASER PHOTOREFRACTIVE KERATECTOMY**

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***Purpose*** : To evaluate the efficacy of 2 topical NSAIDs, 0,1% indomethacin and 0,1% diclofenac solutions, versus a placebo in controlling pain and other signs after excimer laser photorefractive keratectomy (PRK).
***Methods*** : After written consent, 120 informed patients (67 males, 53 females; mean age = 31,1 ± 7,6 yrs) were enrolled in this bicenter, double-masked, randomized, comparative study and assigned to either indomethacin or diclofenac or a placebo treatment. Subjective preoperative evaluation of individual susceptibility to pain evoked by topical application of 0.4% oxybuprocaine vs saline served as a reference for further postoperative pain measurement using visual analog horizontal scales. Ocular and cephalic pain, itching, foreign body sensation, insomnia, photophobia, blepharospasm as well as systemic medication and alcohol intake were monitored for 2 days following photoablation (D0) as well as reepithelialization process.
***Results*** : Compared to the placebo, 0.1% indomethacin solution significantly reduced pain on the first day following excimer laser PRK ($p<0.05$) while 0.1% diclofenac did not reach a significant level ($p=0.46$). At D0, the analgesic intake by oral route was significantly greater in the placebo group ($p<0.05$). In comparison with the placebo and indomethacin groups, the corneal wound healing rate was significantly decreased in diclofenac-treated patients at D2 ($p=0.001$).
***Conclusions*** : These data suggest that 0.1% indomethacin ophthalmic solution may help control the pain induced by excimer laser PRK without any deleterious effect on corneal healing.