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EVALUATION OF TOPICAL KETOCONAZOLE EFFECTS ON THE REGENERATION OF CORNEAL EPITHELIUM - EXPERIMENTAL STUDY IN RABBITS.

JORGE E.N.[1] JORGE E.C.[1] MORAES SILVA M.R.B.[1] VANE, L.A.[2]
[1] Department of Ophthalmology, Universidade Estadual Paulista (S.Paulo, Brazil)
[2] Department of Anesthesiology, Universidade Estadual Paulista (S.Paulo, Brazil)

Purpose 29 male rabbits were submitted to bilateral epithelial ablation of corneas induced by mechanical and chemical methods.The toxicity of topical Ketoconazole (KCZ), used at 2 different concentrations, 2% and 4%, was evaluated, considering the following parameters: rate of re-epithelization and histopathological changes of the cornea. We tested the applicability in this experimental mode of attributes like the characteristics of the cicatrization process, the shape of the cicatrization process and the rate between the minimum and maximum diameter of the re-epithelization area.

Methods The animals were divided in 4 groups: GI: received 2% KCZ in the right eye (GID); GII: 4% KCZ in the right eye (G2D); GIII: control colyrium in the right eye (G3D). GIV: no drops were instilled in the right eye. The left eyes of all animals used in the experimental groups listed above did not receive any kind of treatment, after the epithelial ablation. They were considered the biological control of the opposite treated eye.

Results They were studied by quantitative and qualitative methods with statistical analysis of area under the cicatrization line, the rate between the minimum and maximum diameter of the re-epithelization area and its shape. All the corneas had histopathological analysis.

Conclusions The results demostrated that the use of 2% Ketoconazole has no toxic effect to the cicatrization process of the cornea, when compared to the control groups. In contrast, the use of 4% Ketoconazole caused toxic effects compared to the control groups, considering the parameters evaluated in this experimental study. Shape had greater sensibility to show differences among different groups than rate between diameters. 4% Ketoconazole had toxic effects at histopathological analysis.

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LACK OF CYTOTOXIC EFFECT OF GANCICLOVIR AND ACYCLOVIR ON RABBIT CORNEAL EPITHELIAL CELLS IN VITRO

KHOSRAVI E.[1] ELENA P.P.[1] GOLDSCHMIDT P.[2] BAUDOIN C.[3] and LUYCKX J.[2]

[1] Iris Pharma, Nice (France)
[2] Transphyto, Clermont Ferrand (France)
[3] Department of Ophthalmology, Nice (France)

PURPOSE :
To determine the effect of various concentrations of ganciclovir (GCV) or acyclovir (ACV) in extempore solutions (0.1 %, 0.01 %, 0.001 % and 0.0001 % w/v) on rabbit corneal epithelial cells proliferation and viability, in vitro.

METHODS :
Cell culture :
Rabbit corneal epithelial cells were prepared using corneal epithelium explants method.
Toxicity evaluation :
To examine cell viability and proliferation, 130 000 cells/well were incubated with 0.1 %, 0.01 %, 0.001 % and 0.0001 % GCV or ACV for 24 hours. The cells number and viability were determined by hemacytometer and trypan blue dye test .

RESULTS :
Hereunder the effect of GCV and ACV on cells mortality % after 24 hours contact was given.

Treatment	mortality % (mean ± Sd; n = 9)	Treatment	mortality % (mean ± Sd; n = 9)
Control	8.9 ± 4.1	Control	8.9 ± 4.1
GCV 0.1 %	14.3 ± 6.7	ACV 0.1 %	16.2 ± 3.9
GCV 0.01 %	13.2 ± 5.0	ACV 0.01 %	13.2 ± 5.3
GCV 0.001 %	10.5 ± 3.5	ACV 0.001 %	10.0 ± 3.7
GCV 0.0001 %	8.2 ± 5.7	ACV 0.0001 %	14.0 ± 8.0

For each tested concentration, % of cell mortality was statistically compared to control: (I) for GCV there were non significant differences between the 4 tested concentrations (p>0.05); (II) for ACV the 0.1% concentration showed a significant increase in cell mortality (p<0.05).

CONCLUSION :
These results indicate that GCV at 4 concentrations tested (0.1%, 0.01%, 0.001% and 0.0001%) do not show a toxic effect on rabbit corneal epitheal cells in vitro, while ACV presents a slight however toxic effect at 0.1% concentration.This results may be correlated to the ocular side effects observed in human after topical antiviral administration.

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5-FLUOROURACIL (5-FU) SOLUTIONS HAVE AN ALKALINE pH THAT, WHEN INJECTED ALONE, INCITES AN INFLAMMATORY REACTION IN THE CONJUNCTIVA

MALEK-CHEHIRE N. [1,2], RENARD G. [1,2], LEGEAIS J.-M. [1,2], KELLER N. [2], SAVOLDELLI M. [2], and POULIQUEN Y. [1,2]
[1] Department of Ophthalmology, Hôtel-Dieu de Paris, University of Paris (France)
[2] INSERM U 86, Paris (France)

Purpose. To assess pH-related toxicity of subconjunctival (SC) 5-Fluorouracil (5-FU) as used after glaucoma filtering surgery.
Methods. 16 rabbbits (4 rabbits in each group) received a subconjunctival (SC) injection of 0.5 cc of one of 4 solutions:
- the "worldwide" 5-FU formula (Roche): ("pH 9 5-FU")
  (pH = 9.3 undiluted and 9.1 after dilution to 10 mg/ml).
- the "older french" formula (Roche, before Jan. 1994): ("pH 8 5-FU")
  (pH = 8.3 undiluted and 8.25 after dilution to 10 mg/ml).
- physiologic saline solution adjusted to pH 9.2: ("pH 9 NaCl")
- BSS: ("BSS")

Eyes were enucleated on days 1, 5, 15 and 30. They were fixated with glutaraldehyde and conventionally processed for light (LM) and transmission electron microscopy (TEM).
Results. The first three solutions were responsible for an inflammatory reaction in the conjunctiva. It was most severe for the "pH 9 NaCl" solution which showed some cellular toxic changes on day 5. Intensity was comparable for both 5-FU formulae and no degenerative changes to the fibroblasts were seen.
Conclusions. A single SC injection of a pH 9 solution is toxic to the conjunctiva. Presence of the 5-FU molecule reduces the intensity of the inflammatory reaction. Further studies should evaluate possible damage after 5 or 10 injections. Adjusting the pH of 5-FU solutions prior to SC injections is advisable.

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FML-GENTAMICIN VERSUS FML-NEOMYCIN IN THE TREATMENT OF BACTERIAL CONJUNCTIVITIS

HUGUET P.[1] and JAUCH A.[2]

[1] *Service d'Ophtalmologie, Centre Hospitalier Régional, Tahoua (Niger)*
[2] *International R & D, CIBA Vision Ophthalmics, Bülach (Suisse)*

Purpose To compare the efficacy and safety of FML-Gentamicin (FG) eye drops and FML-Neomycin (FN) eye drops both at a dosage of 5 times daily for eight days in the treatment of bacterial conjunctivitis.

Methods Comparative, randomised, single-masked study in a single centre. 12 clinical signs & symptoms graded from 0-3 were evaluated by slit lamp on day 1, 3-4 and 7-8. Conjunctival swabs were taken before and after therapy and colony counts graded from 0-3 (CFU: 0/1-10/11-50/>50).

Results One hundred and five patients (45 FG; 60 FN) were enrolled. 89 strains of bacteria were isolated from 78 eyes; mostly staphylococci and hemophilus. Both drugs were highly effective in reducing the clinical sum score (FG: from 23 to 2.95; FN: from 22.7 to 4.7) and ocular bacterial count scores (FG: from 0.98 to 0.02; FN: from 0.72 to 0.14). There was a significant lower sum score with FG at dismissal (p=0.005), a trend in favour of FG for doctors' judgement of success of therapy (p=0.072), and a trend in favour of FG of lower bacterial counts after treatment (p=0.07). Moreover, local tolerance with FG was better than with FN (p=0.05). There were 2 transient side effects with FN and no withdrawals in both groups.

Conclusion This study suggests that FML-Gentamicin is possibly more effective and better tolerated than FML-Neo in the treatment of bacterial conjunctivitis.