Evaluation of antibiotic hypersensitivity in hospital setting. In vivo and in vitro testing by using standardized epicutaneous, intradermal, oral provocation tests and a rapid IL-6 release assay on the peripheral mononuclear cells

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Background: Antibiotics are amongst the most frequent causes of drug hypersensitivity.

Aim: To study the appearance of mostly skin related hypersensitivity events due to this very heterogeneous group of drugs in our hospitalized and out-patient material between 2007-2013 in order to analyze their culprit role.

Methods: The total number of patients was 136 that of matching control 29. Most patients were seen at the Emergency Unit of our hospital and sent after consultation as in- or outpatient for further clarification. According their history and symptoms 45% were definitely, 19% probably, 19% possibly hypersensitive to one or more drugs. Within the control group in 67% drugs as causative agents could be ruled out and in 33% their role has emerged as possibility. All tests have been carried out between 2-8 months after the event. In vivo methods included patch testing by pure drugs (10% w/w in petrolatum), intradermal tests by 1 mM drug solutions and oral provocations introducing incremental doses over 3 hrs. In vitro tests were developed to exploit the rapid (20') release of preformed IL-6 from ex vivo T-cells due to sensitizing drugs. Many in vivo–in vitro tests were run in parallel.

Results: Forty two patients and 5 controls were tested with various antibiotics according their histories. The number of positive in vitro tests was 31 and that of negative tests 29. Within the control group 9 negative tests were noted. Most tests (32/60=53%) were performed with β-lactams (penicillins and cephalosporins), followed by clindamycin (8/60=13%), fluoroquinolones (5/60=8%) sulfametoxazole (4/69=7%), doxycycline (3/60=5%), metronidazole (3/60=5%) and clarythromycine (2/60=3%). The highest positivity rate was found to amoxicillin (8/14=57%) but both false negative and false positive results (1-1) relative to in vivo tests were noted. The lowest positivity rate (0/4=0%) could be found with sulfametoxazole. The intradermal tests with 10-3M vancomycin gave false positive results in 3 controls tolerating this drug. Therefore, its test concentration has been lowered to 10-4 M. The phenotypic expression of antibiotic hypersensitivity fell into the following categories: circumscribed (17%) and generalized (30%) maculopapular rash, severe perioperative angioneurotic edema with dyspnoea, cardiac arrest (6,4%), generalized hives, diffuse erythema + fever (4,3%) circumscribed angioneurotic edema or urticaria (27,6%), severe intertriginous and flexural exanthema (SDRIFE), induced asthma, fixed drug eruption, loss of consciousness; one case each (14,7%). Non-immediate reactions were more common.

Conclusion: In vivo and in vitro tests carried out successively are needed to demonstrate drug induced hypersensitivity to antibiotics taking into account the clinical picture and differential diagnostic approach. IL-6 release assay has gained a solid place in the procedure.

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