

427 Efficacy and Safety of Etanercept in an Integrated Multistudy Database of Patients With Psoriasis

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RATIONALE: Etanercept has recently been approved in psoriasis. Here we report the safety and efficacy of etanercept in psoriasis patients across one phase 2 and two phase 3 studies.

METHODS: Comparisons presented between the 25-mg BIW dose (N=415) and placebo (N=414) used data pooled across all 3 studies, and those between the 50-mg BIW dose (N=358) and placebo (N=359) used data pooled across the phase 3 studies. The primary endpoint was $\geq 75\%$ improvement in the Psoriasis Area and Severity Index (PASI) at 12 weeks.

RESULTS: Three percent of patients receiving placebo and 33% receiving 25 mg BIW etanercept achieved a PASI 75 ($p < 0.0001$), while 3% of patients receiving placebo and 49% receiving 50 mg BIW etanercept achieved a PASI 75 ($p < 0.0001$). Across all three studies, 1261 patients received at least 1 dose of etanercept. Etanercept was well tolerated, with an adverse event profile similar to placebo. Injection site reactions were more common with etanercept use (6% placebo, 14% etanercept). At week 12, 2% of patients in the pooled placebo group and 1.8% in the pooled etanercept group discontinued because of adverse events. Serious adverse events occurred in a similar proportion of patients in both groups (1.2% placebo, 1.7% etanercept). No opportunistic infections or tuberculosis were reported.

CONCLUSIONS: Etanercept provided consistent, robust efficacy in the treatment of chronic plaque psoriasis. The adverse event profile of etanercept in patients with psoriasis was similar to that seen with placebo and was consistent with experience from RA populations. No new or unanticipated patterns of adverse events were observed.

428 The Protean Cutaneous Manifestations of Chronic Heavy Metal Overload in Pediatric Patients

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RATIONALE: Quest for an alternative means for solving severe & intractable skin problems in pediatric practice.

METHODS: Retrospective review of consecutive 494 patients who had undergone mineral hair analysis from April 2002 to June 2004 in a private pediatric clinic in Hong Kong. As the author had experienced initial successes with experimental regime on patients diagnosed to have heavy metal overload. The reason for this review was the occurrence of bizarre chronic problems not solved by conventional medical means. This paper was limited to discussion of the protean skin manifestations cured by this novel therapeutic approach.

RESULTS: Out of the 494 consecutive patients who have undergone hair mineral analysis, there were 79 patients with dermatological problems. Majority were eczema. The average age of the patients so treated was 4.8 $\pm$ 3.8 yrs (range 1 -14 yr. old). The major source of heavy metal overload was from the ingestion of contaminated fish by the patients. Ten of the patients had onset of eczema before 6 months of age thought to be related to transplacental or translactational transfer of heavy metals. Alpha Lipoic Acid, a potent antioxidant, hitherto with no report of its use in pediatrics, has been shown to be beneficial with no adverse side effects in the treatment regime. The result has been most encouraging as majority of the patients had marked amelioration or complete eradication of the eczema after 102 $\pm$ 55 days of therapy.

CONCLUSIONS: The use of anti-oxidant in the therapy of early pediatric eczema diagnosed by mineral hair analysis should deserve further study.

429 Sequence and Characterization of Honeybee Venom Acid Phosphatase

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RATIONALE: Acid phosphatase has been shown to be a significant IgE binding protein in honeybee venom, the nature of its IgE binding epitopes is unknown.

METHODS: Peptides produced by tryptic and endoproteinase-GluC digestion of the chromatographically purified protein were sequenced by Edman degradation. MALDI-TOF mass spectrometry was performed on a tryptic digest and the results analyzed using protein prospector. The cDNA was cloned using exact match primers and sequenced and then compared to the partially assembled genomic sequence.

RESULTS: The molecule is a typical histidine acid phosphatase of 373 amino acids with 4 potential N-linked carbohydrates. It is similar to other insect acid phosphatases and mammalian prostatic and lysosomal enzymes. There are 2 disulfide bonds. The signal sequence is 27 amino acids. The sequence is contained in 6 exons of the genomic sequence in contig 16010. The Edman sequenced peptides cover 47% of the molecule and the mass spectrometry peptides 52%; with a total coverage of 67%. The molecular weight of the protein portion is 43.9kDa with an isoelectric point of 5.64.

CONCLUSIONS: Honeybee venom acid phosphatase is an acidic heat-labile protein with potential protein and carbohydrate IgE binding epitopes.

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430 Proteins in the High Molecular Weight Fraction of Honeybee Venom

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RATIONALE: There are a number of IgE binding proteins in the high molecular weight fraction of honeybee venom, we have been able to identify three.

METHODS: The high molecular weight fraction of honeybee venom was separated by reversed phase chromatography and major peaks subjected to amino acid sequencing of the N-terminal and separated tryptic digest peptides. Sequences were cloned by RACE and RT-PCR and compared to honeybee genomic sequences.

RESULTS: Five peptides were isolated from a protein of unknown function, which was cloned and completely sequenced. It is 204 amino acids with 4 potential N-linked carbohydrate sites and no cysteines. N-linked carbohydrate was observed experimentally. It has very large introns in the genomic sequence. Similar proteins are known in other insects. A second protein of 68kDa known to bind IgE was identified as a carboxylesterase, possibly acetylcholinesterase. A putative sequence has been constructed from the genomic DNA. The protein molecular weight is 60kDa with 4 potential N-linked carbohydrates. This protein has also been found by Kettner et al. The third protein of about 78kDa is related to hexamerin 2, an arylphorin storage protein of insects.

CONCLUSIONS: One IgE binding protein is a carboxylesterase, a second is a carbohydrate rich protein of unknown function.

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