The Antivenom and Vaccine Production Center

Polyvalent Snake Antivenom (Equine)

The AVPC polyvalent snake antivenom is a refined and highly purified preparation containing the $F(ab')_2$ fractions of the immunoglobulins raised against the venoms of six terresterial Saudi snakes.

Preparation

The antivenom is prepared by hyperimmunizing healthy Arabian horses using gradually increasing doses of the Saudi snake venoms from: *Bitis arietans, Cerastes cerastes, Echis carinatus, Echis coloratus, Naja haje and Walterinnesia aegyptia* and immunomodulators. Monospecific sera of high titre are purified by different stages of salt fractionation and refined by peptic digestion. The resulting $F(ab')_2$ fragments are clarified by gel adsorbents and multistage filtration followed by proportional mixing and dilution to the required potency.

Composition

Each 1 ml antivenom contains purified immunoglobulin fractions against:

- *Bitis arietans* venom ..... Q.S. to neutralize 25 LD_{50} (minimum)
- *Cerastes cerastes* venom ..... Q.S. to neutralize 25 LD_{50} (minimum)
- *Echis carinatus* venom ..... Q.S. to neutralize 25 LD_{50} (minimum)
- *Echis coloratus* venom ..... Q.S. to neutralize 25 LD_{50} (minimum)
- *Naja haje* venom ..... Q.S. to neutralize 25 LD_{50} (minimum)
- *Walterinnesia aegyptia* venom ..... Q.S. to neutralize 25 LD_{50} (minimum)
- m-Cresol ..... 3.5 mg (maximum)
- Isotonic sodium chloride solution ... Q.S to 1.0 ml

Spectrum of Activity

The polyvalent antivenom is highly specific in neutralizing the toxic effects of the six Saudi snake venoms. The antivenom was also shown to neutralize effectively the haemorrhagic and myonecrotic activities of the viper snake venoms and the neuromascular blocking and cardiotoxic effects of the elapid snake venoms. The antivenom has a wide spectrum of activity and can neutralize the venom of many of the Middle East and North African snakes including:

- *Bitis caudalis*
- *Bitis gabonica*
- *Naja melanoleuca*
- *Naja naja*
- *Naja nigricollis*

Packaging

Box of 10 x 10 ml ampoules
Box of 10 x 20 ml ampoules

Mode of Action

Immunologic interaction of the specific immunoglobulin fractions with the antigenic sites in the toxins and other active components in the venoms resulting in blocking of the active toxicologic sites in the molecules. The strong binding of the venom-antivenom molecules in the central compartment (blood) will also cause a shift of the venom molecules from their binding receptors in the tissues into the central compartment and thus facilitates elimination.

Treatment of Snake Bites

Antivenom is the only specific antidote available at present time for the treatment of venomous snake bites. Effective treatment depends on the intravenous injection of the antivenom **as soon as possible after the snake bite.** Antivenom treatment is indicated if signs of systemic envenoming are present such as:

a. Haemostatic abnormalities such as spontaneous systemic bleeding, incoagulable blood or marked thrombocytopenia (<50,000/mm^3).
b. Hypotension and shock, abnormal ECG, etc.
c. Neurotoxicity.
d. Impaired consciousness.
e. Generalized rhabdomyolysis.

Also, in the absence of systematic envenoming, local swelling involving more than half the bitten limb, extensive blistering or bruising and bites on digits with rapid progression of swelling are indications for antivenom.

Prediction of Antivenom Reactions

Most antivenom reactions are not caused by the acquired Type I, IgE mediated hypersensitivity, but by complement activation by IgG aggregates or Fc fragments. It follows that the skin and conjunctival tests cannot predict early (anaphylactoid) or late (serum sickness) antivenom reactions, but delay the onset of treatment and may sensitise the patient. However, for assurance of the medical faculty a BESREDKA test can be carried out as follows: 0.1 ml of antivenom is injected subcutaneously followed by 15 minutes watch then 0.25 ml of antivenom is injected followed by another 15 minutes watch. If no reaction develops, the calculated dose of the antivenom should be given. In case of positive BESREDKA test or if the patient has a proven sensitivity to horse serum a GOAT antivenom may be given.

Administration and Dosage

Antivenom treatment is indicated as long as signs of systemic envenoming persist and as soon as these signs appear. In bites from the Saudi venomous snakes generally forty (40) ml antivenom are diluted in approximately 5 ml isotonic physiological fluid, /kg body weight and infused intravenously slowly over a period of 30-60 minutes. Alternatively, the antivenom can be injected intravenously undiluted at a rate of 4 ml/minute. No difference in the incidence or severity of antivenom reactions was observed in patients treated by either method. However, it is easier to control antivenom administration by the infusion method than by the intravenous "push technique". The antivenom dose can be repeated every 4-6 hours until definite improvement takes place. **CHILDREN MUST BE GIVEN THE SAME DOSE OF ANTIVENOM AS ADULTS.**

Response to Antivenom

Marked symptomatic improvement may be seen soon after antivenom administration. In shocked patients, the blood pressure may rise and conciousness return. Neurotoxic signs may improve within 30 minutes but generally take several hours. Spontaneous systemic bleeding usually stops within 15-30 minutes and blood coagulability is restored within 6 hours, provided that an adequate antivenom dose was given.

Side Effects, Toxic Reactions and Antidotes

The AVPC polyvalent snake antivenom is a refined highly purified preparation. Despite its low protein content and high purity both early and late allergic reactions may occur in susceptible patients. The early (anaphylactoid) reactions may develop within 10-180 minutes of starting antivenom administration. They are treated by subcutaneous injection of adrenaline (1 mg/ml, 0.5-1 ml for adults and 0.01 ml/kg for children), the dose being repeated if necessary, an antihistamine (e.g., chlorpheniramine maleate, 10 mg intravenously for adults and 0.2 mg/kg intravenously for children) and hydrocortisone (100-200 mg intravenously). The late reactions (serum sickness or immune complex) may develop 5-24 days (average 7 days) after antivenom. They are treated by prednisolone (5 mg six hourly for 7 days for adults and 0.7mg/kg/day in divided doses for 7 days for children). An antihistamine (e.g., chlorpheniramine maleate, 2mg 6 hourly for adults and 0.25 mg/kg/day in divided dose for children) may be added.

Adjunctive Therapy For Snake Bite Poisoning

NEUROTOXIC ENVENOMING. Bulbar and respiratory paralysis may lead to death from aspiration, airway obstruction or respiratory failure. Mechanical measures should be taken to maintain lung ventilation. Anticholinesterases are potentially useful in these states.

HYPOTENSION AND SHOCK. Fresh whole blood, fresh frozen plasma or a plasma expander can be used. Dopamine infusion can be used in cases of persistent or profound hypotension.

OLIGURIA AND RENAL FAILURE. Cautious rehydration, diuretics, peritoneal or haemodialysis or haemofiltration may be undertaken.

LOCAL INFECTION AT THE SITE OF THE BITE. Penicillin, erythromycin or a broad spectrum antibiotic together with a booster dose of tetanus toxoid should be given in cases of wound infection. An aminoglycoside antibiotic such as gentamicin and metronidazole should be added if there is evidence of local necrosis.

Storage

The AVPC polyvalent snake antivenom should be stored at $4 \pm 2^{\circ}$ C in the dark. The shelf life under these conditions is 3 years.

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