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Efficacy of the new batches of monospecific Russell's viper (*Daboia russelii siamensis*) and cobra (*Naja kaouthia*) antivenoms manufactured by Myanmar Pharmaceutical Factory

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Efficacy of new batch of monospecific Russell's viper (*Daboia russelii siamensis*) and cobra (*Naja kaouthia*) antivenoms manufactured by the Myanmar Pharmaceutical Factory was tested according to WHO recommended techniques. The new batch of monospecific Russell's viper antivenom is 1.7 to 5 times less effective in neutralising defibrinogenating, haemorrhagic, necrotic, lethal and procoagulant activities and 64 times in capillary permeability increasing activity compared to the reference. The efficacy of neutralisation of the lethal activity of cobra venom by the new batch of monospecific cobra antivenom is 10 times inferior to that of the reference. Because of inferior performance of the new batch of antivenoms, clinical efficacy and the dose of the antivenom to be given to human snakebite cases need to be studied.

INTRODUCTION

The monospecific Russell's viper (*Daboia russelii siamensis*) (RV) antivenom (1 ml neutralises 2 mg of RV venom) and cobra (*Naja kaouthia*) antivenom (1 ml neutralises 1 mg of the cobra venom) (MPF pamphlets) manufactured by Myanmar Pharmaceutical Factory) (MPF) have been used throughout the country for treating specific snakebites decades ago. It also serves as reference antivenoms. Since 1997, the manufacturer changed venom-antivenom neutralisation ratio of the antivenoms in line with the antivenom manufacturers of the Southeast Asia where 1 ml of the new batch of Russell's viper antivenom will now neutralise 1 mg of Russell's viper venom and that of cobra 0.6 mg. The neutralising efficacy of the biological activities of the new batches is not known and needs to be tested before put into general use. This study concerns with *in vivo* and *in vitro* testing of neutralising efficacy of the antivenoms.

MATERIALS AND METHODS

Neutralisation of different biological properties of the Russell's viper (*D. r. siamensis*) venom of Tharawaddy such as lethality ($5LD_{50}$), coagulant (3MHD), necrotic (3MND), haemorrhagic (3MDD), defibrino-genating (5MDD), and capillary permeability increasing activities (100MCPID), by the new batch of monospecific liquid antivenom (batch no: C98011, exp. 4/2001) was tested according to the WHO recommended techniques [1]. Neutralisation of the $5LD_{50}$ i.v of the cobra (*Naja kaouthia*) venom by the new batch of monospecific liquid antivenom (batch no: A98009, exp. 1/2001) was also tested according to the WHO recommended technique [1].

Table.1. Neutralising dose to different biological properties of Russell's viper (*Daboia russelii siamensis*) venom by monospecific antivenoms

Antivenom	3 MHD 2.53 mg/ml µl	3 MND 2.39mg/ml µl	5 MDD 120 µg/ml µl	100 MCPID 14.4µg/ml µl	$5LD_{50}$ iv 233.7 µg/ml µl	10 MCD 50.25 µg/ml µl
MPF(R)	10	5	3	0.039	3	0.0625
MPF(N)	40	20	5	2.5	12	0.3125
TRC	10	20	5	0.1562	3	0.125
SII	40	40	80	15	6.25	NT

(venom neutralising doses of the TRC and SII antivenoms are included for comparison, ref:3)

MPF(R) = Reference MPF antivenom
MPF(N)= New MPF antivenom
SII= Serum Institute of India
TRC= Thai Red Cross antivenom
NT= not neutralised
LD_{50}iv= lethality
MHD= minimum heamorrhagic dose
MND= minimum necrotic dose
MCD= minimum coagulant dose
MDD= minimum defibrinogenating dose
MCPID= minimum capillary permeability increasing dose

Note: neutralisation of the lethal activity (LD_{50}) is expressed as ED_{50} dose that is the amount of antivenom required to protect 50% death of the experimental animal in 24 hr following injection of the mixture.

RESULTS

Monospecific Russell's viper antivenom

The amount of the antivenom required to neutralize different biological properties of Russell's viper venom are shown in Table 1.

The new batch of antivenom is 1.7 to 5 times less effective in neutralising defibrinogenating, haemorrhagic, necrotic, lethality and coagulant activities and 64 times in capillary permeability increasing activity compared to the reference. Moreover its neutralizing efficacy was inferior to that of the Thai Red Cross and slightly more potent than that of the Indian SII antivenom.

Monospecific cobra antivenom

The new batch of monospecific antivenom requires 200 ul to neutralise $5LD_{50}$ i.v. of the cobra venom (*Naja kaouthia*). The reference (batch no: DE 96767, exp. 7/2001) and the TRC antivenoms require 21.25 ul and 80.6 ul to neutralise $5LD_{50}$ i.v. of the cobra venom respectively [2].

DISCUSSION

Although venom-antivenom neutralizing ratio of the new batch of antivenom is reduced to half of the reference, its neutralising efficacy of the different biological activities of the venom is reduced from 1.75 to 64 times compared to the reference. In particular, 5-64 times reduction in neutralising efficacy of coagulant and capillary permeability increasing activity (MCPID) is not desirable. It is expected that more antivenom will be needed to correct the clotting and permeability defects in treating Russell's viper bite cases than before. It also raises the questions that such variation in the antivenom efficacy could be due to batch-to-batch variation of the antivenom [3] which in turn depends on the quality of immungoen used for raising this particular batch of antivenom. Widely pooled venom should be used for raising antivenom in order to overcome the deficiency [1].

Since the venom neutralising efficacy of the new viper antivenom is much inferior to

those of the reference and the Thai Red Cross antivenom, it is suggested that venom-antivenom neutralization ratio should be aimed at having at least comparable or more potent efficacy than that of the Thai antivenom. Also the neutralising efficacy of lethal activity of the new cobra antivenom is also inferior to those of the reference and the Thai Red Cross antivenoms. Monitoring of the neutralising efficacy of every batch of antivenom should be carried out as a routine.

From the above observations it could be concluded that more clinical studies of the new antivenom on snakebite patients are needed in order to confirm *in vivo* and *in vitro* findings and formulation of the new antivenom should be reviewed in order to produce a high quality antivenom for treating snakebite cases throughout the country.

REFERENCES

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