Case study

Effect of Diethylcarbamazine (DEC) in Relapse cases of Nephrotic Syndrome in Filarial Endemic Region: A case Series

Abstract

INTRODUCTION-Incidence of N.S and filariasis both is high in China, Japan & India.Studies have shown association of filariasis in NS.In Coastal belt of Gujarat Filariasis occurs as the mosquito responsible is still prevalent.Therefore, filariasis association may be causing persistence of edema in NS relapse cases.After a 7^{th} relapse patient was treated successfully with DEC,we decided to study,the effect of Tab.DEC on weight loss and urine protein, in relapse patients of NS.

MATERIAL METHOD-In relapse patients of NS, Tab.DEC given by oral route in dose of 72mg/kg/cycle for 7 days.Weight record and urine protein was measured daily.Steroid as Tab P.R administered at 2 mg/k/d.

RESULTS-1^{st} case was 7^{th} relapse S.D N.S; on P.R and levamisole for 3 years. Tab.DEC was started on D^3 of admission and response seen on D^5.Urine protein become nil on 10^{th} D.O.A, relapse free since 1year.In other 4 cases of 1^{st}, 2^{nd}, 2^{nd} and 7^{th} relapse, response of DEC was seen within 2 days.Thus, after starting tab.DEC weight and urine protein reduced within 2 days in 5 relapse cases.Filaria wasn't detected in blood film of any patient & Elisa test sent in 2 was negative.

CONCLUSION-After starting steroid therapy, no satisfactory response,but after starting Tab.DEC decrease in weight was seen and urine protein become nil.Tab. DEC works well in filariasis and has also effects on immune system.Levamisole used as immunomodulator, also acts as an antifilarial agent. Tab.DEC considered in relapse cases of NS in Filaria endemic regions & it's cost-effective and safe.

Keywords
NS Nephrotic syndrome; UTI urinary tract infection; DEC diethyl carbamazine citrate; T temperature; AG abdominal girth; URTI upper respiratory tract infection; H.C Heat Coagulation; D.O.A day of admission; P.R prednisolone; C.P crystalline penicillin; S.D steroid dependant; S.S steroid sensitive; S.R steroid resistant

INTRODUCTION

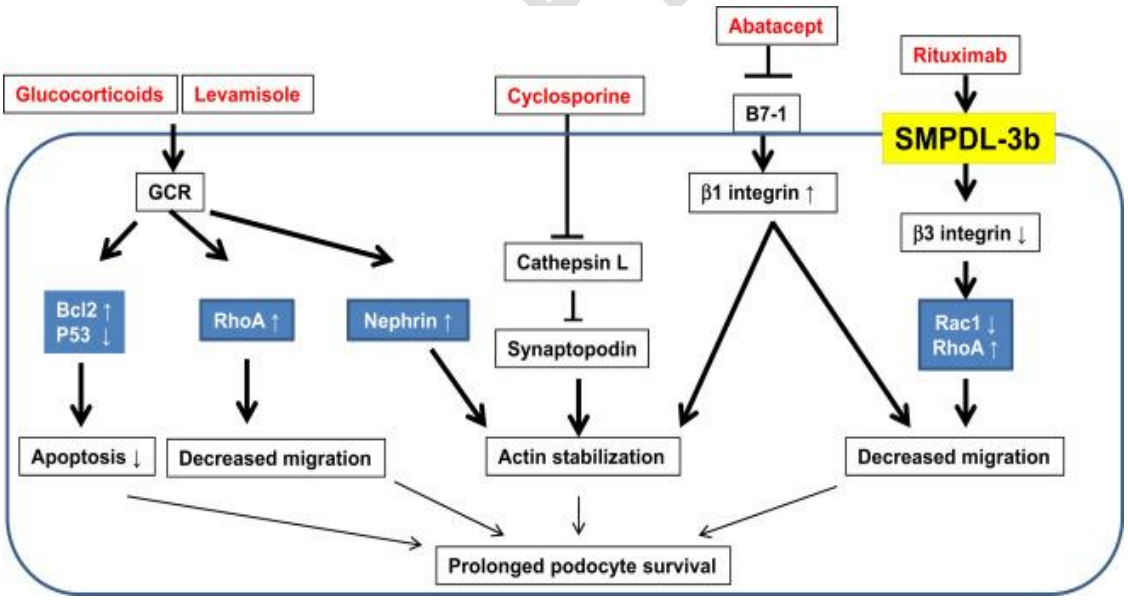
N.S is characterized by heavy(nephrotic range) proteinuria as >3.5gm/24hr or a urine protein creatinine ratio >2, hypoalbuminemia (< 2.5 g/dl), hyperlipidaemia(cholesterol >200mg/dl), and edema.[1]

P.R suppresses autoimmunity in N.S & so induces remission early. But long term use of P.R can cause steroid toxicity in frequent relapsers, S.R & S.D N.S.[2]

In 1966, new drug levamisole was discovered[3] and due to its immunemodulator property[4], its use had been increased in frequent relapsers, S.R & S.D N.S. But its side effects like leucopenia, rash, seziures limits its use in N.S[5].

As per figure 1 Levamisole attenuates podocyte apoptosis and increase in RhoA activity and decrease in degradation of synaptopodin protein; and so prolonging podocyte survival[6].

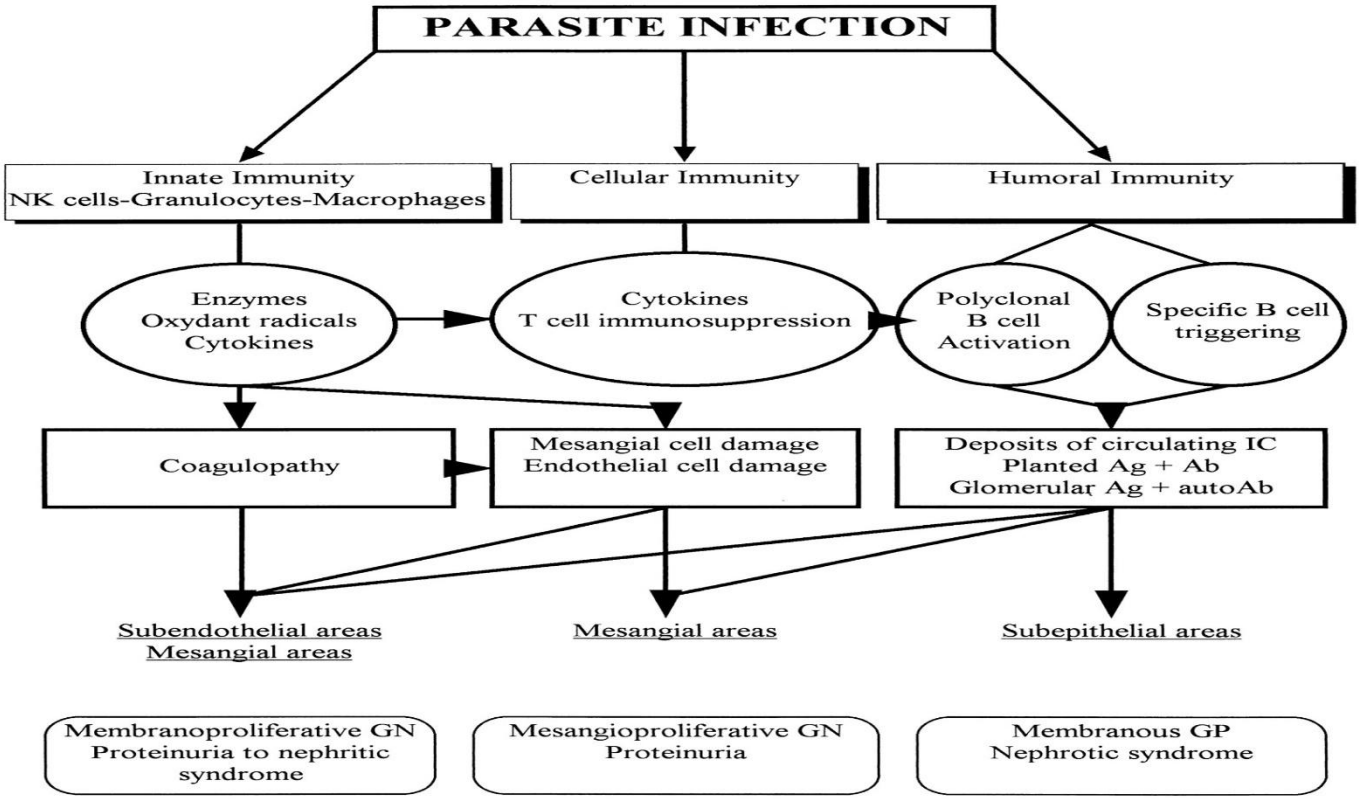
Figure 1 Mechanism of action of Drugs used in N.S [6]



Incidence of N.S was quite high in China, Japan, India and many Asian countries in 1950s[7]& incidence of lymphatic filariasis was also quite high in those countries.[8]As per figure 2 there is a clear association of filariasis and N.S.[9] In the Coastal belt of Gujarat, filariasis still occurs as the mosquito responsible for it , therefore filariasis association causing persistence of edema in N.S is possible.

After filarial infection of human body the generated toxins affects several compartments of the immune system. And play a role in fighting parasitic infections & in the pathogenesis of associated glomerulopathies.During infection, released inflammatory mediators directly damage the different glomerular cell types & participate in the activation of specific subsets of T and B cells, resulting in different levels of antigen, antibody & immune complexes.Depending on the site of the immune-complex deposition and on the type of primary damaged glomerular cells, different glomerular lesions develope.[10]

Figure 2 Effect of Parasitic Infection [9]



DEC is an anti-parasitic agent used in the treatment of lymphatic filariasis, tropical pulmonary eosinophilia, and loiasis & acts by inhibiting arachidonic acid metabolism.DEC is administered by oral route in the dose of 72mg/kg/cycle spread over 5-15 days(in our study we were giving for 10 m/k/d for 7 days).Side effect of DEC due to release of antigens from dying filariae are fever, skin rash, and swollen tender glands in neck, visual disturbance, nausea, dizziness, itching.[11] It's Safe in pregnancy.

Levamisole as immunomodulator for N.S is more effective in filarial endemic countries and beneficial effect of levamisole are reported from south east asia countries.[12] As we see glomerular pathology occurs because of parasitic infections, instead of using levamisole, we can use better specific antifilarial agent which has lower side effects.

DEC works well in filariasis and other parasitic infections and due to serious side effects of levamisole & due to possible association of filariasis with N.S, it can be used in N.S as it's cost effective and safety is better than levamisole.

Method

Here we are discussing effect of DEC in minimal change N.S who had responded to steroids and who presented again with relapse. DEC is not 1st line treatment of N.S here we were using when they came with relapse.

In these 5 cases of minimal change N.S;DEC was administered by oral route in the dose of 72mg/k/cycle for 7days (Table 1).After starting it,daily weight record and urine protein was measured daily(Figure 3-7).Steroid as Tab P.R was administered at 2m/k/d.
No adverse events were detected by using DEC & Filaria wasn't detected in midnight thick blood film of any patient. Elisa test done in 2 patients was negative.

Table 1: Case Details

History	Examination	Treatment
A.4 Y/F: Eyelid and pedal swelling since 7 day abdomen distension since 2-3 day decrease urine output since 2 days UTI (Ecoli +ve) 7^{th} relapse S.S	T Normal Eyelids swelling Pedal edema (pitting),transverse umbilicus AG-64cm BP-94/68mmHg	Inj.ciprofloxacin (7day) Tab.levamisole (4day) Tab.P.R(20mg) (8day) Tab. DEC (7day) Tab zinc(12day)
B.2 Y/M: Swelling of eyelid since 3days cough and cold since 2days Tonsilitis 4^{th} relapse steroid dependent	T-Normal AG-64cm BP-96/70mmHg Throat-congested, Tonsil enlarged Eyelids swelling Pedal edema +(pitting)	Inj. amoxiclav (5dy) Tab.P.R (6days) Tab.DEC for 7days
C.5.5 Y/M: fever 4day, Eyelid swelling 4 day, Swelling over abdomen 2 day, UTI (urine pus cells) 2^{nd} relapse S.S	T-Normal AG-64cm BP-96/70mmHg Pedal edema +transverse umbilicus	Inj.ciprofloxacin (10 d) Tab.P.R (10 d) Tab.amoxycillin(1day) Tab.DEC (7day) Tab zinc(11day)
D.6 Y/F: eyelid swelling-2dy Pedal swelling-2dy Cough-2dy URTI 2^{nd} relapse S.S	T-Normal AG-60cm BP- 100/70mmHg Throat-congested and Tonsil enlarged Eyelid swelling Pedal edema (pitting)	Inj.amoxiclav(4dy) Tab.P.R(4dy) Tab.DEC for 7 day
E.6Y/M: eyelid swelling since 3 day, swelling over abdomen since 3 day tonsillitis 1^{st} relapse S.S	T-Normal AG-62cm, BP-98/66mmHg Throat-congested PA-visible veins, edema over abdomen, liver+2cm	Inj.C.P(5d) Inj.amoxyclav (4day) Tab.P.R (9day) Tab.DEC (7day)

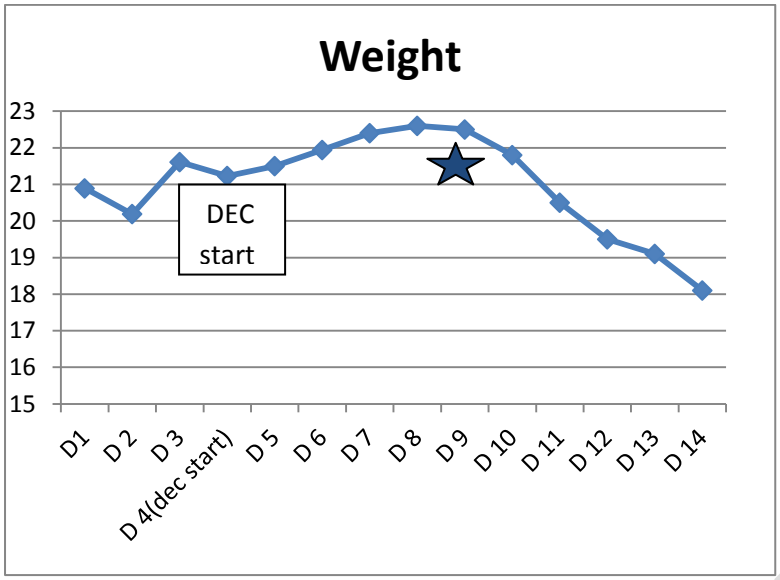
Table 2: Investigations on admission

Investigations	**Case 1**	**Case 2**	**Case 3**	**Case 4**	**Case 5**
T. Protein (g/dl)	3.9	4	4.02	3.92	3.2
S. Albumin (g/dl)	1.42	1.5	1.42	1.63	2.1
S. Globulin (g/dl)	2.48	2.5	2.60	2.29	2.8
A/ G ratio	0.57	2.5	0.55	0.71	0.75
S Cholesterol (mg/dl)	525	385	467	321	320
24hr Urine Protein **(**mg/24hr)	>2000	670	452	395	410
Urine Protein Creatinine ratio (mg/mg)	7.9	9.19	12.85	12.5	8

Normal values: T. protein 6-8g/dl; S. Albumin 3.5-5g/dl; S.Globulin-0.5-3g/dl; A/G ratio-0.8-2.0; S. cholesterol <200mg/dl; 24hr urine protein 30-150mg/24hr; Urine protein creatinine ratio <0.2mg/mg

Course during treatment

Figure 3: Case A-4yr female- 7th Relapse



★ ----Shows urine H.C becomes nil

Figure 4: Case B 2yr male 4th Relapse

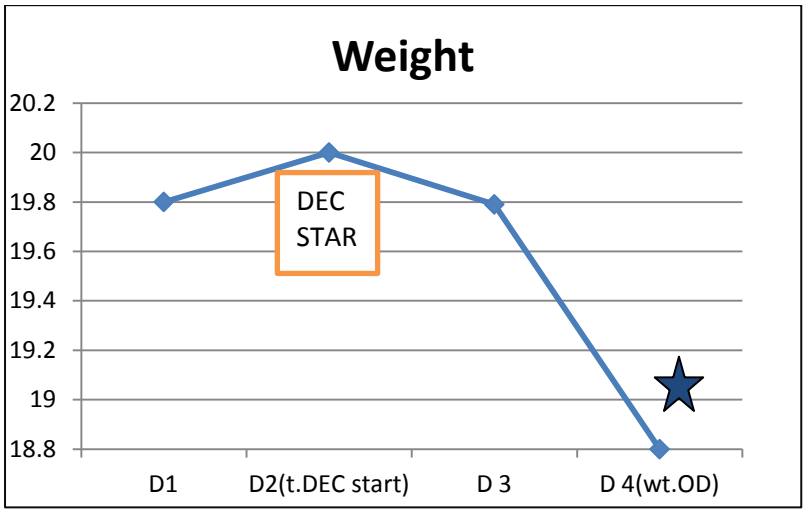


Figure 5: Case C. 5.5yr male -2nd relapse

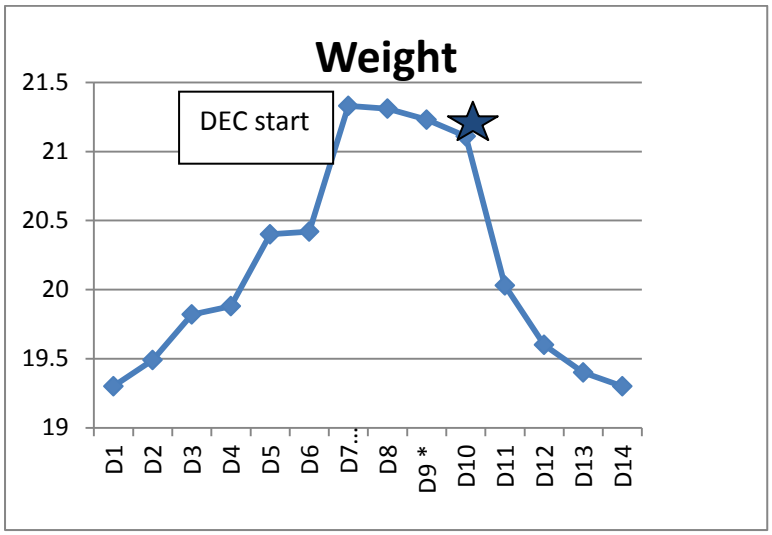


Figure 6: Case D-6yr Female – 2nd relapse

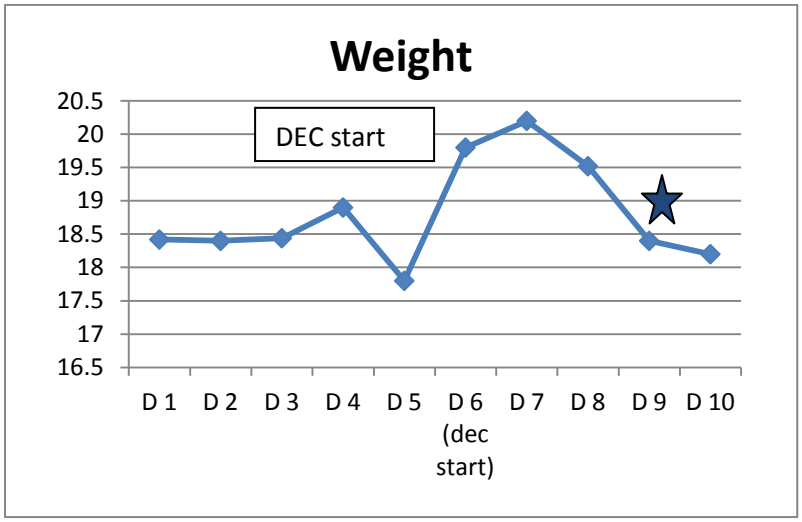
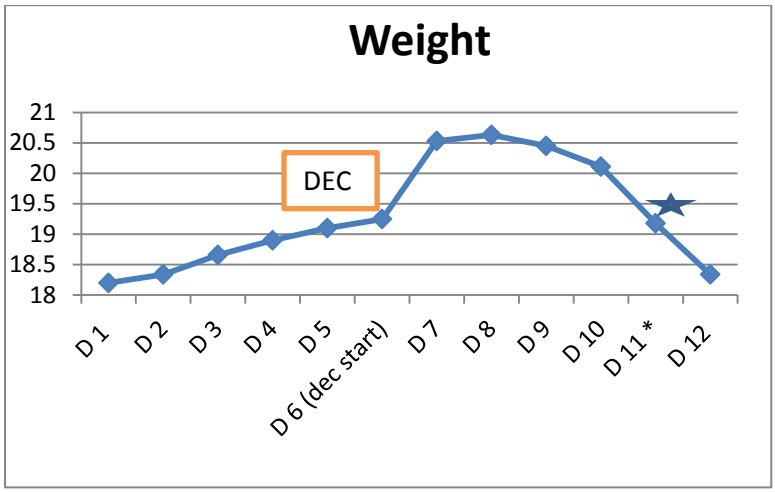


Figure 7: Case E .6yr Male -1st Relapse



★ ----Shows urine H.C becomes nil

Discussion:

It is a denovo study in N.S patients. Initially reports were done to find out any foci of infection and as per report symptomatic management was done. Still in all these cases edema and heavy range proteinuria, didn't disappear so considering connection of N.S with filariasis we started tab.DEC. After starting DEC as effect occur initially weight loss starts slowly and urine cloudication becomes clear day by day.

In the index case A, with 7th Relapse, foci of infection was U.T.I.so treatment for UTI started. Daily twice weight record and twice daily urine H.C was continued. Till 4rd day no recovery was seen so considering relapse and no any recovery seen even after starting antibiotics so started DEC on 3rd D.O.A. Edema started to reduce on 5th D.O.A and slowly it disappeared on 8th D.O.A, H.C became clear on 9th D.O.A (figure 3).

In 2nd case B, 4th Relapse, foci of infection was chronic tonsillitis so considering bacterial infection we started antibiotics and then daily twice weight record and twice daily urine H.C was done .but no response came so DEC started on 4th D.O.A and after that edema gradually started to reduce on 6th day .(figure 4).

In 3rd case C,2nd Relapse, foci of infection was UTI and treatment for UTI started, & daily twice weight record and twice daily urine H.C was done. Even after 7 day no any signs of recovery seen so DEC started on 7rd D.O.A and after that edema reduced on 9th D.O.A and H.C became clear on 10th D.O.A (figure 5).

In 4th case D, 2nd Relapse, foci of infection was due to URTI and antibiotic started & twice weight record and twice daily urine H.C was done. Even after 6day no changes in edema and proteinuria seen so DEC started on 6th D.O.A and after that edema started to resolve slowly from 7th D.O.A and H.C became clear on 9th D.O.A (figure 6).

In 5th case E ,admission done and foci of infection was URTI and symptomatic and specific treatment started and daily twice weight record and twice daily urine H.C was done.But no response till 6th day so DEC started on 6nd D.O.A and after that edema started to reduce on 9th D.O.A & H.C became clear on 4thD.O.A (figure 7).

Conclusion

As per above study, After Starting DEC, weight and urine protein started to reduce within 2 days.
Tab. DEC works well in filariasis and has also effects on immune system. Levamisole used as immunomodulator, also acts as an antifilarial agent. Tab. DEC may be considered in relapse cases of NS in Filaria endemic regions. It is cost-effective and safe. Further trials with controls and efforts to detect antigen is recommended.

Recommendation

What is already known?
Levamisole is used for S.D N.S. It is also a wormicidal drug acting on filarial worms. Filaria has been linked with minimal change N.S and filarial antigen has been observed in kidney biopsy.

What this Study adds?
We are reporting this case series because with N.S, the effect of DEC is appear as it reduce edema within 3-4 days of administration.

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