PROTOCOLLO : FILTRAZIONE A CASCATA NELL'EPATITE CRONICA ATTIVA HCV+

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STUDIO DI FATTIBILITÀ:
PROTOCOLLO FC / IFNα / RIBAVIRINA
PZ ECA HCV+ GENOTIPO I
NON RESPONSIVI A IFNα / RIBAVIRINA

LETTERATURA IL 40% DEI PAZIENTI CON ECA HCV+ NON RISPONDE ALLA TERAPIA STANDARD; UNA RIDUZIONE DELLE COPIE DI HCV-RNA È STATA OSSERVATA IN PAZIENTI SOTTOPOSTI A FC.

FC & VIREMIA HCV. EVIDENZE? (*)

IN UNO STUDIO PILOTA 4 PAZIENTI AFFETTI DA HCV SOTTOPOSTI A TRAPIANTO DI FEGATO DA VIVENTE, SONO STATI SOTTOPOSTI A CICLO DI FC, OLTRE A INTERFERONE E RIBAVIRINA, PER ABBATTERE LA CARICA VIRALE (HCV RNA).

I PAZIENTI HANNO RICEVUTO CICLI DI FC (MAX 5 PROCEDURE) IN CONCOMITANZA DELL'INIZIO DELLA TERAPIA FARMACOLOGICA. I LIVELLI DI HCV RNA SI SONO RIDOTTI DRASTICAMENTE (*>90.0%*).

AD UN ANNO DAL TRAPIANTO IL VIRUS ERA SILENTE.

LA COMBINAZIONE FC / INTERFERONE / RIBAVIRINA SI È DIMOSTRATA EFFICACE TRATTAMENTO PER ABBATTERE I LIVELLI DI HCV RNA.

(*) IMPACT OF DOUBLE-FILTRATION PLASMAPHERESIS IN COMBINATION WITH INTERFERON AND RIBAVIRIN IN LIVING DONOR LIVER TRANSPLANT RECIPIENTS WITH HEPATITIS C. *MASAHIKO TANIGUCHI ET ALL. TRANSPLANTATION* 2006;81: 1747–1749.

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Original Article

Double filtration plasmapheresis and interferon combination therapy for chronic hepatitis C patients with genotype 1 and high viral load

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Aim: The efficacy and safety of double filtration plasmapheresis (DFPP) plus interferon (IFN) combination therapy were compared with those of IFN therapy alone in 193 chronic hepatitis C patients having a high hepatitis C virus ribonucleic acid load of difficult-to-treat genotype 1b.

Methods: All patients received either interferon alpha-2b (IFN-α-2b) monotherapy or combination therapies with ribavirin and IFN-α-2b or pegylated interferon alpha-2b (PEG-IFN-α-2b). Each patient individually decided whether to receive concomitant DFPP. DFPP was immediately followed by IFN treatment, and up to five sessions were given during the first week.

Results: Sixty patients decided to receive DFPP. In the DFPP plus PEG-IFN-α-2b therapy group ($n = 30$), viral load reduction at 4 weeks after the start of treatment was greater than in non-DFPP ($n = 74$) (2.47 *vs* 1.52, log, $P = 0.010$), and the sustained virus response was also higher (77.8% *vs* 50.0%), even in cases of re-treated patients (relapsers or non-responders to previous IFN therapies). Adverse events, mild and transient, were observed in 38.3% of all DFPP-treated patients.

Conclusion: DFPP plus IFN combination therapy produced a great reduction of viral load during the early stage of treatment and achieved a high sustained virus response, suggesting that this combination therapy may be a new modality for chronic hepatitis C patients at difficult-to-treat states.

Key words: combination therapy, double filtration plasmapheresis, early viral reduction, non-responder, relapser, sustained virus response

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Dynamics of hepatitis C viremia after plasma exchange

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Background/Aims: **The dynamics of hepatitis C viremia after perturbation by plasma exchange was addressed in two infected patients with symptomatic cryoglobulinemia. This approach may offer an alternative to studying patients treated with antivirals in order to understand the dynamics of hepatitis C virion exchange among different compartments *in vivo*.**

Methods: **Plasma exchange sessions were conducted every 24 h for 3 consecutive days; hepatitis C virus RNA copy numbers were evaluated in sequential plasma samples collected before (−24, −12, −8, and 0 h) and at short intervals (at 1, 3, 6, and 12 h) after each session.**

Results: **After each plasma exchange session viremia dropped by 45.3–93.3% in patient 1, and by 60.5–72.7% in patient 2, paralleling (or, in some cases, exceeding) the amount of fluid exchanged. No mobilization of cell-free hepatitis C virus from extra-vascular sites was documented during the 2-h plasma exchange. The dynamics of hepatitis C viremia after each procedure was also evaluated. Pre-plasma exchange levels were restored within 3–6 h in both patients, and the mean doubling times of residual viremia were 4.6 h and 4.5 h for patients 1 and 2, respectively.**

Conclusions: **The results, in agreement with recent evidence indicating that the turnover of hepatitis C virions is a highly dynamic process, extend previous evaluations by documenting that large amounts of newly-produced virions are introduced into the vascular compartment within a few hours of the drop in hepatitis C viremia caused by plasma exchange.**

Key words: **Doubling time; HCV, viremia; Plasma exchange.**

End Point

Fattibilità del protocollo
Safe procedura

Cinetica HCV-RNA nella FC

Risultati clinici a +3 mesi; +1 anno; +2 anni

Criteri di risposta al trattamento:
risposta completa (RC): HCV-RNA=0;
risposta parziale (RP): riduzione HCV-RNA>50%;
non responder (NR): riduzione HCV-RNA<50%.

FC & VIREMIA HCV: PROTOCOLLO B.A.

PAZIENTI HCV+ GENOTIPO I - NON RESPONDER A IFN + RIBAVIRINA

VIREMIA BASALE>100KUI/mL, PERSISTENZA TRANSAMINASI ELEVATE, HBsAg-, ASSENZA CONTROINDICAZIONI ALL'AFERESI TERAPEUTICA.

SEP. CELL. COBE SPECTRA – CIRCUITO TPE
FILTRAZIONE A CASCATA:
CARTUCCIA CASCADEFLO EC50W
50 ML PRO KG
1 PROCEDURA/7GIORNI/X 3
(VENERDÌ FC, SABATO IFN + RIBAVIRINA)
DETERMINAZIONE VIREMIA HCV PRE AFERESI DA SP
INDICE DI SOTTRAZIONE VIREMIA INTRA PROCEDURA INLET – OUTLET A 1.000/2.000/3.000 PLASMA FRAZIONATO

pazienti arruolati: 10
M/F 9/1
età 35-52 anni
HIV+ in 7 casi.

UPN pz	Iniziali	Età	HIV
1	FF	35	HIV-
2	VA	42	HIV+
3	CP	42	HIV+
4	PGL	44	HIV-
5	CC	45	HIV+
6	BM	45	HIV+
7	MD	52	HIV-
8	MM	46	HIV+
9	CP	45	HIV+
10	GD	44	HIV+

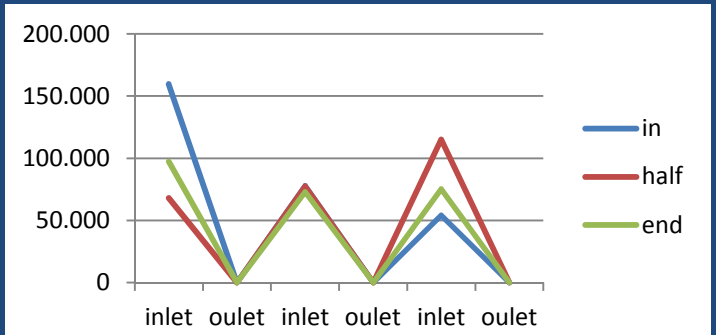
Reoferesi (FC)		Follow-up (fino a 1 anno)		
Timing	Studio cinetica HCV-RNA		mensile	trimestrale
1° FC: tempo 0	basale (pre-FC)	HCV-RNA	x	
2° FC: + 7 giorni	in corso di FC (50% del processato)	HIV-RNA	x	
3° FC: + 14 giorni	fine FC	CD4/mm3	x	
IFN a +24 ore dopo ogni FC		funzionalità epatica	x	
Ribavirina		funzionalità tiroidea		x
		autoimmunità		x

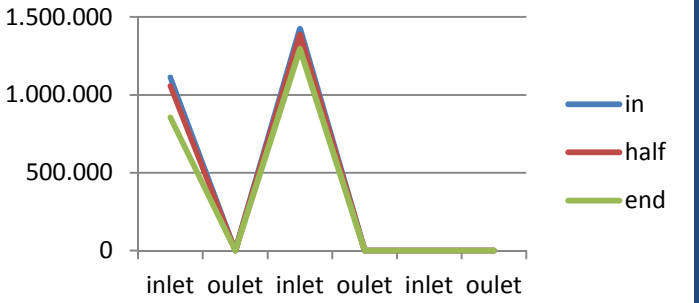
End Point

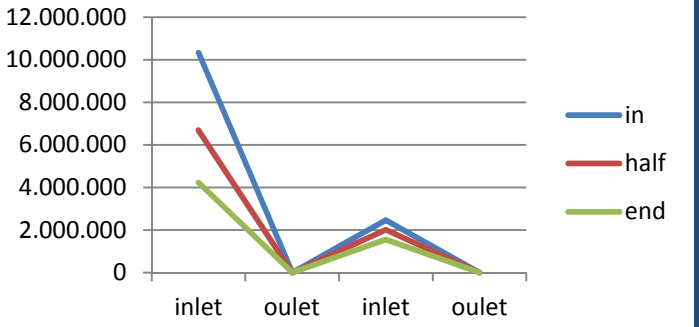
Tutti i soggetti hanno terminato il protocollo FC

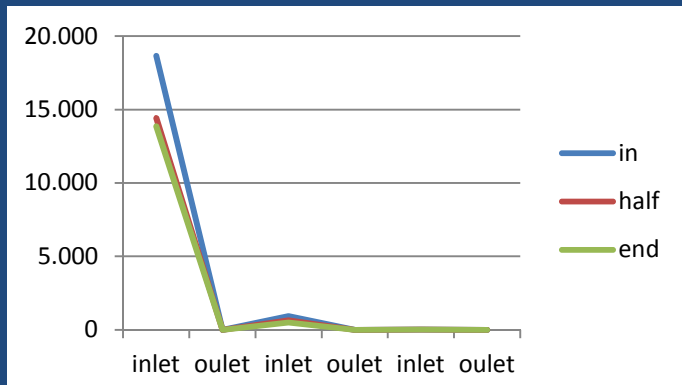
Safe: 1 episodio di ipotensione allo stacco

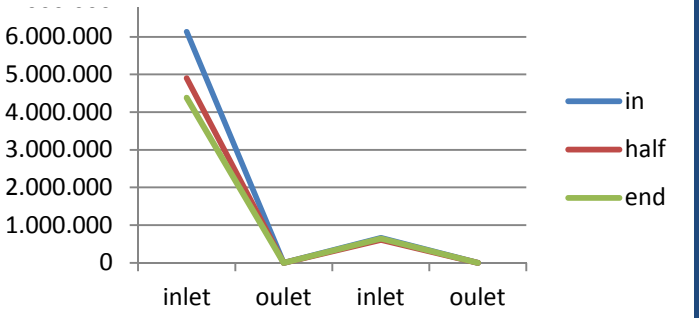
Cinetica HCV-RNA / FC
EC50W : DROP HCV viremia











End Point

una riduzione dell'entità della sintomatologia soggettiva da "IFN"

+3 mesi:

RC ottenuta in 4 casi

RP in 3

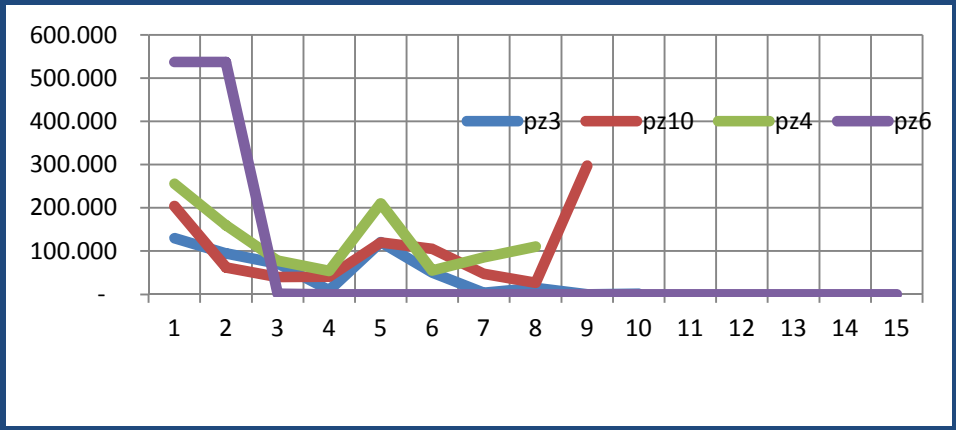
NR in 3 pazienti.

+12 mesi

RC confermata in 3 pazienti, ripresa della viremia con valori analoghi a quelli basali in 7 pazienti

+24 mesi

RC in 2/10 pazienti, con persistenza di viremia ad alta carica in 8/10 casi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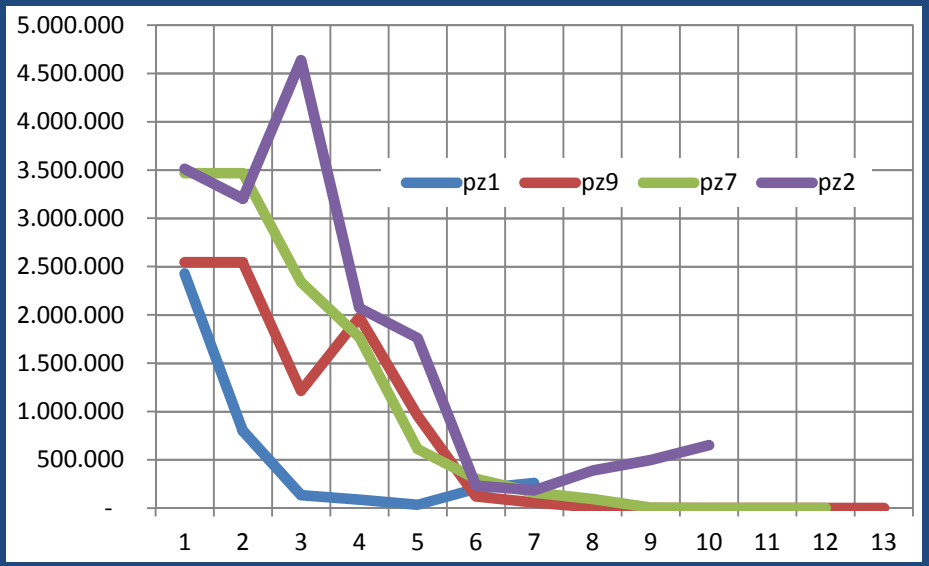
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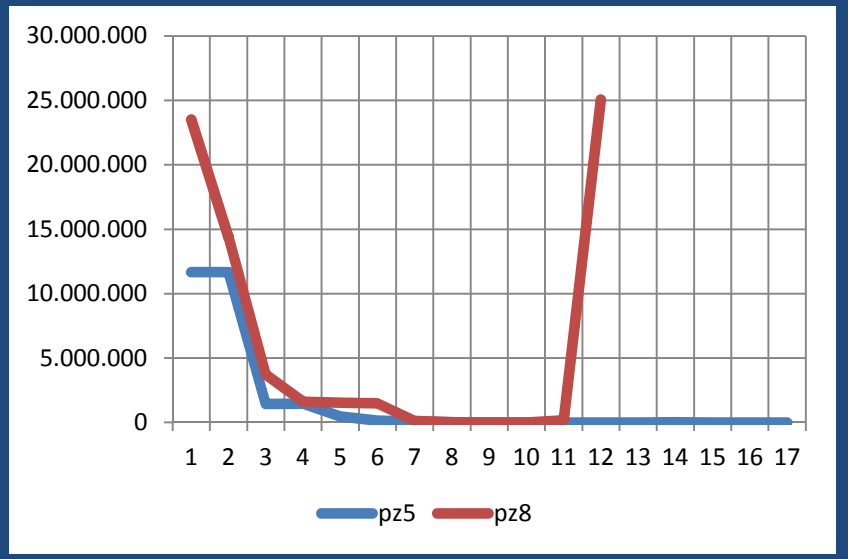
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REVIEW

Current topics on therapeutic apheresis

Ken Yamaji

In the case of IFN/Rib therapy, it is said that the complete response rate is high when the HCV RNA response occurs soon after start of treatment and that the efficacy of IFN therapy is low in cases with a high viral load. Therefore, the therapeutic effect of IFN therapy might be enhanced by lowering the viral load by means of concomitant DFPP. With respect to DFPP, replacement fluids

Double-filtration plasmapheresis (DFPP) for chronic hepatitis C

Since 20% of so-called refractory cases with genotype 1b chronic hepatitis C with a high viral load responded completely to 24-h concomitant therapy with interferon/ribavirin (IFN/Rib) therapy, 48-week concomitant therapy with peginterferon/ribavirin (PEG-IFN/Rib) therapy was approved in 2004. The complete response rate improved to about 50%, and it is now considered to be a standard therapy, but further improvement in therapeutic effect is being sought.

The hepatitis C virus (HCV) is said to have a particle diameter of 55–65 nm. Since physical removal is possible by means of double-filtration plasmapheresis (DFPP) using a secondary membrane with a pore size of 30 nm, clinical research was conducted at multiple institutions in hopes that the therapeutic effect would be improved by combining it with IFN/Rib therapy and PEG-IFN/Rib therapy [10]. It was found that the decrease in viral load and the virological response increased significantly with concomitant therapy with DFPP as compared with IFN/Rib or PEG-IFN/Rib monotherapy.

In the case of IFN/Rib therapy, it is said that the complete response rate is high when the HCV RNA response occurs soon after start of treatment and that the efficacy of IFN therapy is low in cases with a high viral load. Therefore, the therapeutic effect of IFN therapy might be enhanced by lowering the viral load by means of concomitant DFPP. With respect to DFPP, replacement fluids

Prospettive future

Boceprevir (Vitrelis) inibitore orale proteasi HCV

ECA HCV genotipo I associato a Peg IFN α e Ribavirina

Terapia 1° linea / terapia 2° linea in soggetti non responsivi