

# Efficacy of NaCl nebulized hypertonic solutions in cystic fibrosis

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**Abstract.** *Introduction:* CFTR deficiency produces poor water secretions. We studied the effects of nebulized hypertonic solution. *Methods:* 30 CF patients, each patient considered a control of himself, were followed to evaluate the therapeutic efficacy by spirometric indices. *Outcomes:* Results, statistically significant, indicate best results for small/medium airways. *Conclusion:* Nebulized hypertonic saline achieves the best results in heterozygous F508del, BCC negative, BMI > 5<sup>th</sup> ([www.actabiomedica.it](http://www.actabiomedica.it))

**Key words:** hypertonic saline, CFTR, inhalation therapy, cystic fibrosis

## Introduction

Mucociliary clearance is an important mechanism of defense of the airways from respiratory infectious agents and inhaled inerts. Homeostasis of epithelial secretions of exocrine glands is regulated by several transmembrane proteins like channels for sodium absorption (amiloride-sensitive) and chlorine secretion (CFTR) (1).

### *Therapeutic approach*

The discovery of the cystic fibrosis gene led to new therapies aimed at:

- 1) correction of genetic defect (using viral vectors);
- 2) closure of the sodium channel;
- 3) opening of an alternative Cl-channel;
- 4) repair of the CFTR protein defect;
- 5) aerosol moisturizers - hypertonic solutions.

### *Aerosolized hypertonic solutions*

Robinson's finding (2) about the effect of aerosolized hypertonic solution (in association with

Amiloride) raised the question about the efficacy of hypertonic solution used alone.

## Material and methods

At the Apulia Cystic Fibrosis Centre, we enrolled 30 patients with cystic fibrosis (17 females and 13 males) between 7 and 36 years of age (Tab. 1). Each patient was considered a control of himself. In the first part of the study, lung function was evaluated before administration of hypertonic solution (NaCl 6,75%). Therefore, the main spirometric indices (FEV<sub>1</sub>, FVC, PEF, MEF<sub>75</sub>, MEF<sub>50</sub>, MEF<sub>25</sub>, MMEF) were evaluated. Patients were monitored during the first year in order to evaluate therapeutic efficacy through chest examination and spirometric tests.

## Outcomes

The averages of the results after administration of aerosolic hypertonic solution for one year showed a slight decrease in FVC (2%), FEV<sub>1</sub> (1%) and MEF<sub>25</sub> (4%) and a significant increase in the MEF<sub>50</sub> (4%) and MEF<sub>75</sub> (5%). These differences are more evident for small and medium airways.

Table 1. Casistic

	1	2	3	4	5	6	7	8	9	10
SEX	F	M	M	M	F	M	M	F	F	M
AGE	15	22	10	16	23	18	11	35	11	32
DIAGNOSIS	2/4/1986	15/9/1980	17/7/1992	23/5/1990	18/2/1984	7/3/1983	3/11/1986	13/10/1994	23/4/1993	10/1/1986
GENETICS	ETER ΔF	ETER ΔF	ETER ΔF	ETER ΔF	ETER ΔF	ETER ΔF	ETER ΔF	NON ΔF	NON ΔF	OMO ΔF
PSEUDOMONAS	SI	SI	SI	SI	SI	SI	SI	SI	SI	SI
CEPACIA	SI	NO	NO	SI	SI	SI	SI	NO	SI	NO
START	7/10/1999	10/1/2000	29/9/2000	21/7/1999	16/11/1999	23/6/1999	22/4/1999	28/1/2000	9/9/1999	14/7/1999
1 YEAR BEFORE										
FVC	61%	105%	93%	73%	91%	59%	64%	87%	76%	29%
FEV1	50%	92%	90%	51%	79%	59%	55%	65%	66%	21%
PEF	72%	99%	81%	57%	59%	70%	49%	67%	55%	47%
MEF25	14%	66%	39%	14%	38%	36%	13%	24%	22%	7%
MEF50	25%	68%	73%	21%	64%	43%	30%	34%	32%	9%
MEF75	48%	80%	89%	31%	66%	63%	52%	51%	48%	22%
AUXOLOGY										
WEIGHT c	7,6	10,9	69,8	1,4	4,8	0	3,7	60,6	15,4	0,6
HEIGHT c	9,2	11,9	36,3	2,6	35,9	0	9,7	78,8	38,6	21,2
1 YEAR LATER										
FVC	64%	104%	106%	53%	86%	68%	45%	83%	48%	28%
FEV1	53%	104%	114%	39%	72%	57%	37%	65%	46%	20%
PEF	64%	91%	116%	51%	55%	72%	51%	65%	53%	46%
MEF25	19%	96%	78%	9%	31%	21%	9%	24%	31%	6%
MEF50	30%	88%	145%	15%	58%	32%	22%	40%	31%	8%
MEF75	42%	86%	127%	34%	58%	51%	52%	59%	40%	33%
AUXOLOGY										
WEIGHT c	10,8	12,9	50	0	7,8	0	0	39	5,7	0,9
HEIGHT c	22,7	11,9	25,5	0	35,9	0	1	78,8	24,2	23,6

Table 1. Casistic

	11	12	13	14	15	16	17	18	19	20
SEX	F	F	M	M	M	F	F	F	F	F
AGE	18	23	35	30	7	30	30	12	25	11
DIAGNOSIS	21/7/1993	13/7/1983	3/4/1978	2/9/1982	17/12/1997	2/9/1992	1/9/1989	10/6/1992	10/10/1987	29/1/1997
GENETICS	ETER ΔF	ETER ΔF	NON ΔF	OMO ΔF	NON ΔF	OMO ΔF	NON ΔF	OMO ΔF	NON ΔF	NON ΔF
PSEUDOMONAS	SI	SI	SI	SI	SI	SI	SI	SI	SI	SI
CEPACIA	NO	NO	NO	NO	NO	NO	NO	SI	NO	SI
START	18/1/2000	25/2/2000	8/2/2000	27/1/2000	13/9/2000	12/8/2000	24/3/2000	15/5/2000	26/2/2000	28/5/1999
1 YEAR BEFORE										
FVC	72%	77%	58%	59%	117%	63%	50%	72%	60%	77%
FEV1	73%	57%	25%	39%	123%	51%	34%	74%	49%	87%
PEF	73%	64%	21%	45%	82%	77%	26%	89%	46%	57%
MEF25	61%	18%	9%	12%	83%	19%	9%	39%	13%	85%
MEF50	78%	28%	8%	17%	105%	37%	14%	76%	27%	58%
MEF75	82%	40%	11%	26%	81%	60%	22%	95%	51%	56%
AUXOLOGY										
WEIGHT c	49,2	10,4	9,2	6,6	21,2	59,1	2,6	16,6	5,2	5,6
HEIGHT c	26,1	5,2	39,4	3,7	3,4	64,8	1,7	34,5	0,5	6,7
1 YEAR LATER										
FVC	86%	96%	70%	55%	115%	67%	53%	45%	57%	54%
FEV1	82%	85%	26%	36%	125%	54%	37%	44%	43%	56%
PEF	92%	90%	21%	43%	101%	62%	31%	51%	57%	50%
MEF25	45%	47%	7%	12%	87%	15%	9%	19%	12%	28%
MEF50	79%	65%	8%	16%	115%	32%	12%	37%	20%	41%
MEF75	100%	89%	10%	22%	108%	59%	24%	53%	38%	54%
AUXOLOGY										
WEIGHT c	52,8	11,3	12,3	3,8	33	34,1	12	3,2	8,9	0,4
HEIGHT c	17,1	5,2	42,5	5,2	2,4	70,9	2,1	11,1	0,7	1

Table 1. Casistic

	21	22	23	24	25	26	27	28	29	30	MEDIA
SEX	F	M	F	M	F	F	F	M	F	M	
AGE	23	15	20	17	14	36	18	15	33	24	21
DIAGNOSIS	4/9/1985	12/10/1988	1/3/1982	22/12/1994	6/9/1987	9/11/1999	1/4/1991	25/10/1986	6/4/1998	1/1/1978	
GENETICS	OMO ΔF	ETER ΔF	NON ΔF	ETER ΔF	ETER ΔF	ETER ΔF	NON ΔF	ETER ΔF	NON ΔF	OMO ΔF	
PSEUDOMONAS	SI	SI	SI	SI	SI	SI	SI	SI	SI	SI	
CEPACIA	SI	SI	NO	NO	SI	NO	NO	NO	NO	NO	
START	25/6/1999	11/10/2000	30/8/1999	6/6/2000	13/8/1999	26/10/2000	8/2/2000	23/8/1999	19/6/2000	23/5/2000	
1 YEAR BEFORE											
FVC	50%	58%	107%	83%	83%	70%	72%	74%	99%	67%	74%
FEV1	42%	39%	104%	73%	76%	58%	57%	62%	95%	38%	63%
PEF	67%	64%	119%	91%	88%	49%	78%	65%	81%	42%	66%
MEF25	11%	11%	57%	27%	20%	25%	20%	31%	85%	12%	31%
MEF50	28%	13%	100%	49%	68%	37%	26%	30%	72%	13%	43%
MEF75	68%	30%	123%	81%	91%	52%	46%	41%	87%	21%	57%
AUXOLOGY											
WEIGHT c	4,2	2,4	34,1	5,4	5	4,2	0,4	2,4	69,2	0,5	
HEIGHT c	2,5	2,9	17,1	8,5	5,6	19,2	0,4	16,9	21,8	18,9	
1 YEAR LATER											
FVC	52%	30%	108%	78%	98%	78%	84%	83%	104%	74%	72%
FEV1	42%	25%	105%	63%	87%	67%	60%	69%	99%	39%	62%
PEF	70%	51%	116%	69%	105%	71%	81%	63%	83%	52%	67%
MEF25	11%	7%	55%	23%	19%	32%	0%	21%	65%	12%	28%
MEF50	23%	12%	100%	41%	98%	52%	20%	36%	111%	12%	47%
MEF75	73%	42%	128%	67%	110%	72%	50%	55%	92%	22%	62%
AUXOLOGY											
WEIGHT c	1,9	0	31,6	12,9	4,5	6,3	0,1	0,3	73,6	0,3	
HEIGHT c	2,1	0,1	11,5	20,6	1,4	21,8	0,1	6,1	21,8	23,6	

For each spirometric index, Pearson's correlation coefficient ( $r$ ) was measured to establish the significance of the study with the following results:

Then the patients were divided into cohorts according to genetics and the results showed a slight but statistically significant improvement for F508del heterozygous patients with a mean age of 18 years against not-F508del patients with a mean age of 23 years. The slight worsening of F508del homozygous patients (Tab. 2) is related both to increased genotypic expression and to the mean age of these patients (25 years) which is different from F508del heterozygous (Tab. 3) and not-F508del (Tab. 4).

Table 2.

Spirometric index	r	p value
FVC	0,8242	<0,0001 (two tailed)
FEV <sub>1</sub>	0,8820	<0,0001 (two tailed)
MEF <sub>25</sub>	0,7580	<0,0001 (two tailed)
MEF <sub>50</sub>	0,8486	<0,0001 (two tailed)
MEF <sub>75</sub>	0,8436	<0,0001 (two tailed)

Moreover, patients were divided according to infection by Burkholderia cepacia. B.cepacia negative patients achieved a significant increase in all spirometric indices after administration of hypertonic solution (Tab. 5), although the mean age was 24 years against 15 years of B.cepacia positive patients (Tab. 6).

Another important result was obtained in seventeen patients with a better nutritional status (weight > 5th centile) and mean age of 23 years. These patients achieved an improvement of lung function with an increase in all spirometric parameters (Tab. 7), unlike the group of thirteen patients with body weight <5th percentile and a mean age of 18 who presented a worsening of these parameters (Tab. 8).

## Conclusion

The introduction of aerosolic hypertonic saline solution brought the best results in F508del heterozygous patients with B.cepacia and auxological development > 5th centile (Tab. 9). These data confirm the

Table 3. Genetic eterozygotes DF508

	1	2	3	4	5	6	7	11	12	22	24	25	26	28	MEDIA
SEX	F	M	M	M	F	M	M	F	F	M	M	F	F	M	
AGE	15	22	10	16	23	18	11	18	23	15	17	14	36	15	18
DIAGNOSIS	2/4/86	15/9/80	17/7/92	23/5/90	18/2/84	7/3/83	3/11/86	21/7/93	13/7/83	12/10/88	22/12/94	6/9/87	9/11/99	25/10/86	
GENETICS	ETER ΔF	ETER ΔF	ETER ΔF	ETER ΔF	ETER ΔF	ETER ΔF	ETER ΔF	ETER ΔF	ETER ΔF	ETER ΔF	ETER ΔF	ETER ΔF	ETER ΔF	ETER ΔF	
PSEUDOMONAS	SI	SI	SI	SI	SI	SI	SI	SI	SI	SI	SI	SI	SI	SI	
CEPACIA	SI	NO	NO	SI	SI	SI	SI	SI	NO	NO	SI	NO	SI	NO	
START	7/10/99	10/1/00	29/9/00	21/7/99	16/11/99	23/6/99	22/4/99	18/1/00	25/2/00	11/10/00	6/6/00	13/8/99	26/10/00	23/8/99	
<b>1 YEAR BEFORE</b>															
FVC	61%	105%	93%	73%	91%	59%	64%	72%	77%	58%	83%	83%	70%	74%	76%
FEV1	50%	92%	90%	51%	79%	59%	55%	73%	57%	39%	73%	76%	58%	62%	65%
PEF	72%	99%	81%	57%	59%	70%	49%	73%	64%	64%	91%	88%	49%	65%	70%
MEF25	14%	66%	39%	14%	38%	36%	13%	61%	18%	11%	27%	20%	25%	31%	30%
MEF50	25%	68%	73%	21%	64%	43%	30%	78%	28%	13%	49%	68%	37%	30%	45%
MEF75	48%	80%	89%	31%	66%	63%	52%	82%	40%	30%	81%	91%	52%	41%	60%
<b>AUXOLOGY</b>															
WEIGHT c	7,6	10,9	69,8	1,4	4,8	0	3,7	49,2	10,4	2,4	5,4	5	4,2	2,4	
HEIGHT c	9,2	11,9	36,3	2,6	35,9	0	9,7	26,1	5,2	2,9	8,5	5,6	19,2	16,9	
<b>1 YEAR LATER</b>															
FVC	64%	104%	106%	53%	86%	68%	45%	86%	96%	30%	78%	98%	78%	83%	77%
FEV1	53%	104%	114%	39%	72%	57%	37%	82%	85%	25%	63%	87%	67%	69%	68%
PEF	64%	91%	116%	51%	55%	72%	51%	92%	90%	51%	69%	105%	71%	63%	74%
MEF25	19%	96%	78%	9%	31%	21%	9%	45%	47%	7%	23%	19%	32%	21%	33%
MEF50	30%	88%	145%	15%	58%	32%	22%	79%	65%	12%	41%	98%	52%	36%	55%
MEF75	42%	86%	127%	34%	58%	51%	52%	100%	89%	42%	67%	110%	72%	55%	70%
<b>AUXOLOGY</b>															
WEIGHT c	10,8	12,9	50	0	7,8	0	0	52,8	11,3	0	12,9	4,5	6,3	0,3	
HEIGHT c	22,7	11,9	25,5	0	35,9	0	1	17,1	5,2	0,1	20,6	1,4	21,8	6,1	

Table 4. Genetic omozygotes DF508

	10	14	16	18	21	30	MEDIA
SEX	M	M	F	F	F	M	
AGE	32	30	30	12	23	24	25
DIAGNOSIS	10/1/86	2/9/82	2/9/92	10/6/92	4/9/85	1/1/78	
GENETICS	OMO ΔF	OMO ΔF	OMO ΔF	OMO ΔF	OMO ΔF	OMO ΔF	
PSEUDOMONAS	SI	SI	SI	SI	SI	SI	
CEPACIA	NO	NO	NO	SI	SI	NO	
START	14/7/99	27/1/00	12/8/00	15/5/00	25/6/99	23/5/00	
<b>1 YEAR BEFORE</b>							
FVC	29%	59%	63%	72%	50%	67%	57%
FEV1	21%	39%	51%	74%	42%	38%	44%
PEF	47%	45%	77%	89%	67%	42%	61%
MEF25	7%	12%	19%	39%	11%	12%	17%
MEF50	9%	17%	37%	76%	28%	13%	30%
MEF75	22%	26%	60%	95%	68%	21%	49%
<b>AUXOLOGY</b>							
WEIGHT c	0,6	6,6	59,1	16,6	4,2	0,5	
HEIGHT c	21,2	3,7	64,8	34,5	2,5	18,9	
<b>1 YEAR LATER</b>							
FVC	28%	55%	67%	45%	52%	74%	54%
FEV1	20%	36%	54%	44%	42%	39%	39%
PEF	46%	43%	62%	51%	70%	52%	54%
MEF25	6%	12%	15%	19%	11%	12%	13%
MEF50	8%	16%	32%	37%	23%	12%	21%
MEF75	33%	22%	59%	63%	73%	22%	44%
<b>AUXOLOGY</b>							
WEIGHT c	0,9	3,8	34,1	3,2	1,9	0,3	
HEIGHT c	23,6	5,2	70,9	11,1	2,1	23,6	

Table 5. Genetic not-DF508

	8	9	13	15	17	19	20	23	27	29	MEDIA
SEX	F	F	M	M	F	F	F	F	F	F	
AGE	35	11	35	7	30	25	11	20	18	33	23
DIAGNOSIS	13/10/94	23/4/93	3/4/78	17/12/97	1/9/89	10/10/87	29/1/97	1/3/82	1/4/91	6/4/98	
GENETICS	NON ΔF	NON ΔF	NON ΔF	NON ΔF	NON ΔF	NON ΔF	NON ΔF	NON ΔF	NON ΔF	NON ΔF	
PSEUDOMONAS	SI	SI	SI	SI	SI	SI	SI	SI	SI	SI	
CEPACIA	NO	SI	NO	NO	NO	NO	SI	NO	NO	NO	
START	28/1/00	9/9/99	8/2/00	13/9/00	24/3/00	26/2/00	28/5/99	30/6/99	8/2/00	19/6/00	
1 YEAR BEFORE											
FVC	87%	76%	58%	117%	50%	60%	77%	107%	72%	99%	80%
FEV1	65%	66%	26%	123%	34%	49%	87%	104%	67%	95%	71%
PEF	67%	55%	21%	82%	26%	46%	57%	119%	78%	81%	63%
MEF25	24%	22%	9%	83%	9%	13%	85%	67%	20%	85%	41%
MEF50	34%	32%	8%	105%	14%	27%	58%	100%	26%	72%	48%
MEF75	51%	48%	11%	81%	22%	51%	56%	123%	46%	87%	58%
AUXOLOGY											
WEIGHT c	60,6	15,4	9,2	21,2	2,6	5,2	5,6	34,1	0,4	69,2	
HEIGHT c	78,8	38,6	39,4	3,4	1,7	0,5	6,7	17,1	0,4	21,8	
1 YEAR LATER											
FVC	83%	48%	70%	115%	53%	57%	54%	106%	84%	104%	78%
FEV1	65%	46%	26%	125%	37%	43%	56%	105%	60%	99%	66%
PEF	65%	53%	21%	101%	31%	57%	50%	116%	81%	83%	66%
MEF25	24%	31%	7%	87%	9%	12%	28%	55%	0%	65%	32%
MEF50	40%	31%	8%	115%	12%	20%	41%	100%	20%	111%	50%
MEF75	59%	40%	10%	108%	24%	38%	54%	128%	60%	92%	60%
AUXOLOGY											
WEIGHT c	39	5,7	12,3	33	12	8,9	0,4	31,6	0,1	73,6	
HEIGHT c	78,8	24,2	42,5	2,4	2,1	0,7	1	11,5	0,1	21,8	

Table 6. Positive Burkholderia cepacia infection

	1	4	5	6	7	9	18	20	21	22	25	MEDIA
SEX	F	M	F	M	M	F	F	F	F	M	F	
AGE	15	16	23	18	11	11	12	11	23	15	14	15
DIAGNOSIS	2/4/86	23/5/90	18/2/84	7/3/83	3/11/86	23/4/93	10/6/92	29/1/97	4/9/85	12/10/88	6/9/87	
GENETICS	ETER ΔF	ETER ΔF	ETER ΔF	ETER ΔF	ETER ΔF	NON ΔF	OMO ΔF	NON ΔF	OMO ΔF	ETER ΔF	ETER ΔF	
PSEUDOMONAS	SI	SI	SI	SI	SI	SI	SI	SI	SI	SI	SI	
CEPACIA	SI	SI	SI	SI	SI	SI	SI	SI	SI	SI	SI	
START	7/10/99	21/7/99	16/11/99	23/6/99	22/4/99	9/9/99	15/5/00	28/5/99	25/6/99	11/10/00	13/8/99	
1 YEAR BEFORE												
FVC	51%	73%	91%	59%	64%	76%	72%	77%	50%	58%	83%	69%
FEV1	50%	51%	79%	59%	55%	66%	74%	87%	42%	39%	76%	62%
PEF	72%	57%	59%	70%	49%	55%	89%	57%	67%	64%	88%	66%
MEF25	14%	14%	38%	36%	13%	22%	39%	85%	11%	11%	20%	28%
MEF50	25%	21%	64%	43%	30%	32%	78%	58%	28%	13%	68%	42%
MEF75	48%	31%	66%	63%	52%	48%	95%	56%	68%	30%	91%	59%
AUXOLOGY												
WEIGHT c	7,6	1,4	4,8	0	3,7	15,4	16,6	5,6	4,2	2,4	5	
HEIGHT c	9,2	2,6	35,9	0	9,7	38,6	34,5	6,7	2,6	2,9	5,6	
1 YEAR LATER												
FVC	64%	53%	86%	68%	45%	48%	45%	54%	52%	30%	98%	58%
FEV1	53%	39%	72%	57%	37%	46%	44%	56%	42%	25%	87%	51%
PEF	64%	51%	55%	72%	51%	53%	51%	60%	70%	51%	105%	61%
MEF25	19%	9%	31%	21%	9%	31%	19%	28%	11%	7%	19%	19%
MEF50	30%	19%	58%	32%	22%	31%	37%	41%	23%	12%	98%	36%
MEF75	42%	34%	58%	51%	52%	40%	53%	54%	73%	42%	110%	55%
AUXOLOGY												
WEIGHT c	10,8	0	7,8	0	0	5,7	3,2	0,4	1,9	0	4,5	
HEIGHT c	22,7	0	35,9	0	1	24,2	11,1	1	2,1	0,1	1,4	

Table 7. Negative Burkholderia cepacia infection

	2	3	8	10	11	12	13	14	15	16	17	19	23	24	26	27	28	29	30	MEDIA
SEX	M	M	F	M	F	F	M	M	M	F	F	F	F	M	F	F	F	M	F	M
AGE	22	10	35	32	18	23	35	30	7	30	30	25	20	17	36	18	15	33	24	24
DIAGNOSIS	15/9/80	17/7/82	13/10/84	18/1/86	21/7/93	13/7/83	3/4/78	2/9/82	17/12/97	2/9/92	1/9/89	10/10/87	1/3/82	22/12/94	8/11/95	1/4/91	25/10/86	6/4/98	1/1/78	
GENETICS	ETER ΔF	ETER ΔF	NON ΔF	OMO ΔF	ETER ΔF	ETER ΔF	NON ΔF	OMO ΔF	NON ΔF	OMO ΔF	NON ΔF	NON ΔF	NON ΔF	ETER ΔF	ETER ΔF	NON ΔF	ETER ΔF	NON ΔF	OMO ΔF	
PSEUDOMONAS	SI	SI	SI	SI	SI	SI	SI	SI	SI	SI	SI	SI	SI	SI	SI	SI	SI	SI	SI	SI
CEPACIA	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO
START	10/1/80	29/9/80	28/1/85	14/7/99	18/1/80	25/2/80	8/2/80	27/1/80	13/9/80	12/8/80	24/3/80	26/2/80	20/6/99	6/6/80	26/10/80	8/2/80	23/8/99	19/6/80	23/5/80	
1 YEAR BEFORE																				
FVC	105%	93%	87%	29%	72%	77%	58%	59%	117%	82%	50%	60%	107%	83%	70%	72%	74%	99%	67%	76%
FEV1	92%	90%	65%	21%	73%	57%	25%	39%	123%	51%	34%	49%	104%	73%	58%	57%	82%	85%	38%	63%
PEF	99%	81%	67%	47%	73%	64%	21%	45%	82%	77%	26%	46%	119%	91%	49%	78%	65%	81%	42%	66%
MEF25	66%	39%	24%	7%	61%	18%	9%	12%	83%	19%	9%	13%	57%	27%	25%	20%	31%	85%	12%	32%
MEF50	68%	73%	34%	9%	78%	28%	8%	17%	105%	37%	14%	27%	100%	49%	37%	26%	38%	72%	13%	43%
MEF75	80%	89%	51%	22%	82%	69%	11%	26%	81%	60%	22%	51%	123%	81%	52%	46%	41%	87%	21%	56%
AUXOLOGY																				
WEIGHT c	10,9	89,8	60,8	0,8	49,2	10,4	9,2	6,8	21,2	59,1	2,8	5,2	34,1	5,4	4,2	0,4	2,4	89,2	0,5	
HEIGHT c	11,9	36,3	78,8	21,2	26,1	5,2	39,4	3,7	3,4	64,8	1,7	0,5	17,1	8,5	19,2	0,4	16,9	21,8	18,9	
1 YEAR LATER																				
FVC	104%	106%	83%	28%	86%	96%	70%	55%	115%	67%	53%	57%	100%	78%	78%	84%	83%	104%	74%	89%
FEV1	104%	114%	65%	20%	82%	85%	26%	36%	125%	54%	37%	43%	105%	63%	67%	80%	89%	99%	39%	68%
PEF	91%	116%	65%	46%	92%	90%	21%	43%	101%	82%	31%	57%	116%	69%	71%	81%	63%	83%	52%	71%
MEF25	96%	78%	24%	6%	45%	47%	7%	12%	87%	15%	9%	12%	55%	23%	32%	0%	21%	65%	12%	34%
MEF50	88%	145%	46%	8%	79%	65%	8%	16%	115%	32%	12%	26%	100%	41%	52%	30%	36%	111%	12%	52%
MEF75	88%	127%	59%	33%	100%	89%	10%	22%	109%	59%	24%	38%	128%	67%	72%	50%	55%	92%	22%	65%
AUXOLOGY																				
WEIGHT c	12,9	50	39	0,9	52,8	11,3	12,3	3,8	33	34,1	12	8,9	31,8	12,9	6,3	0,1	0,3	73,6	0,3	
HEIGHT c	11,9	25,5	78,8	23,8	17,1	5,2	42,5	5,2	2,4	78,9	2,1	0,7	11,5	20,6	21,8	0,1	6,1	21,8	23,6	

Table 8. Weigh < 5<sup>th</sup>

	4	6	7	10	14	18	20	21	22	25	27	28	30	MEDIA
SEX	M	M	M	M	M	F	F	F	M	F	F	M	M	
AGE	16	18	11	32	30	12	11	23	15	14	18	15	24	18
DIAGNOSIS	23/6/90	7/3/83	3/11/86	10/1/86	2/9/82	10/8/92	29/1/97	4/9/85	12/10/88	6/9/87	1/4/91	25/10/86	1/1/78	
GENETICS	ETER ΔF	ETER ΔF	ETER ΔF	OMO ΔF	OMO ΔF	OMO ΔF	NON ΔF	OMO ΔF	ETER ΔF	ETER ΔF	NON ΔF	ETER ΔF	OMO ΔF	
PSEUDOMONAS	SI	SI	SI	SI	SI	SI	SI	SI	SI	SI	SI	SI	SI	
CEPACIA	SI	SI	SI	NO	NO	SI	SI	SI	SI	SI	NO	NO	NO	
START	21/7/99	23/6/99	22/4/99	14/7/99	27/1/00	15/5/00	28/5/99	25/6/99	11/10/00	13/8/99	8/2/00	23/8/99	23/5/00	
1 YEAR BEFORE														
FVC	73%	59%	64%	29%	59%	72%	77%	50%	58%	83%	72%	74%	67%	64%
FEV1	61%	59%	55%	21%	39%	74%	87%	42%	39%	76%	67%	62%	38%	54%
PEF	67%	70%	49%	47%	45%	89%	67%	67%	64%	88%	78%	65%	42%	63%
MEF25	14%	36%	13%	7%	12%	39%	85%	11%	11%	20%	20%	31%	12%	24%
MEF50	21%	43%	30%	9%	17%	76%	58%	28%	13%	68%	26%	30%	13%	33%
MEF75	31%	63%	52%	22%	26%	95%	56%	68%	30%	91%	46%	41%	21%	49%
AUXOLOGY														
WEIGHT c	1,4	0	3,7	0,6	6,6	16,6	5,6	4,2	2,4	5	0,4	2,4	0,5	
HEIGHT c	2,6	0	9,7	21,2	3,7	34,5	6,7	2,5	2,9	5,6	0,4	16,9	18,9	
1 YEAR LATER														
FVC	53%	68%	45%	28%	55%	45%	54%	52%	30%	98%	84%	83%	74%	59%
FEV1	39%	57%	37%	20%	36%	44%	56%	42%	25%	87%	60%	69%	39%	47%
PEF	51%	72%	51%	46%	43%	51%	50%	70%	51%	105%	81%	63%	52%	60%
MEF25	9%	21%	9%	6%	12%	19%	28%	11%	7%	19%	0%	21%	12%	13%
MEF50	15%	32%	22%	8%	16%	37%	41%	23%	12%	98%	20%	36%	12%	29%
MEF75	34%	51%	52%	33%	22%	53%	54%	73%	42%	110%	50%	55%	22%	50%
AUXOLOGY														
WEIGHT c	0	0	0	0,9	3,8	3,2	0,4	1,9	0	4,5	0,1	0,3	0,3	
HEIGHT c	0	0	1	23,6	5,2	11,1	1	2,1	0,1	1,4	0,1	6,1	23,6	

Table 9. Weigh > 5<sup>h</sup>

	1	2	3	5	8	9	11	12	13	15	16	17	19	23	24	26	29	MEDIA
SEX	F	M	M	F	F	F	F	F	M	M	F	F	F	F	M	F	F	
AGE	15	22	10	23	35	11	18	23	35	7	30	30	25	20	17	36	33	23
DIAGNOSIS	2/4/86	15/3/80	17/7/92	18/2/84	13/10/94	23/4/93	21/7/93	13/7/83	3/4/78	17/12/97	2/9/92	1/9/89	10/10/87	1/3/82	22/12/94	9/11/99	6/4/98	
GENETICS	ETER AF	ETER AF	ETER AF	ETER AF	NON AF	NON AF	ETER AF	ETER AF	NON AF	NON AF	OMO AF	NON AF	NON AF	NON AF	ETER AF	ETER AF	NON AF	
PSEUDOMONAS	SI	SI	SI	SI	SI	SI	SI	SI	SI	SI	SI	SI	SI	SI	SI	SI	SI	SI
CEPACIA	SI	NO	NO	SI	NO	SI	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO
START	7/10/99	10/1/00	29/9/00	10/11/99	28/1/00	9/9/99	10/1/00	25/2/00	8/2/00	13/9/00	12/8/00	24/3/00	26/2/00	30/6/99	6/6/00	26/10/00	19/6/00	
1 YEAR BEFORE																		
FVC	61%	105%	93%	91%	82%	76%	72%	77%	58%	117%	63%	50%	60%	107%	83%	70%	99%	81%
FEV1	50%	92%	90%	79%	65%	66%	73%	57%	25%	123%	51%	34%	49%	104%	73%	58%	95%	70%
PEF	72%	99%	81%	58%	67%	55%	73%	64%	21%	82%	72%	26%	46%	119%	91%	49%	81%	68%
MEF25	14%	66%	39%	38%	24%	22%	61%	18%	9%	83%	19%	9%	13%	57%	27%	25%	85%	36%
MEF50	25%	68%	73%	64%	34%	32%	78%	28%	8%	105%	32%	14%	27%	100%	49%	37%	72%	50%
MEF75	48%	80%	89%	66%	51%	48%	82%	40%	11%	81%	60%	22%	51%	123%	81%	52%	87%	63%
AUXOLOGY																		
WEIGHT c	7,6	10,9	69,8	4,8	60,5	15,4	49,2	10,4	9,2	21,2	59,1	2,6	5,2	34,1	5,4	4,2	69,2	
HEIGHT c	9,2	11,9	36,3	35,9	78,8	38,6	26,1	5,2	39,4	3,4	64,8	1,7	0,5	17,1	8,5	19,2	21,8	
1 YEAR LATER																		
FVC	64%	104%	106%	86%	83%	48%	80%	90%	70%	115%	67%	53%	57%	100%	78%	78%	104%	83%
FEV1	53%	104%	114%	72%	65%	46%	82%	85%	26%	129%	54%	37%	43%	105%	63%	67%	99%	73%
PEF	64%	91%	116%	55%	65%	53%	52%	90%	21%	101%	62%	31%	57%	116%	69%	71%	83%	73%
MEF25	19%	96%	78%	31%	24%	31%	45%	47%	7%	87%	15%	9%	12%	55%	23%	32%	65%	40%
MEF50	30%	88%	145%	58%	40%	31%	79%	65%	8%	115%	32%	12%	20%	100%	41%	52%	111%	60%
MEF75	42%	86%	127%	58%	59%	40%	100%	89%	10%	108%	59%	24%	38%	128%	67%	72%	92%	71%
AUXOLOGY																		
WEIGHT c	10,8	12,9	50	7,8	39	5,7	52,8	11,3	12,3	33	34,1	12	8,9	31,6	12,9	6,3	73,6	
HEIGHT c	22,7	11,9	25,5	35,9	78,8	24,2	17,1	5,2	42,5	2,4	70,9	2,1	0,7	11,5	20,6	21,8	21,8	

Table 10. Positive response

	1	2	3	11	12	13	15	16	17	23	25	26	27	28	29	30	MEDIA
SEX	F	M	M	F	F	M	M	F	F	F	F	F	F	F	M	F	M
AGE	18	22	10	18	23	35	7	30	30	20	14	36	18	15	33	24	22
DIAGNOSIS	2/4/86	15/9/80	17/7/92	21/7/93	13/7/83	2/4/78	17/12/97	2/9/92	1/9/89	1/3/82	6/9/87	8/11/99	1/4/91	25/10/86	6/4/98	1/1/78	
GENETICS	ETER AF	ETER AF	ETER AF	ETER AF	ETER AF	NON AF	NON AF	OMO AF	NON AF	NON AF	NON AF	ETER AF	ETER AF	NON AF	ETER AF	NON AF	OMO AF
PSEUDOMONAS	SI	SI	SI	SI	SI	SI	SI	SI	SI	SI	SI	SI	SI	SI	SI	SI	SI
CEPACIA	SI	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	SI	NO	NO	NO	NO	NO
START	7/10/99	10/1/00	29/9/00	18/1/00	25/2/00	8/2/00	13/9/00	12/8/00	24/3/00	30/6/99	12/8/99	26/10/00	8/2/00	23/8/99	19/6/00	23/5/00	
1 YEAR BEFORE																	
FVC	61%	105%	93%	72%	77%	58%	117%	63%	50%	107%	83%	70%	72%	74%	99%	67%	79%
FEV1	50%	92%	90%	73%	67%	25%	123%	51%	34%	104%	78%	58%	57%	62%	95%	58%	68%
PEF	72%	99%	81%	73%	64%	21%	82%	77%	26%	119%	88%	49%	78%	65%	81%	42%	70%
MEF25	14%	66%	39%	61%	18%	9%	83%	19%	9%	87%	20%	25%	20%	31%	85%	12%	36%
MEF50	25%	68%	73%	78%	28%	8%	105%	37%	14%	100%	68%	37%	26%	30%	72%	13%	49%
MEF75	48%	80%	89%	82%	40%	11%	81%	60%	22%	123%	91%	52%	46%	41%	87%	21%	61%
AUXOLOGY																	
WEIGHT c	7,6	10,9	69,8	49,2	10,4	9,2	21,2	59,1	2,6	34,1	5	4,2	0,4	2,4	69,2	0,5	
HEIGHT c	9,2	11,9	36,3	26,1	5,2	39,4	3,4	64,8	1,7	17,1	5,6	19,2	0,4	16,9	21,8	18,9	
1 YEAR LATER																	
FVC	64%	104%	106%	86%	86%	70%	115%	67%	53%	108%	88%	78%	84%	83%	104%	74%	87%
FEV1	53%	104%	114%	82%	86%	26%	129%	54%	37%	105%	87%	67%	60%	69%	99%	39%	76%
PEF	64%	91%	116%	82%	90%	21%	101%	62%	31%	116%	103%	71%	81%	63%	83%	52%	77%
MEF25	19%	96%	78%	45%	47%	7%	87%	15%	9%	86%	19%	32%	0%	21%	65%	12%	38%
MEF50	30%	88%	145%	78%	66%	8%	115%	32%	12%	100%	98%	52%	20%	36%	111%	12%	63%
MEF75	42%	86%	127%	100%	89%	10%	108%	59%	24%	128%	110%	72%	60%	55%	82%	22%	73%
AUXOLOGY																	
WEIGHT c	10,8	12,9	50	52,8	11,3	12,3	33	34,1	12	31,6	4,6	6,3	0,1	0,3	73,6	0,3	
HEIGHT c	22,7	11,9	25,5	17,1	5,2	42,5	2,4	70,9	2,1	11,5	1,4	21,8	0,1	6,1	21,8	23,6	

multifactorial origin of Cystic Fibrosis and the difficulty in establishing the prognosis of these patients. Not only the genetic expression of the disease (Fig. 1), but also the possible infection with *B.cepacia* (Fig. 2) and nutritional status (Fig. 3) seem to play an important role in the prognosis of these patients and in the response to new therapies.

This study was completed in 2001 and since then the hypertonic saline has been used in our patients. Its administration is preceded by premedication with beta2 stimulants. The first dose is always performed during hospitalization and there have never been observed any side effects.

A few patients complained of a salty taste, which was corrected by decreasing NaCl concentration to 2.87%. Most patients prefer ultrasonic nebulizers because they need less time and they have the possibility to heat the mixture. This treatment is always well-tolerated for the proven effectiveness in reducing the time of expectoration.

In 2006, the Robinson group published an interesting case-control, double-blind study (3) using 7%

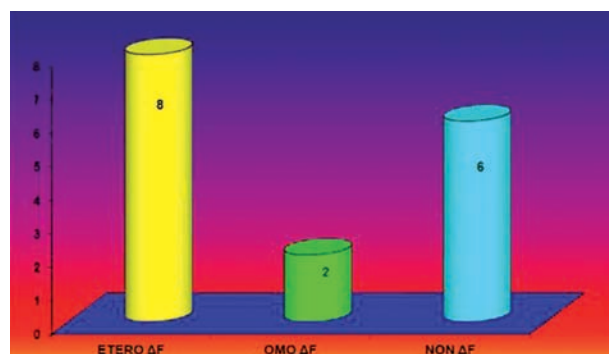


Figure 1. Positive response for genetic mutation

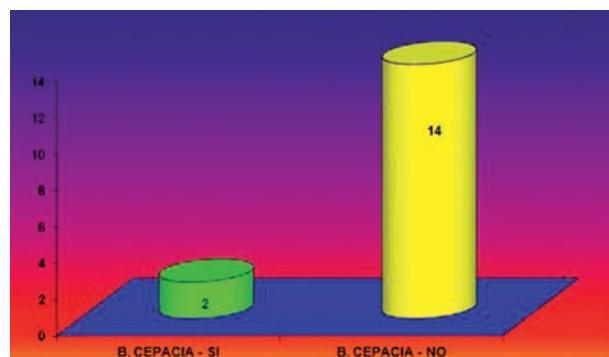


Figure 2. Positive response for Burkholderia cepacia infection

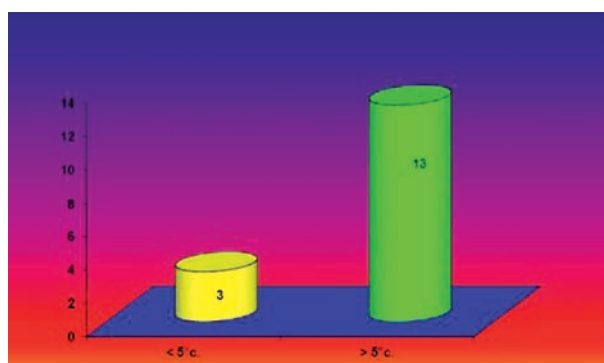


Figure 3. Positive response for weight

NaCl solution in the study group and 0.9% solution in the control group. The result was a greater increase in FEV1 and FCV for the group treated with hypertonic solution respectively of 3.2% and 2.8%. These differences were more significant for patients over 18 years of age. A decrease in number of exacerbations (0.39 vs. 0.89), days with exacerbation (6 vs 17) and an increase of days free from exacerbations (76% vs 62%) were also observed. Even considering only the symptoms, the outcome is still more favorable for the group treated with hypertonic solution. The days of antibiotic therapy were still lower in the study group (11 vs 50) as well as the days lost from school or work (7 vs 24). The incidence of side events was lower in the group treated with hypertonic solution (2.89 vs 5.17). There was not any difference in the number of new infections, except for coliforms that attack exclusively the control group, neither in the prevalence of *S. aureus* and *Ps. Aeruginosa*, while a highest concentration of *Ps. Aeruginosa* was found in the children of the study group under 18 years of age at week 4. No difference was found between the two groups in terms of concentrations of IL6, IL8, IL10 and TNF. The results are significant in terms of quality of life: fewer exacerbations, less care, fewer days lost, and lower costs. The benefits are due to the improvement of mucociliary clearance. On the other hand, the lack of differences in inflammatory activity between the two groups confirms the safety of hypertonic solution. Fewer exacerbations over a longer period will preserve the integrity of the respiratory system and the respiratory function.

Compliance of Apulian patients, after a 6-year follow-up, supports the evidence that the subjective



assessment of therapy agrees with the experimental results.

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