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Could emotional processing influence pain perception and quality of life in chronic kidney disease and hemodialyzed patients

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Abstract

Background and Objectives: The incidence of chronic pain is 11-24% in general population, whereas it affects 50% of hemodialyzed subjects and is often secondary to comorbidities, CKD-related complications and certain clinical procedures.
Consequently, a better approach in evaluating pain as a "symptom" and in managing it adequately is required for these patients.

Methods: 33% of the 300 patients enrolled properly consigned the questionnaires.
The mean age of dialyzed patients was 52.2±11.2 years, whereas 54.9±10.7 years was the mean age for CKD patients. Moreover, 53 healthy subjects, ages 20-65, have been included in the study as control group.
Specific psycho-diagnostic tests were administered: EPI, ASQ, SF-36, REM-71, TAS-20, SCL-90.

Results: We have observed that the mean values of quality of life and pain assessment tests for HD and CKD patients were lower than the control group on every dimension. Moreover, comparing the two nephropatic populations, HD patients were characterized by statistically significant lower values than CKD subjects, both for mental and physical dimensions.
The SF36 human body graph highlighted that 17 out of 49 CKD patients suffered from severe pain, but only 3 of them were treated with analgesics (paracetamol and metamizole). In HD group, 38 patients reported severe pain and 30 of them were treated with analgesic drugs.

Conclusions: Our data underlined that an introverted-psychotic personality trait, associated to an insecure and avoidant attachment style, closely and positively related to primitive defensive mechanisms, determined in nephropatic patients alterations of emotional processes of pain perception which is probably exacerbated by the worsening of the alexithymic status.
For these reasons, the monitoring of expressive modalities of emotions must be performed regularly in both CKD and HD patients, through periodic administration of questionnaires and psychological support.

Keywords: pain, hemodialysis, chronic kidney disease, alexithymia, dialysis, defense mechanisms

Introduction

CKD prevalence is evaluated between 11 and 13% worldwide, whereas, in Italy, it was estimated around 9.3% in adults (11.93% in female and 6.49% in male). According to these data, projecting prevalence figures over the entire adult Italian population, CKD should affect more than 4.4 million subjects, whereas 55.000 patients should require renal replacement therapies [1].

As a result of the continuous growth of the nephropatic population, increased attention has been focused on pain management. Despite its high impact on quality of life, pain is undertreated in 75% of hemodialyzed and CKD subjects, probably due to the lack of information about symptoms [2].

The incidence of chronic pain is 11-24% in the general population, whereas it affects 50% of hemodialyzed subjects [1]. In particular, chronic pain could be secondary to comorbidities (uremic osteodystrophy, peripheral polyneuropathy, carpal tunnel syndrome, peripheral vascular disease, ischemic myocardial disease, gout, polycystic disease, lithiasic disease, pyelonephritis, calciphylaxis, cancer) and CKD-related complications [1]. Furthermore, in patients undergoing hemodialysis, pain could be associated to specific procedures (venopuncture, worsening of arthrosis pain due to long immobility during HD session, headache, cramps, central vein catheter related infections, amyloidosis) [1]. Consequently, a better approach in evaluating pain as a symptom and managing it is required for these patients [3].

The Joint Commission on Accreditation of Healthcare Organizations (JCAHO) and the American Pain Society (APS) consider, in fact, pain as the fifth vital sign and recommend to measure its intensity in all patients, in addition to blood pressure, heart rate, respiratory rate and body temperature

evaluation [3].

Furthermore, it is well known that pain is closely related to physical and mental issues, thus having significant biological, psychological and social causes and consequences [4, 5, 6].

In order to expand the potential targets of pain treatment and therefore to minimize the prevalence of its negative impacts, bio-psycho-social factors, that are most consistently associated with pain and pain-related outcomes, should be identified.

A potential factor that may contribute to the development and maintenance of chronic pain is alexithymia [7, 8, 9]. This condition, whose name derives from Greek and literally means "a lack of words for feelings", describes a personality trait associated with an inability to regulate negative affection. It represents a disturbance of both cognitive and affective functioning, characterized by difficulty in recognizing or describing one's emotions [10].

It was demonstrated that alexithymia is positively associated with pain intensity and interference, and negatively associated with vitality in a sample of individuals with neuromuscular disease and chronic pain [9, 11]. Moreover, the effects of alexithymia on pain may be mediated by negative affect and the TAS-20 DIF scale score has been identified as the most consistent factor associated with chronic pain and pain-related dysfunction [11, 12].

The aim of our study was to evaluate, in nephropatic populations, whether pain perception is related to clinical symptoms alone, or it is caused and/or worsened by alexithymia. The latter, influenced by several factors, was related to attachment styles, defense mechanisms and dysfunctional traits.

Materials and Methods

Study Cohort

300 patients were enrolled and 100 of them (33%) properly consigned the questionnaires.

In particular, 55 (34%) patients on hemodialysis completed the tests correctly, whereas the remaining patients (105 subjects, 66%) did not fill in entirely the questionnaires or missing data were found. A similar rate was achieved in the CKD group (49 patients, 35%).

The mean age of dialyzed patients was 52.2±11.2 years, whereas 54.9±10.7 years was the mean age assessed in CKD patients.

Among CKD patients, disease staging breakdown was as follows: stage II (7 subjects), stage III (24 patients), stage IV (14 subjects). No distinctions were made by gender.

Moreover, 53 healthy subjects, aged 20-65 years, have been included in the study as control group.

The baseline characteristic of the studied population was reported in Table 1.

Psycho-diagnostic testing and definitions

Specific psycho-diagnostic tests were administered:

The Eysenck Personality Inventory (EPI) analyzes three potential personality traits: 1) extraversion (tending to enjoy human interactions, with optimism and emotional involvement); 2) neuroticism (tending to instability and turmoil); 3) psychoticism (revealing a minimal interest in interpersonal relationships: a concept linked more to schizoid than "psychotic" status) [13].

The Attachment Style Questionnaire (ASQ) is a tool highlighting and measuring attachment styles in interpersonal relationships and addresses: "Confidence", "Discomfort with closeness"; "Need for approval"; "Preoccupation with relationships"; "Relationships as secondary" [14].

The Response Evaluation Measure (REM-71) is a self-report, 71-item questionnaire for the assessment of 21 defensive mechanisms which structure personality in managing psychological processes of introspection and external relationships. This test is mainly based on 2 factors: F1 (constituted of 14 defenses which distort reality) and F2 (including other 7 defensive mechanisms, adapted to reality) [15].

The 20-Items Toronto Alexithymia scale (TAS-20) represents the most psychometrically valid measurement of alexithymia and is composed of 20 items divided in three main areas which analyze: (F1) difficulty identifying feelings and distinguishing between feelings and the bodily sensations of emotional arousal; (F2) difficulty describing feelings to others; (F3) externally-oriented thinking [12].

The Symptom Check list (SCL)-90 is a self-report test tool assessing psychological symptom status of individuals from "healthy controls" to "disordered ones". Moreover, negative effects are measured with the depression and anxiety scales of this test. Different areas allow to evaluate: Somatization; Obsessive–compulsive disorder; Interpersonal Sensitivity; Depression; Anxiety; Hostility; Phobic anxiety; Paranoid ideation; Psychoticism [16].

The Short Form (SF) -36 Health Survey is a validated self-administered questionnaire evaluating quality of life (QoL) that is both brief and precise. The test is based on the consideration that the subject is a reliable source of data and provides a unique point of view which could not be collected in other ways and is complementary in many areas to the clinical perspective [7].

A pharmacological anamnesis about analgesic drugs was also made. Age, sex, marital status, educational level are factors that could potentially influence pain and were therefore assessed and controlled in all analyses.

The study was approved by the institutional review board and the local Ethics Committee. All patients gave written informed consent.

Statistical Analysis

Statistical analyses were performed with NCSS for Windows (version 4.0) and the MedCalc (version 11.0; MedCalc Software Acacialaan, Ostend, Belgium) software. Data were presented as mean ± SD for normally distributed values. Differences between groups were established by unpaired t test or by ANOVA followed by Bonferroni's test for normally distributed values and by Kruskal-Wallis analysis followed by Dunn's test for nonparametric values. Two-sided values of $p<0.05$ were considered significant in all analyses.

Results

HD patient profile

HD patients were characterized by an ambivalent- anxious attachment style, as revealed by ASQ test, with a deep discomfort for relational intimacy and difficulties in identifying feelings, in describing them to others and in

analyzing other's feelings, as emerged by TAS-20. Figure 1A, Figure 2.

Immature thoughts and maladaptive defense mechanisms were prevalent (Factor 1), as expressed by a great use of acting out, scission, dissociation, passive aggressive behavior, repression, reaction formation, conversion and autistic retirement, and measured by the REM test. In the control group, more "mature" defense mechanisms were observed. Figure 3.

Moreover, EPI test revealed a higher prevalence of psychotic personality in dialyzed patients when compared to CKD and Healthy Subjects (HS) (15.8±7.3 vs 5.1±2.6; $p < 0.0001$), associated to exaggerated expression of emotions and self-dramatization, probably due to the progression of the chronic disease. Figure 1B.

These data are also confirmed by SCL-90 test, which highlighted the tendency of this cohort of patients to develop obsessive thoughts, passive aggression, social isolation and autistic behaviour. Figure 4.

CKD patient profile

As detected in HD patients, CKD subjects were affected by an ambivalent-anxious attachment style, but associated to a greater, as compared to HD subjects, discomfort for relational intimacy and difficulties in identifying feelings, in describing them to others and in analyzing own feelings. Moreover, a prevalence of F3 component (externally-oriented thinking) was assessed, linked to a poor tendency towards introspection, with a consequent disaffection against internal emotional mechanisms. Figure 2.

Less mature defensive mechanisms were observed in CKD patients than in the healthy control group, based on prevalent immature thoughts and a dominant factor 1 over factor 2 of REM test, by using acting out, scission, dissociation, passive aggressiveness, repression and reactive formation. These conditions were less present in CKD than in HD patients, but more expressed than in the healthy group. Figure 3.

EPI results highlighted a prevalent tendency toward psychoticism, whereas SCL-90 data assessed obsessive thinking, passive aggressiveness and behaviors based on social retirement, autism and isolation. Figure 1B, Figure 4.

Quality of life and pain assessment

The mean scores for each SF36 dimension and the differences between each treatment group for all enrolled patients are shown in Figure 4.

We have revealed that the mean scores for HD and CKD patients were lower than the control group on every dimension. Moreover, comparing the two nephropatic populations, HD patients were characterized by statistically significant lower values than CKD subjects, both for mental and physical dimensions.

Moreover, analyzing the body pain subscale of the SF-36 test, no differences were assessed between dialyzed and healthy subjects (-2.1±12.7 vs - 4.3±16; p:0.42), whereas CKD patients were characterized by higher values when compared to HD (25.1±31.2 vs -2.1±12.7; $p < 0.0001$) and HS (25.1±31.2 vs - 4.3±16; $p < 0.0001$).

The SF36 human body graph highlighted that 17 out of 49 CKD patients suffered from severe pain, but only 3 of them were treated with analgesics (paracetamol and metamizole). In the HD group, 38 patients reported severe pain and 30 of them were treated with analgesic drugs. In particular, paracetamol was administered to 10 patients, whereas non steroidal anti-inflammatory drugs (NSAIDs), such as nimesulide, ketorolac or diclofenac were prescribed in 7 patients. Only 1 patient was treated with Tramadol. 13 subjects reported a not well defined analgesic therapy, whereas 1 patient treated his pain through physiotherapy sessions. These patients were characterized by the lowest SF36 values, highlighting a poor quality of life.

These data can be associated with the greater anxiety CKD patients may feel for a further progression of renal disease, whereas in HD patients the main problem could be related to dialytic treatment issues.

Alexithymia

TAS-20 data highlighted higher scores in HD than CKD patients, in all three factors identifying alexithymia and demonstrating that alexithymia construct appeared to be a very frequent personality trait in patients treated with dialysis. Figure 2.

The results obtained for TAS-20 in hemodialyzed patients were as follows: 35 subjects (64%) showed alexithymia, 12 (22%) possible alexithymia, while 8 patients (14%) were not alexithymic.

Among CKD population, alexithymia was detected in 14 subjects (29%), whereas borderline profiles and negative results have been assessed in 16 (32%) and 19 (39%) patients, respectively. Figure 2.

In particular, the F1 component, assessing difficulties in identifying feelings, was higher in HD than HS (16.4 ± 6.8 vs 13.3 ± 5.7, p: 0.01), whereas no differences have been found between HD and CKD patients (16.4 ± 6.8 vs 15.4 ± 6.7, p: 0.43) and CKD and healthy subjects (15.4 ± 6.7 vs 13.3 ± 5.7, p: 0.09). Analyzing factor 2, evaluating difficulties to describe other people's feeling, we observed the highest scores in HD group (16.6 ± 4), greater than those revealed both in CKD patients and HS (13.2 ± 4.3, p: 0.0001; 13.9± 3.9, p: 0.0007, respectively).

Interestingly, we have assessed that CKD patients were characterized by lower values than HS, but without reaching a statistically significant difference (p: 0.38).

Similarly, HD patients presented higher levels of factor 3 (30.3 ± 4.8) than CKD (24.5± 6.7, p: 0.0007) and HS (22.2 ± 6.6, $p < 0.0001$), demonstrating higher tendency for external thoughts, associated to a minimal consideration of own pain, than those observed in the CKD group.

Only in this component of TAS-20, we have found a difference between the HD and CKD groups. Table 2.

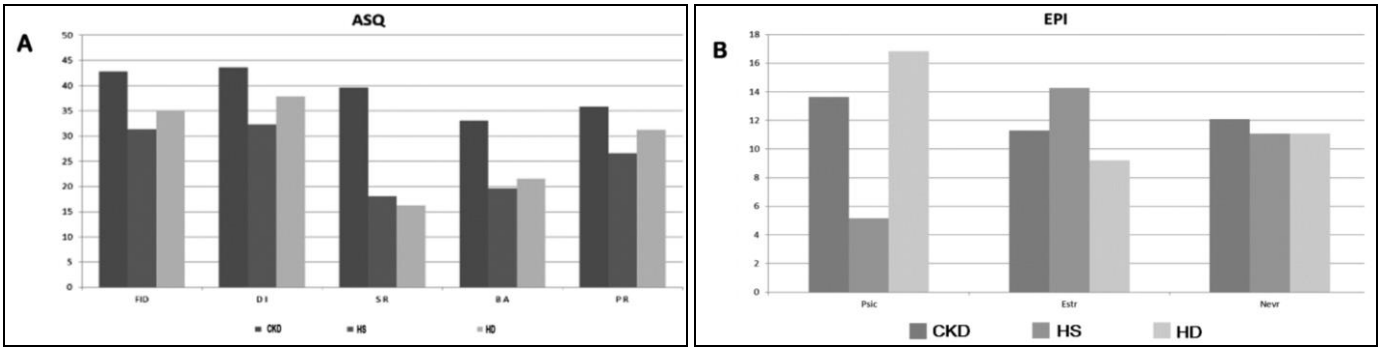

Fig 1: ASQ and EPI test in chronic kidney disease patients, healthy subjects and hemodialyzed patients. FID, Confidence; DI, Discomfort with closeness; SR, Relationship as secondary; BA, Need for Approval; PR, Preoccupation with Relationship; Psic, Psychoticism; Estr, Extraversion ; Nevr, Neuroticism

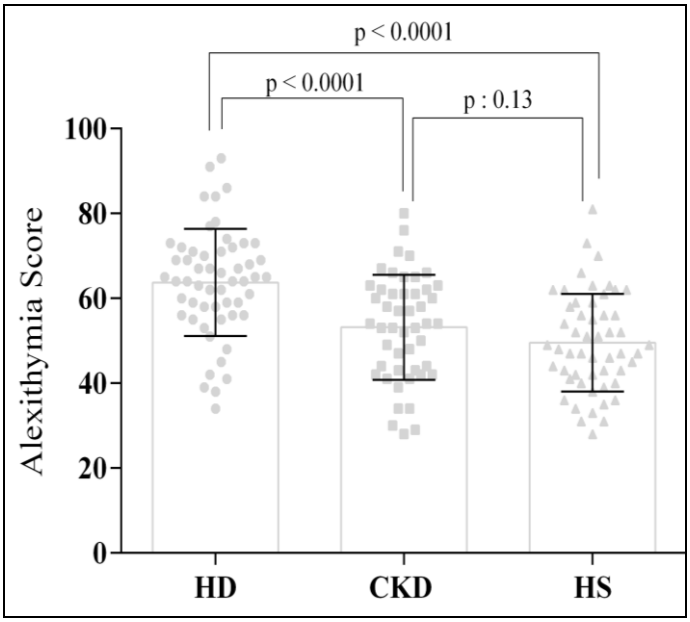

Fig 2: TAS-20 Results

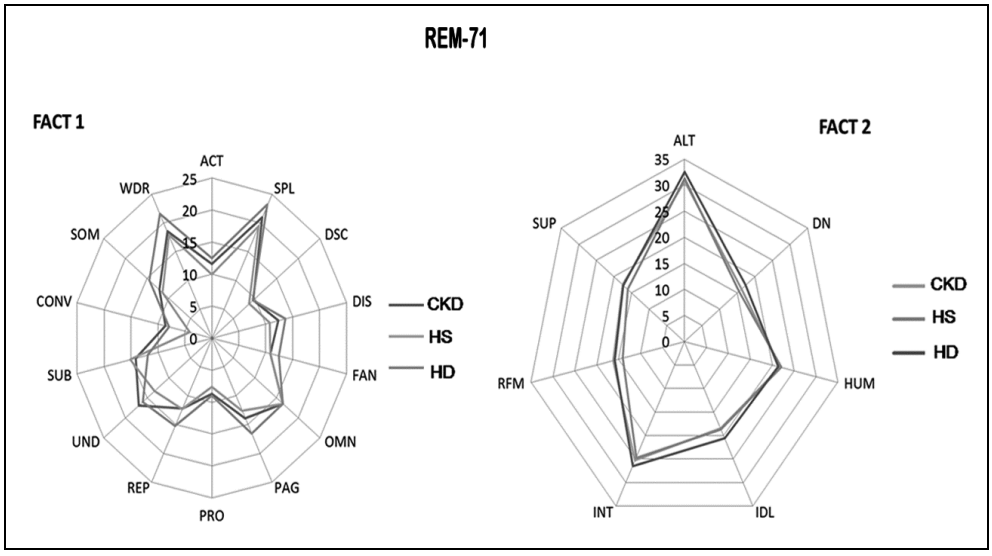

Fig 3: REM 71 results. FACT 1, immature defense mechanisms; FACT 2, mature defense mechanisms. ACT, Acting out; ALT, Altruism; CONV, Conversion; DIS, Displacement; DN, Denial; DSC, Dissociation; FAN, Fantasy; HUM, Humor; IDL, Idealization; INT, Intellectualization; OMN, Omnipotence; PAG, Passive Aggression; PRO, Projection; REP, Repression; RFM, Reaction Formation; SOM, Somatization ; SPL, Splitting; SUB, Sublimation; SUP, Suppression; UND, Undoing; WDR, Withdrawal

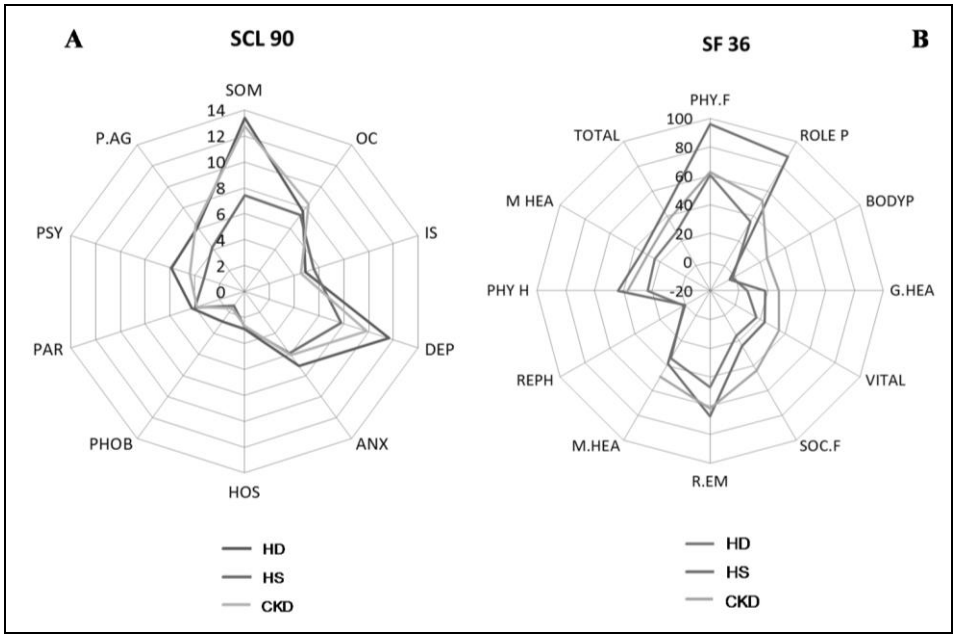

Fig 4: SCL 90 and SF36 scores. ANX, Anxiety ; BODY P, Bodily Pain; DEP, Depression; G.HEA, General Health; HOS, Hostility; IS, Social Issues; M.HEA, Mental Health; M HEA, Mental Health; OC, Obsessive Compulsive; P.AG, Passive Aggressive; PAR, Paranoid Ideation; PHOB, Phobic Anxiety ; PHY F, Physical Functioning; PHY H, Physical Health; PSY, Psychoticism; R.EM, Role- emotional; REPH, Reported Health; ROLE P, Role Physical; SOC.F, Social Functioning; SOM, Somatization; VITAL, Vitality.

Table 1: Baseline demographic, clinical and laboratory data of the patient population. ADPKD, Autosomal Dominant Polycystic kidney disease; AVF, Arteriovenous Fistula; CKD, Chronic Kidney Patients; HD, Hemodialysis; GN, Glomerulonephritis; Others, other causes of renal disease included cancer, gout, abuse of drugs, nephrolithiasis;

	CKD patients (n:49)	**HD patients (n:55)**
Gender, male	28	38
Mean Age, years	54.9±10.7	52.2±11.2
Marital status, n	41	46
Schooling		
None, n(%)	5 (10)	14 (25)
Elementary School	17 (35)	12 (22)
Secondary School	8 (16)	19 (35)
High School	12 (25)	8 (14)
University	7 (14)	2 (4)
Renal disease etiology		
Nephroangiosclerosis	18 (37)	16 (29)
Diabetes mellitus	8 (16)	9 (16)
ADPKD	12 (25)	9 (16)
GN	4 (8)	8 (14)
Others	7 (14)	13 (25)
Pain severity		
Absent	3 (6)	2 (4)
Soft	3 (6)	4 (7)
Mild	9 (18)	2 (4)
Moderate	17 (35)	9 (16)
Severe	17 (35)	24 (44)
Worst	0	14 (25)
Pain location		
Head	18 (37)	29 (53)
Vertebral column	34 (69)	24 (44)
Muscles	30 (61)	13 (24)
Thorax	9 (26)	12 (22)
Superior Arm (AVF)	-	13 (24)
Inferior Arm	-	14 (25)
Analgesic therapy	3 (6)	30 (55)

Table 2: TAS sub-scale and total scores distribution of the study population. Data are presented as mean ± standard deviation. TAS, Toronto alexithymia scale; DIF, Difficulty Identifying Feelings; DDF, Difficulty Describing Feelings; EOT, Externally Oriented Thinking.

Alexithymia subgroups	HD (n:55)	CKD (n:49)	HS (n:53)
Total	63.7±12.6	63.7±12.3	63.7±11.5
DIF (F1)	16.4±6.8[a]	15.4±6.6[ns]	13.3±5.7[ns]
DDF (F2)	16.6±4[b,c]	13.2±4.3[ns]	13.9±3.9
EOT (F3)	30.3±4.8[d,e]	24.5±6.7[ns]	22.2±6.6

F1: [a] HD vs HS p: 0.01; [ns] HD vs CKD p > 0.05; [ns] CKD vs HS p > 0.05
F2: [b] HD vs HS p: 0.007; [c] HD vs CKD p: 0.0001; [ns] CKD vs HS p > 0.05
F2: [d] HD vs HS p: < 0.0001; [e] HD vs CKD p: 0.0001; [ns] CKD vs HS p > 0.05

Univariate Correlation

In HD patients, TAS-20 values were negatively related to EPI test, exclusively with nevrotic component (0.01; r: - 0.33). In particular, the subclasses F1 (0.04; r: - 0.27; R^2: .07) and F2 (0.04; r: - 0.27; R^2: .07) determined the correlation both explaining the 10% variance.

An important difference was noted for CKD group, in which a relation between alexithymia and EPI was confirmed, but only with the psychotic component and the F3 element of TAS test (p<0.0001; r: - 0.63; R^2: .40)

A close and inverse relation has been detected in the CKD group among ASQ and TAS-20, whereas no correlations have been found in HD patients.

In particular, TAS-20 F3 was related to the ASQ "Relationships as secondary" component (p> 0.0001; r: - 0.43) and the coefficient of determination shows that 20% of the variance of one of the variables is explained by the variation values of the other variable.

No correlations have been found between alexithymia scale and SCL-90 parameters, including depression and anxiety subunits, both in CKD and dialyzed patients.

On the contrary, TAS 20 was found inversely related to SF-36 (r: - 0.20; p:0.02) in HD patients.

In particular, F1 component was responsible of the most correlations found (TAS 20 F1 vs SF-36 G.HEA r: - 0.43; p:0.0009; TAS 20 F1 vs SF-36 R. EM r: - 0.37; p:0.004; TAS 20 F1 vs SF-36 Role P r: - 0.30; p:0.02; TAS 20 F1 vs SF-36 M.HEA r: - 0.28; p:0.03; TAS 20 F1 vs SF-36 M HEA r: - 0.48; p:0.0002; TAS 20 F1 vs SF-36 PHY.H r: - 0.30; p:0.02; TAS 20 F1 vs SF-36 SOC.F r: - 0.33; p:0.01; TAS 20 F1 vs SF-36 TOT r: - 0.41; p:0.001), whereas no relations have been assessed when the subscales F2 and F3 were inserted in the model.

Analyzing CKD population, an inverse relationship has been found between TAS-20 and SF-36 G.HEA (r: - 0.47; p:0.0008), SF-36 VITAL (r: - 0.42; p:0.003), SF-36 M.HEA (r: - 0.52; p:0.0002) and SF-36 SOC.F (r: - 0.29; p:0.04).

According to subgroup analysis, F1 was related to SF-36 PHY.F (r: - 0.39; p:0.006), SF-36 R. EM (r: - 0.52; p:0.0002), SF-36 Role P (r: - 0.34; p:0.01), SF-36 VITAL (r: - 0.42; 31p:0.03), SF-36 M.HEA (r: - 0.42; p:0.002).

Discussion

We have clearly demonstrated the necessity to better evaluate pain in the nephropatic population and strive for an adequate management of analgesic therapies.

We have also underlined the importance of assessing physical symptoms, in order to link them to specific pathological processes or psychopathological conditions, such as alexithymia.

Pain characterized all patients with end stage renal disease enrolled in the study, as confirmed by other reports highlighting that almost 50% of HD patients reports pain [5].

Osteoarticular lesions represented the main cause of pain in these patients, principally due to an impaired calcium-phosphorus metabolism, often independently of advanced age, as observed in our cohort who was constituted by a relative low number of elderly patients. The dialysis technique could be another source of pain, often linked to arteriovenous fistula creation and puncture.

Several studies assessed that the severity of symptoms, such as tiredness, itching, thirst, articular pain and sleep disorders, was positively related to anxiety and/or depression levels. In fact, in HD patients, somatic symptoms are closely associated with anxiety and depression, influencing the self-perceived healthy status [17, 5]. Moreover, it was demonstrated that depression plays a pivotal role in the inter-dialytic weight gain, affecting quality of life of HD patients [18].

Takaki revealed that itching HD patients with low self-efficacy will be more depressive and anxious than non-itching patients, whereas itching patients who report a high degree of emotion-oriented coping will be more anxious than non-itching patients [18].

It is clear that the evaluation of psychiatric status must be included in the clinical management of HD patients, with the goal of developing specific and focused interventions.

Analyzing data obtained from TAS-20, we revealed that alexithymia is more pronounced in advanced renal disease patients, secondary to a greater involvement of psyche of subjects affected by chronic and progressive physical disease, and impacting on the affective sphere and emotional processing.

We detected, in fact, an affective slipping, ranging from primary difficulties in feeling identification, which, in CKD patients, are associated with issues with describing others' feelings and external thinking, to a progressive negative processing, associated with somatic depletion which, consequently, complicated the alexithymic status.

In HD patients, three dialysis sessions a week cause severe prostration, creating a progressively worsening outlook influencing emotional processing which is also involved and directing it toward negative focus and determining self- and hetero directed affective difficulties.

The results of this research confirm the existence of an association between alexithymia and attachment styles, highlighting a negative relation with secure attachment style, as also confirmed by numerous previous studies [10, 19].

In particular, it has been demonstrated that emotional

regulation strategies are influenced by emotional development and by quality of attachment relationships [20, 21].

This relation could evidence that the attachment style could explain the variation in values of alexithymia, based on the etiological explanatory models of alexithymia, which show that an insecure attachment style has a negative influence on the emotional regulation capacity [19].

Our study has limitations that must be addressed in further studies. For instance, a study could be undertaken considering, in the same patient group, disease progress from the early stages of the CKD to the last stages of HD.`

Conclusions

In conclusion, alexithymia, based on an impaired cognitive capacity to elaborate and regulate emotions, determines a tendency towards negative and not-differentiated states, causing, in these patients, difficulties to feel positive emotions, such as delight, happiness and love. In these patients alexithymia is associated with social anhedonia and an insecure attachment style.

Our data underlined that an introverted-psychotic personality associated to an insecure and avoidant attachment style, closely and positively related to primitive defensive mechanisms, determined, in nephropatic patients, alterations of the emotional processing of pain perception, which could be probably exacerbated by the worsening of the alexithymic status.

For these reasons, the monitoring of expressive modalities of emotions must be evaluated in both CKD and HD patients, through periodic administration of questionnaires and psychological support. If alexithymia is not identified early and preventive measures are not correctly put in place, it could determine negative effects on the individual's interpersonal relationships.

Moreover, the results of this study may help to develop strategies for therapeutic interventions or educational programs to prevent and mitigate these difficulties in the nephropathic population.

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