



## Three-in-one procedure for failed spinal surgery improved pain, disability scores and serum inflammatory milieu: Three-years follow-up

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### ABSTRACT

**Background:** None of the various treatment modalities for failed back surgery syndrome (FBSS) is satisfactory.

**Aim of the study:** Comparison of subjective and laboratory outcomes of the 3-in-1 procedure to percutaneous screw and rod spinal fixation (PSRF) for FBSS patients determined at the end of Phase II of the study (3-year follow-up after surgery).

**Patients & Methods:** This is phase II (follow-up at 3 years) of patients undergoing 3-in-1 procedure (Group B) or PSRF (Group A) as regard pain and disability scores and cytokines levels.

**Results:** At phase of the study, pain and disability scores were still significantly lower in all patients with significantly lower scores in group B than in group A. In comparison to the results obtained at the end of Phase I, the 3-in-1 procedure provided better outcome than PSRF only and number of patients graded the outcome as excellent-to-good was significantly higher than in patients of group B than group A. At the end of both phases, serum inflammatory cytokines' levels were significantly decreased and anti-inflammatory cytokines' levels were significantly increased in all patients compared to preoperative levels with significant difference in favor of patients of group B. the percentages of change in pain and disability scores at end of Phase II were significantly correlated with the percentage of change of serum anti-inflammatory cytokines' levels in both groups.

**Conclusion:** After 36 m after the 3-in-1 procedure pain scores were significantly decreased with improved disability scores and inflammatory milieu than in patients having FBSS only.

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Failed back surgery syndrome; cytokines; pain scores; disability scores; percutaneous screw and rod spinal fixation; thermal radiofrequency

## 1. Introduction

The incidence of failed back-surgery syndrome (FBSS) ranges between 10% and 40% with or without fusion. [1,2] Normally, back is dynamic structure, while the failed back is no longer dynamic [3]; such discrepancy results in recurrence of symptoms that may be aggravated than before the first surgery [4] and patients may become unresponsive to medical conservative treatment and their quality of life (QOL) could be easily compromised [5].

Various medications, reoperations and interventions had been suggested as treatment options for FBSS, unfortunately, evidence of its clinical outcome has not been clearly determined. [6] Thus, treatment of each FBSS patient must be selective to provide long-term pain control with reduction of costs and avoiding fewer effective modalities. [7]

Potential advantages of minimally invasive techniques for spinal surgery include reduction of intraoperative blood loss, requirements for postoperative (PO) analgesia and length of hospital stay, so as to allow early resumption of daily activities and return to work. [8,9] Screws act as a rigid and stable anchor points that

are bridged and connected with a rod as part of a construct for gripping spinal segment to get spinal fusion. [10]

Lumbar spine facet joint injection where the superior articular process connects to the base of the transverse process is the ideal site for medial branch infiltrations. [11] Injection mixture of corticosteroid and local anesthetic allows pain reduction [12] and proper selection of patient who may get benefit on thermal radiofrequency neurotomy (TRFN) [13] Efficacy facet joint injections depends on the anti-inflammatory and antiedematous effect of steroids in addition to its immunosuppressive action and to the inhibition of neural transmission within the nociceptive C fibers through reduction of lamina II GABAergic synaptic transmission resulting in a selective decrease in the processing of nociceptive inputs. [14]

Thermal techniques including TRFN induce mechanical decompression with thermally induced modifications of intradiscal cytokines involved in disc disease. [15] TRFN also destroy nociceptors in the periphery of the annulus. [13] Moreover, at temperature more than 70°C, fusion of collagen fibers in the annulus

occurs with shrinkage at the periphery of the disc. [16] Combined TRFN and steroid nerve block produced substantial improvement in terms of long-term pain relief and QOL. [17]

The 3-in-1 procedure was previously applied by the authors (Phase I) and entailed percutaneous TRNF of the median branch of the facet nerve, percutaneous screw and rod insertion and finally interlaminar epidural injection of triamcinolone. The 3-in-1 procedure showed superior short outcome than percutaneous screw and rod spinal fixation (PSRF). [18] The purpose of this study was to compare subjective and laboratory outcomes of the 3-in-1 procedure (applied during Phase I of the study) to the PSRF alone for FBSS patients at the end of 30-m follow-up.

## 2. Patients & methods

Figure 1 is a flow diagram that shows the progress of our study phases. This prospective comparative follow-up study was carried out in Anesthesia Departments, Faculty of Medicine, Tanta & South Valley Universities in conjunction with Medical

Biochemistry Department, Faculty of Medicine, Benha University and Rejuvenation Center, Benha, Egypt, between 2017 and 2020.

The study protocol was approved by the Local Ethical Committee to continue follow-up evaluation of patients previously had the 3-in-1 procedure (Group B) or PSRF (Group A) as interventional management of FBSS patients. [18] Patients accepted to attend the follow-up visits, to give blood sample for estimation of assigned laboratory investigations and signed fully informed written consents were included in the study. Preoperative and 6-m PO data of the enrolled patients were extracted out of their hospital files to be compared to data obtained at re-evaluation sessions till end of 30-m PO (Phase II).

## 3. Clinical outcome measures

### 3.1. Primary outcome

Pain severity was assessed using an 11-point numeric rating scale (NRS) where 0 indicates no pain and 10 indicates worst pain imaginable. [19,20] Back and leg pain during day and night was assessed and total NRS pain score was calculated.

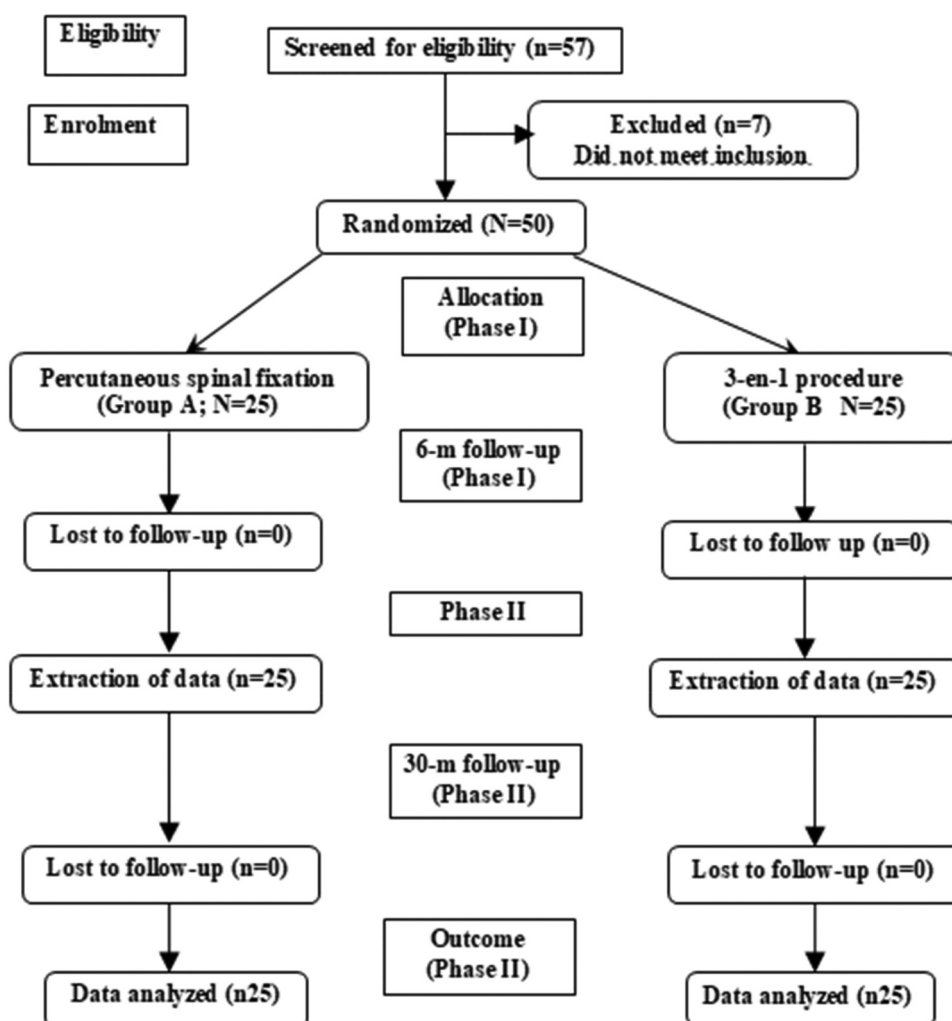


Figure 1. Consort flow diagram of the different study phases.

#### 4. Secondary outcomes

- (1) Disability secondary to pain was assessed using the Oswestry Low Back Pain Disability Questionnaire [21,22] that covers 10 items for evaluation of pain intensity, personal care, lifting, walking, sitting, standing, sleeping, sex life, social life and travelling. Each item was scored from 0 to 5 according to increased disability and a total Oswestry Disability index (ODI) scores was calculated. Disability was graded as minimal (ODI = 0–20), moderate (ODI = 20–40), severe (ODI = 40–60), crippled (ODI score = 60–80) and ODI score of 80–100 indicates that the patient is either bed-bound or exaggerating his or her symptoms [22,23]. Pain and disability scores were compared to previous scores and percentages of change in relation to preoperative and 6-m PO scores were evaluated. [24,25]
- (2) Pain medication requirements were recorded using a 0- 4-point scale with 0 indicates no medication used; 1 indicates occasional use of pain medications; 2 indicate regular use of non-opioid medications, 3 indicates occasional use of opioid medications and 4 indicates regular use of opioid medications.
- (3) Patients' evaluation of outcome was graded according to Odom's criteria into Excellent: relief of all preoperative symptoms and all abnormal findings were improved; Good: minimal persistence of preoperative symptoms and all abnormal findings were improved or unchanged; Fair: definite relief of some preoperative symptoms, while other symptoms were unchanged or slightly improved; Poor: all preoperative symptoms and signs were unchanged or exacerbated. [26]

#### 5. Blinding

The anesthetist who gathered data from patients at 36 m post-operatively was not aware of the study protocol.

#### 6. Sampling & investigations

Venous blood samples (5 ml) were collected from the antecubital vein under complete aseptic conditions and were kept in a plan container, allowed to clot and then serum was separated by centrifugation at 3000 rpm for 10 minutes, collected in sterile Eppendorf tube and stored at  $-80^{\circ}\text{C}$  till be assayed. Blood samples were collected and numbered by an assistant who was blinded about type of surgery.

#### 7. Laboratory tests

Serum levels of estimated markers were measured using enzyme-linked immunosorbent assay (ELISA) kits according to the manufacturer's instructions and were read using a 96 well microplate ELISA reader (Dynatech. MR 7000).

- (a) Human TNF- $\alpha$  was measured with the enzyme linked immunoassay (ELISA) kit (catalogue no. ab179886, abcam Inc., Cambridge, USA) by quantitative sandwich enzyme immunoassay technique. [27]
- (b) Human IL-1 $\beta$  with the enzyme linked immunoassay (ELISA) kit (catalogue no. ab46052, abcam Inc., Cambridge, USA) by quantitative sandwich enzyme immunoassay technique. [28]
- (c) Human IL-6 with the enzyme linked immunoassay (ELISA) kit (catalogue no. ab46042, abcam Inc., Cambridge, USA) by quantitative sandwich enzyme immunoassay technique. [29]
- (d) Human IL-10 was measured with the enzyme linked immunoassay (ELISA) kit (catalogue no. ab215089, abcam Inc., San Francisco, USA) by quantitative sandwich enzyme immunoassay technique. [30]

#### 8. Statistical analysis

Obtained data were presented as mean $\pm$ SD, ranges, numbers and percentages. Results were analyzed using paired t-test, One-way ANOVA Test and Chi-square test. Possible relationships were investigated using Pearson linear regression analysis. Statistical analysis was conducted using the IBM SPSS (Version 23, 2015) for Windows statistical package. P value  $<0.05$  was considered statistically significant.

#### 9. Results

Table 1 showed no statistically significant difference between studied groups as regard demographic data. At the end of Phase II (30-m of follow-up), total NRS pain scores were still significantly lower, in patients of both groups, in comparison to their preoperative scores with significantly lower total pain scores of patients of group B in comparison to patients of group A. The median percentage of decrease at the end of Phase II, in relation to preoperative pain scores, was significantly higher in patients of group B in comparison to that of patients of group A. On contrary, the median percentage of change in NRS scores at the end of Phase II in comparison to that recorded at the end of Phase I (6th month' scores) were non-significantly better in group B in comparison to group A. Unfortunately, 25 patients showed worsened pain scores at the end of

**Table 1.** Demographic and clinical data of studied patients.

Data		Group A	Group B
Age (years)	<60 years	8 (32%)	11 (44%)
	>60 years	17 (68%)	14 (56%)
Gender	Mean age	61.4 ± 6.9	60.4 ± 6.3
	Males	10 (40%)	9 (36%)
Weight (kg)	Females	15 (60%)	16 (64%)
		81.3 ± 4.6	82.5 ± 5.2
Height (cm)		167.8 ± 3.1	168.2 ± 3.3
BMI (kg/m <sup>2</sup> )		28.9 ± 1.6	29.2 ± 1.8
Duration since previous surgery (months)		38.1 ± 9.5	39.3 ± 10.2
Duration of pain (months)		9.4 ± 1.8	10.6 ± 2.4
L2-3			3 (12%)
			9 (36%)
L3-4			
Affected level			
L4-5			6 (24%)
			7(28%)
L5-S1			
Number of affected segments	One segment	7 (28%)	7 (28%)
	Two segments	11 (44%)	9 (36%)
	Three segments	6 (24%)	7 (28%)
	Four segments	1 (4%)	2 (8%)

Notes: Data are presented as numbers and mean ± SD; percentages are in parentheses; BMI = body mass index.

Phase II with non-significantly higher frequency of patients had worsened pain in group A in comparison to group B; 60% vs. 44% (Table 2).

At the end of Phase II, ODI scores showed non-significant difference in comparison to scores determined at the end of Phase I in both groups. However, ODI scores that were determined at the end of Phase II were significantly lower in patients of group B on comparison to scores of patients of group A. Moreover, the percentage of change was significantly better in patients of group B in comparison to patients of group A. Lastly, the frequency of patients had improved disability was higher in patients of group B, while the frequency of patients had worsened disability was higher among patients of group A (Table 2).

At end of Phase II, patients' requirements for analgesia were significantly reduced in group B, but non-significantly increased in group A in comparison to their respective requirement scoring at the end of Phase I. Moreover, analgesia requirement scoring for patients of group B was significantly lower than that of patients of group A. Furthermore, the frequency of patients required analgesia was decreased in group B, while the frequency of patients required analgesia in group A was increased with significant difference in favor of groups B (Table 2).

According to Odom's criteria, the frequency of patients of group B who found the outcome excellent was significantly higher than in group A; 52% vs. 24%, while the frequency of patients found the outcome fair-to-good was significantly lower in group B in comparison to group A; 8% vs. 32% (Figure 1)

Serum levels of TNF- $\alpha$  and IL-1 $\beta$  were significantly decreased, while serum levels of IL-6 were non-significantly decreased and serum IL-10 were non-

significantly increased in samples of patients of group A that obtained at the end of Phase I and Phase II in comparison to their preoperative levels. On the other hand, in samples of patients of group B that were obtained at the end of Phase I and Phase II, serum levels of TNF- $\alpha$ , IL-1 $\beta$  and IL-6 were significantly decreased, while serum levels of IL-10 were significantly increased in comparison to their preoperative levels. Moreover, the percentage of change of estimated levels of studied cytokines in relation to preoperative levels showed significant differences between both groups in favor of group B. Estimated levels of TNF- $\alpha$  and IL-1 $\beta$  in 36-m samples of patients of both groups were non-significantly higher in comparison to 6-m sample levels. In patients of group A, serum levels of IL-6 were non-significantly increased, while serum levels of IL-10 were non-significantly decreased in comparison to 6-m levels, while in patients of group B, the difference was significant (Table 3).

The percentages of change in NRS and ODI scores at the end of Phase I and Phase II in relation to preoperative scores were significantly correlated with the percentage of decrease in serum levels of TNF- $\alpha$  and IL-6 and the percentage of increase of serum IL-10 levels in both groups (Table 4).

## 10. Discussion

The results obtained at the end of Phase II of the study (36-m after surgery) indicated the efficacy of spinal fixation using percutaneous screw and rod spinal fixation, alone or as a part of the 3-in-1 procedure for management of FBSS patients as evidenced by the maintained significant reduction of pain and disability scores till 36-m PO in comparison to preoperative scores. These findings supported the previous studies

**Table 2.** Outcome data of patients of both groups determined at 36-m PO.

Parameters		Group A	Group B	P value		
<b>Total NRS score</b>						
Score	Preoperative	6.75 ± 0.78	6.93 ± 0.9	0.455		
	6-m PO	2.27 ± 0.36*	1.47 ± 0.36*	<0.0001		
	12-m PO	2.54 ± 0.5*†	1.49 ± 0.38*	<0.0001		
	18-m PO	2.8 ± 0.54*†	1.65 ± 0.49*†	<0.0001		
	24-m PO	3.13 ± 0.69*†	1.73 ± 0.6*†	<0.0001		
	30-m PO	3.59 ± 0.84*†	1.96 ± 0.78*†	<0.0001		
	36-m PO	4.14 ± 1.04*†	2.08 ± 0.83*†	<0.0001		
	Change in relation to preoperative pain score		39 ± 12.4	70.6 ± 9.23	<0.0001	
Change in relation to 6-m score	Decreased	0	0	0.024		
	No change	3 (4%)	10 (40%)			
	Increased by (%)	by ≤50	3 (12%)	5 (20%)		
		>50-100	10 (36%)	8 (32%)		
		>100	9 (36%)	2 (8%)		
Mean	96.8 ± 34.2	66.5 ± 31.1	0.008			
<b>ODI score</b>						
Score	Preoperative	33.2 ± 6.2	30.92 ± 5.52	0.176		
	6-m PO	16.52 ± 2.86*	14.48 ± 2.45*	0.0094		
	12-m PO	16.76 ± 3.63*	14.4 ± 2.36*	0.009		
	18-m PO	17 ± 3.85*	14 ± 2.61*	0.0023		
	24-m PO	16.84 ± 4.59*	14.04 ± 2.86*	0.0127		
	30-m PO	17.36 ± 4.49*	13.92 ± 3.8*	0.0052		
	36-m PO	17.6 ± 4.64*	14.1 ± 4.62*	0.0099		
	Change in relation to preoperative ODI scores		46.7 ± 12	55.8 ± 11.3	0.008	
Change in relation to 6-m score	Decreased	8 (32%)	15 (60%)	0.147		
	No change	2 (8%)	1 (4%)			
	Increased by (%)	by ≤20	6 (24%)	2 (8%)		
		>20-40	8 (32%)	4 (16%)		
		>40-60	1 (4%)	3 (12%)		
Mean	-6.5 ± 21.2	4.8 ± 28.7	0.121			
<b>Pain medications</b>						
Requirement	Decreased	3 (12%)	7 (28%)	0.023		
	No change	12 (48%)	16 (64%)			
	Increased	10 (40%)	2 (8%)			
score	PO duration	6-m	36-m	6-m	36-m	
		0	4 (16%)	3 (12%)	8 (32%)	5 (20%)
	1	11 (44%)	9 (36%)	10 (40%)	17 (68%)	
	2	8 (32%)	13 (52%)	6 (24%)	3 (12%)	
	3	2 (8%)	0	1 (4%)	0	
	Mean	P = 0.322		P = 0.605		
	1.4 ± 0.71		0.92 ± 0.57	0.011		
<b>Odom's criteria</b>						
PO duration	6-m	36-m	6-m	36-m		
	Excellent	3 (12%)	6 (24%)	6 (24%)	13 (52%)	0.034
	Good	7 (28%)	11 (44%)	13 (52%)	10 (40%)	
	Fair	10 (40%)	7 (28%)	5 (20%)	2 (8%)	
	Poor	5 (20%)	1 (4%)	1 (4%)	0	
	P = 0.051		P = 0.123			

NRS: numeric rating scale; ODI: Oswestry Low Back Pain Disability Questionnaire; P: indicates the significance of difference between both groups; \* indicates significance of difference versus the preoperative measurement; † indicates significance of difference versus the preceding measurement; P < 0.05: indicates significant difference; P > 0.05: indicates non-significant difference

that documented the long-term improvement of ODI and pain scores after instrumented fusion of FBSS patients [31–35].

The 3-in-1 procedure maintained significantly lower ODI and pain scores in comparison to preoperative scores and to the 36-m scores of patients had PSRF only. Moreover, in comparison to the 6-m scores the 3-in-1 procedure provided better outcome than PSRF only. This maintained efficacy could be attributed to the complimentary effect of TRFN and local steroid injection in addition to the effect of PSRF. These results support that previously documented by Rahimzadeh et al. [36] who reported the effectiveness of adding hyaluronidase to the epidural injectate for management of chronic back pain (CBP) in patients with FBSS. Also, Rapčan et al. [37] and Ceylan et al. [38]

reported significant improvement of leg and back pain after 12-months of epiduroscopic hyaluronidase and steroid injection with mechanical lysis. The reported efficacy of steroid and hyaluronidase injection was attributed by Helm li & Racz [39] to the ability of hyaluronidase to facilitate the spread of medications in extracellular matrix by breaking down polysaccharides in the interstitial space.

Concerning the effectiveness of RF, the obtained results are in accordance with Arsanious et al. [40] who found combined pulsed RF followed by TRFN of medial branch of lumbar dorsal ramus improves outcome. Also, Do et al. [41] reported superior pain relief by intra-articular RF than by steroid injection for CBP. Moreover, Chen et al. [42] reported significantly greater improvement in ODI and pain scores and



**Table 3.** Serum levels of studied cytokines estimated at the end of the study phases.

Variable	Time	Group A	Group B	P value
TNF- $\alpha$ (pg/ml)	Preoperative	63.112 $\pm$ 28.13	68.432 $\pm$ 20.126	0.466
	End of Phase I	44.184 $\pm$ 19.6	29.58 $\pm$ 17.59	0.008
	P1 value	0.008	<0.001	
	End of Phase II	46.24 $\pm$ 21.4	39.96 $\pm$ 13.37	0.219
	P1 value	0.021	<0.001	
IL-1 $\beta$ (pg/ml)	P2 value	0.725	0.023	
	% of change*	26.91 $\pm$ 10.72	42 $\pm$ 7.1	<0.001
	Preoperative	7.61 $\pm$ 2.56	7.47 $\pm$ 2.13	0.835
	End of Phase I	5.63 $\pm$ 1.49	5.11 $\pm$ 1.68	0.253
	P1 value	0.0017	0.00007	
IL-6 (pg/ml)	End of Phase II	6.16 $\pm$ 2	5.28 $\pm$ 1.34	0.074
	P1 value	0.031	0.00007	
	P2 value	0.289	0.697	
	% of change*	18.6 $\pm$ 7.4	28 $\pm$ 10.8	0.0008
	Preoperative	5.168 $\pm$ 1.63	5.354 $\pm$ 1.74	0.698
IL-10 (pg/ml)	End of Phase I	4.3 $\pm$ 1.52	3.53 $\pm$ 0.94	0.038
	P1 value	0.057	0.00003	
	End of Phase II	4.6 $\pm$ 1.47	3.61 $\pm$ 1	0.045
	P1 value	0.239	0.00008	
	P2 value	0.417	0.187	
IL-10 (pg/ml)	% of change*	9.9 $\pm$ 6.25	25 $\pm$ 8.6	<0.001
	Preoperative	13.12 $\pm$ 3.81	13.57 $\pm$ 4.23	0.694
	End of Phase I	15.12 $\pm$ 4.84	20.34 $\pm$ 5.05	0.0005
	P1 value	0.111	<0.0001	
	End of Phase II	14.1 $\pm$ 4.1	16.4 $\pm$ 4.46	0.055
IL-10 (pg/ml)	P1 value	0.394	0.026	
	P2 value	0.410	0.0052	
	% of change*	7.38 $\pm$ 3.56	22.38 $\pm$ 9.8	<0.0001

TNF- $\alpha$ : Tumor necrosis factor- $\alpha$ ; IL: Interleukin; P: indicates the significance of difference between both groups; P1: indicates significance of difference versus the preoperative measurement; P2 indicates significance of difference versus sample obtained at the end of Phase I; \*: indicates the percentage of change in relation to preoperative levels; P < 0.05: indicates significant difference; P > 0.05: indicates non-significant difference

**Table 4.** Pearson's correlation between % of change of NRS and ODI scores and percentage of change in studied cytokines' serum levels at the end of Phase II in patients of both groups in relation to preoperative cytokine's levels.

Dependent variable	Independent variables	Group A		Group B		
		r	p	r	p	
% of change of NRS score	% of change of serum levels of	TNF- $\alpha$	0.578	0.002	0.537	0.006
		IL-1 $\beta$	0.290	0.159	0.344	0.092
		IL-6	0.432	0.031	0.729	<0.001
		IL-10	0.438	0.029	0.425	0.034
% of change of ODI score	% of change of serum levels of	TNF- $\alpha$	0.400	0.047	0.476	0.016
		IL-1 $\beta$	0.415	0.039	0.300	0.145
		IL-6	0.189	0.365	0.419	0.037
		IL-10	0.411	0.041	0.544	0.005

NRS: numeric rating scale; ODI: Oswestry Low Back Pain Disability Questionnaire; TNF- $\alpha$ : Tumor necrosis factor- $\alpha$ ; IL: Interleukin; r: Pearson's coefficient; P: indicates the significance of calculated Pearson's coefficient; P < 0.05: indicates significant difference; P > 0.05: indicates non-significant difference

QOL that led to improved function of patients had chronic lumbar and sacroiliac joint pain and treated by RFN than controls.

In line with the maintained effect of RF, Lee et al. [43] and Çetin & Yektaş [44] documented that conventional RFN of medial branch in patients with lumbar facet joint pain effectively decreases pain scores and allowed better QOL and daily activities till 12 [43] and 24 months [44], respectively. Thereafter, Ibrahim et al. [45] found RFN of sensory nerve branches along S1-3 lateral foramina and L4-S1 medial branches is minimally invasive procedure that significantly relieved lumbar back pain for 24 months. Recently, Speldewinde [46] reported sustained success rate of 69% in reduction of sacroiliac ligament/joint complex

pain with improvement in physical and psychological function for 12 months after TRFN. Further, in support of safety of RF application after insertion of the pedicle and screws, Elwood et al. [47] reported no complications due to hardware temperature and Eckmann et al. [48] detected no motor weakness after thermal neurotomy.

Forty patients (80%) found the outcome was excellent-to-good with significantly higher frequency with the 3-in-1 procedure (92%) in comparison to PSRF alone (68%). Similarly, Woiciechowsky & Richter [49] reported that RFN for CBP resulted in acceptable-to-excellent results in 68% of patients with pain reduction rate of 47% for an average duration of 7.8-m and Arıcı & Kılıç [50] documented that TRF for facet arthropathy

is a safe and effective procedure and about 69% found outcome is excellent-to-good with a median duration of pain relief of 10.2 months.

Preoperative serum levels of inflammatory cytokines; IL-1 $\beta$ , IL-6 and TNF- $\alpha$  were significantly higher, while serum levels of anti-inflammatory cytokine, IL-10, were significantly lower in comparison to volunteers' levels. At 6- and 36-m PO, serum levels of inflammatory cytokines were significantly decreased and serum IL-10 levels were significantly increased in all patients in comparison to preoperative levels with significant difference in favor of patients had the 3-in-1 procedure. These findings indicating either a possible role of disturbed cytokines' milieu in pathogenesis of the primary disc disease, or in failure of the previous spinal surgery or it may be secondary to failed surgery and this disturbance could be corrected by proper treatment of disc disease. In support of this assumption, percentages of change in NRS and ODI scores at 36-m were significantly correlated with percentage of decrease in serum levels of TNF- $\alpha$  and IL-6 and increase of serum IL-10 levels in both groups.

These findings and attribution are in accordance with that experimentally reported by Gorth et al. [51] who documented the role of inflammatory cytokines in pathogenesis of intervertebral disc disease and Zhong et al. [52] who found spinal Src family of protein tyrosine kinases contribute to radicular pain by activation of p38 MAPK pathway and increasing spinal expression of inflammatory cytokines in rats with autologous nucleus pulposus. Recently, Zhang et al. [53] (2020) detected high expression rates of TNF- $\alpha$  and IL-1 $\beta$  in degenerate goat discs. Clinically, the obtained results are coincident with Bäckryd et al. [54] who detected significantly higher serum IL-6 levels in patients with FBSS with peripheral neuropathic pain and Kamieniak et al. [55] who reported significantly higher and lower serum levels of TNF- $\alpha$  and IL-10, respectively in patients had FBSS. Moreover, Stover et al. [56] suggested the need for targeting of IL-6, TNF- $\alpha$ , and IL-1 $\beta$  for pain modulation in degenerative intervertebral discs and multiple clinical trials evaluated the efficacy of TNF- $\alpha$  and IL-6 inhibitors in treating CBP. [57]

## 11. Conclusion

36 min after surgery, the 3-in-1 procedure approved its efficacy for reduction of pain and disability scores of FBSS patients and improved the associated disturbance in cytokines' milieu with lessened inflammatory reaction. Thus, it is recommended as a safe and effective management strategy for FBSS patients especially those intolerant to or had contraindications for medical treatment. However, follow-up for longer duration or wider scale studies are mandatory to establish the obtained results.

## Disclosure statement

No potential conflict of interest was reported by the author(s).

## Declaration

The Authors declare that there is no conflict of interest.

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