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Original Contribution

Research Designs in Interventional Pain Management: Is Randomization Superior, Desirable or Essential?

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In the hierarchy of research designs, the results of randomized, controlled trials are considered to be evidence of the highest grade, whereas observational studies are viewed as having less validity because they reportedly overestimate treatment effects. This hierarchy approach to study design has been promoted widely in modern medical literature; in spite of overwhelming evidence that evidence-based medicine includes all types of evidence, and randomized, double-blind studies should not necessarily be considered to represent the best available evidence. In fact, randomized, double-blind studies face insurmountable challenges in interventional pain management. The value of the so-called gold standard of randomized, double-blind trials has been questioned.

This study was undertaken to evaluate if randomization does provide the protective statistical shield that some think it provides in an interventional pain management population. In this study we compared randomized and non-randomized samples. Randomization was accomplished by the use of random number tables and random sampling into four groups, three or two groups. Non-randomization was achieved by allocation into various groups by two different means.

The results of this evaluation showed that there was only one significant difference when patients were allocated by means of non-randomization among the groups or compared to the total sample. In contrast, randomization showed significant differences in seven parameters.

The results of this study conclude that in interventional pain management settings, non-randomized sampling is valid.

Keywords: Evidence-based medicine, randomized trial, double-blind trial, controlled trial, internal validity, external validity, interventional pain management

The acme of clinical research is the randomized, double-blind, controlled trials, but such trials must be undertaken responsibly and are extremely difficult to conduct in interventional pain management. Randomized, controlled trials were introduced into clinical medicine when streptomycin was evaluated in the treatment of tuberculosis (1). Since then, randomized, controlled trials have become the gold standard for assessing the effectiveness of therapeutic agents (2-4). Sacks et al (5) compared published randomized, controlled studies with those that used observational designs. In this landmark evaluation, they showed that the agent being tested was considered effective in 44 of 56 trials (79%) in observational studies utilizing historical controls, whereas the agent was considered positive in only 10 of 50 (20%) randomized, controlled trials. Thus, Sacks et al (5) concluded that bias in patient selection may irretrievably weigh the outcome of historically controlled trials in favor of new therapies in observational studies. Advocates of evidence-based medicine classify studies according to the grades of evidence on the basis of the research design, using internal validity as the criterion for hierarchical rankings. The highest grade is reserved for research involving at least one properly randomized, controlled trial; and the lowest grade is applied to descriptive studies and expert opinion; observational studies, cohort studies and case-controlled studies, falling at intermediate levels (7, 8). Thus, this hierarchical approach to study design has been promoted widely in individual reports, meta-analysis, consensus statements and educational materials for practitioners.

Evidence-based medicine has been defined by many with contradictory definitions (9). Evidence-based medicine must include all types of evidence, including clinical experience (10-28). However, in spite of the descriptions of evidence-based medicine as including all types of evidence, presently all the decisions are made based on so-called evidence-based medicine derived from

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randomized, double-blind, controlled trials. Numerous stumbling blocks posing challenges to randomized, double-blind trials in interventional pain management have been described (29-36).

The concept that assignment of the subjects randomly to either experimental or controlled status is the perfect science has also been questioned (37). Randomized trials often not only trade internal validity for external validity, but randomization also makes patient recruitment difficult (37). Randomization literally means selection similar to the tossing of a coin, which essentially ensures that the physician responsible for the assignment is not consciously or unconsciously allocating certain patients to a particular group. Thus, criticism has been advanced against various types of non-randomized allocations, including assigning volunteers to the treatment group and those who do not volunteer to the control group, allocation into groups based on alternate days, alternate numbers or another assigned preformed methodology. Finally, it is believed that randomization ensures that the two groups will differ only by chance. However, it does not guarantee that in practice, the balance will be actually achieved through the randomization.

Considering the numerous difficulties with randomization, including patient recruitment, it is not clear that without the manipulation by one of the investigators, other modes of allocation are unbiased and produce similar results in all groups of patients. The distinction between randomization and other non-randomized types of allocation has not been established. This study was undertaken to evaluate various features of patients, presenting to an interventional pain management setting and to compare these features utilizing various types of allocations, including randomization.

METHODS

This study was designed to evaluate all of the patients seen in one pain management location by one physician during 2001. There were no inclusion or exclusion criteria. Information with respect to gender, age, height, weight, duration, the mode of onset of pain, history of previous surgical intervention and referral pattern was collected for all patients. Further information included data collection of multiple dimensions of pain, psychological status and management.

Phase I or Non-randomized analysis: This phase included analysis of total sample and allocation into four groups by two different means. Initially an evaluation of the total sample with demographic features, regions involved, psychological status, non-physiological features, and clinical approach with results of their follow-ups was performed.

The first part of analysis consisted of allocation of all the patients into four groups. They were assigned a serial number chronologically from 1 to 372 based on their initial date of visit. Patients were allocated into Group I from number 1 to 93; into Group II from 94 to 186; into Group III from 187 to 279; and into Group IV from 280 to 372.

The second part of analysis consisted of allocation of all the patients into another set of four groups. By their assigned serial number, all the patients were divided into four groups, each corresponding to their assigned number, i.e., 1, 5, 9, 13, etc. - Group I; 2, 6, 10, 14, etc. - Group II; 3, 7, 11, 15, etc. - Group III, 4, 8, 12, 16 etc.- Group IV.

Phase II or Randomized analysis: All 372 patients were divided into either two groups, three groups or four groups by utilizing random tables and finally analyzing 100 patients, divided into 4 groups, with random sampling. Random sampling included 100 of the 372 patients divided into four groups: All the patients were provided with serial numbers from 1 to 372, according to the initial visit date. Subsequently, 25 patients were selected randomly from serial numbers 1 to 93 using random tables and grouped into Group I; 25 patients from 94 to 186 were grouped into Group II, 25 patients from 187 to 279 were grouped into Group III, and from 280 to 372 into group IV.

Data were recorded on a database using Microsoft® Access®; the SPSS version 9.0 statistical package. This package was used to generate the frequency tables and chi-squared statistic was used to test the significance difference between groups. Fischer's exact test was used wherever expected value was less than five. Student's t test was used to test mean difference between groups, and Analysis of variance (ANOVA) is used when comparing more than two groups. Results were considered statistically significant if the p value was less than 0.05.

RESULTS

Phase I Analysis

Results of Phase I analysis are illustrated in Tables 1 and 2.

The data from the total sample is used as baseline data indicating a spectrum of various features in patients presenting to interventional pain management setting. Further analysis consisted of allocation of these patients into four groups based on the date of their initial visit, or allocation by the assigned numbers. The results are illustrated in Tables 1 and 2 with no differences noted between the groups or compared to the total sample in most categories, except in Group I where the percentage of dropouts was 39%, which was significantly higher

Table 1. *Results of non-randomized patient allocation into four groups, by serial number based on initial date of visit*

Demographic features	Total N=372	Group I N=93	Group II N=93	Group III N=93	Group IV N=93
Male	**40%**	43%	34%	41%	43%
Female	**60%**	57%	66%	59%	57%
Age (yrs.)	**47 + 0.8**	47 + 1.6	47 + 1.7	47 + 1.4	48 + 1.7
Height (inches)	**67 + 0.2**	67 + 0.37	67 + 0.38	67 + 0.44	68 + 0.41
Weight (lbs.)	**180 + 2.4**	179 + 4.4	178 + 4.0	177 + 4.1	188 + 5.5
Duration of pain (months)	**102 + 6.4**	94 + 11.5	97 + 13.5	101 + 11.4	114 + 14.6
Gradual onset	**51%**	58%	51%	54%	43%
History of surgery	**29%**	29%	32%	27%	29%
Physician- referral	**69%**	66%	67%	73%	69%
Spinal pain					
Cervical	**47%**	40%	47%	49%	53%
Thoracic	**22%**	23%	22%	25%	19%
Lumbar	**79%**	75%	82%	80%	81%
Total	**93%**	89%	93%	95%	96%
Non-spinal pain					
Headache (non-cervicogenic)	**17%**	24%	14%	20%	11%
Abdominal / chest wall	**7%**	11%	7%	7%	3%
RSD	**11%**	18%	13%	10%	3%
Number of region involved					
One region	**100%**	100%	100%	100%	100%
Two regions	**56%**	57%	55%	57%	56%
Three regions or more	**22%**	26%	23%	27%	12%
Psychological status					
Depression	**58%**	52%	53%	66%	62%
Generalized anxiety disorder	**54%**	47%	50%	63%	56%
Somatization disorder	**34%**	27%	25%	44%	39%
Non-physiologic features					
Non-physiologic symptoms	**15%**	19%	11%	16%	13%
Non-physiologic signs	**15%**	17%	15%	14%	15%
Symptom magnification	**24%**	26%	18%	33%	22%
Clinical approach					
Interventional procedures	**74%**	73%	75%	72%	74%
Non-interventional approach	**19%**	19%	15%	20%	23%
Evaluation only	**7%**	8%	10%	8%	3%
Dropout rate	**25%**	39%#	30%	17%	13%

# Indicates significant difference with total sample

Table 2. *Results of non-randomized patient allocation into four groups by sequential allocation of serial numbers*

Demographic features	Group I N=93	Group II N=93	Group III N=93	Group IV N=93	Total N=372
Male	39%	48%	40%	34%	**40%**
Female	61%	52%	60%	66%	**60%**
Age (yrs.)	47 + 1.4	47 + 1.7	46 + 1.6	48 + 1.7	**47 + 0.8**
Height (inches)	67 + 0.3	67 + 0.4	67 + 0.4	66 + 0.4	**67 + 0.2**
Weight (lbs.)	185 + 4.0	184 + 4.8	178 + 5.5	173 + 4.5	**180 + 2.4**
Duration of pain (months)	84 + 10.2	100 + 11.2	105 + 14.3	118 + 14.6	**102 + 6.4**
Gradual onset	45%	50%	52%	59%	**51%**
History of surgery	36%	28%	28%	26%	**29%**
Physician-referral	69%	68%	71%	67%	**69%**
Spinal pain					
Cervical	48%	54%	45%	42%	**47%**
Thoracic	23%	18%	27%	20%	**22%**
Lumbar	77%	81%	83%	76%	**79%**
Total	93%	93%	96%	89%	**93%**
Non-spinal pain					
Headache (non-cervicogenic)	15%	16%	16%	22%	**17%**
Abdominal / chest wall	5%	7%	7%	7%	**7%**
RSD	12%	13%	7%	14%	**11%**
Number of regionsinvolved					
One region	100%	100%	100%	100%	**100%**
Two regions	55%	63%	56%	50%	**56%**
Three regions or more	22%	21%	20%	23%	**22%**
Psychological status					
Depression	58%	63%	55%	56%	**58%**
Generalized anxiety disorder	57%	50%	58%	52%	**54%**
Somatization disorder	33%	36%	34%	31%	**34%**
Non-physiologic features					
Non-physiologic symptoms	14%	16%	17%	12%	**15%**
Non-physiologic signs	13%	17%	17%	14%	**15%**
Symptom magnification	27%	26%	26%	20%	**24%**
Clinical approach					
Interventional procedures	75%	68%	73%	79%	**74%**
Non-interventional approach	17%	21%	22%	17%	**19%**
Evaluation only	8%	11%	5%	4%	**7%**
Dropout rate	25%	28%	20%	24%	**25%**

compared to total dropouts, which was 25% (Table 1), when patients were allocated by serial numbers.

Phase II Analysis

Table 3 shows random numbers utilized in analysis.

Table 4 shows the results of Phase II analysis with randomization into various groups. Significant differences were noted as follows: 1) involvement of cervical region was higher in Group II compared to Group I, when patients were randomized into two groups; 2) incidence of symptom magnification was lower in Group II and III,

Table 3: *Random numbers utilized in randomization*

Randomization into Two Groups						Randomization into Three Groups						Randomization into Four Groups								Random Sampling			
I			II			I		II		III		I		II		III		IV		I	II	III	IV
1	137	262	4	121	236	4	206	2	199	1	158	1	176	7	196	3	214	4	188	5	10	17	3
2	140	264	7	122	237	8	207	3	202	6	160	2	177	26	201	5	216	8	191	16	12	26	28
3	142	265	12	123	240	11	211	5	204	14	161	6	180	29	204	9	218	14	197	33	30	35	74
5	143	267	14	124	241	13	214	7	209	15	165	10	181	38	206	16	219	17	198	37	32	36	90
6	147	269	16	126	242	16	222	9	210	17	166	11	182	40	210	20	223	18	199	40	34	82	96
8	148	270	17	127	244	21	224	10	212	19	169	12	183	43	215	23	229	19	205	70	38	88	97
9	152	271	18	129	246	24	225	12	217	20	171	13	185	52	235	31	230	27	207	95	57	105	115
10	154	272	20	130	250	25	227	18	218	22	173	15	190	54	237	37	231	36	208	107	60	125	156
11	155	274	23	131	251	26	229	29	219	23	174	21	202	57	241	39	234	41	217	111	91	138	158
13	156	276	25	132	252	28	234	30	220	27	177	22	203	59	242	45	236	46	221	112	93	171	172
15	157	280	26	135	253	32	235	31	228	33	180	24	209	76	243	47	244	48	224	123	94	193	189
19	158	281	27	136	255	34	239	36	232	35	189	25	211	77	245	50	246	49	225	124	122	198	207
21	161	284	31	138	261	42	241	37	236	40	191	28	220	79	247	56	248	53	227	128	145	218	211
22	164	287	36	139	263	52	242	38	237	44	201	30	222	83	249	58	258	55	228	130	147	230	212
24	167	288	37	141	266	55	243	39	238	45	203	32	226	86	250	62	261	60	232	190	187	235	215
28	170	289	38	144	268	57	245	41	244	46	205	33	238	91	251	63	263	65	233	199	194	248	233
29	171	290	41	145	273	58	247	43	248	48	208	34	239	93	252	64	266	70	240	204	195	259	245
30	173	291	43	146	275	59	249	47	250	49	213	35	254	94	253	68	270	78	255	206	217	271	252
32	176	293	45	149	277	62	251	50	252	53	215	42	256	96	260	69	278	81	259	209	223	274	278
33	177	295	46	150	278	67	254	51	253	60	216	44	257	98	269	72	280	84	268	239	229	289	305
34	180	297	47	151	279	68	256	54	255	61	221	51	262	102	273	75	286	95	272	281	254	300	328
35	181	298	49	153	282	69	258	56	259	63	223	61	264	104	283	82	291	97	275	298	273	307	329
39	182	299	50	159	283	72	262	65	260	64	226	66	265	107	285	87	294	101	277	327	290	309	353
40	183	300	51	160	285	73	263	66	264	70	230	67	267	108	289	88	297	106	279	346	330	315	359
42	184	302	52	162	286	76	270	74	265	71	231	71	271	110	290	89	305	109	281	357	371	335	369
44	190	304	53	163	292	77	274	85	267	75	233	73	274	118	301	100	306	112	282				
48	191	309	55	165	294	78	277	86	269	79	240	74	276	121	303	111	307	113	284				
54	196	310	56	166	296	82	279	92	271	80	246	80	287	123	304	114	317	117	288				
57	198	312	59	168	301	83	282	93	272	81	257	85	293	129	308	115	318	126	292				
58	200	313	63	169	303	84	283	98	276	87	261	90	295	130	311	116	326	134	296				
60	201	316	64	172	305	88	286	99	280	89	266	92	299	131	312	122	328	137	298				
61	202	319	65	174	306	90	288	104	281	91	268	99	300	141	313	124	331	138	302				
62	203	321	72	175	307	103	289	105	284	94	273	103	309	145	315	125	333	139	310				
66	204	323	73	178	308	109	291	106	287	95	275	105	316	146	320	127	334	144	314				
67	205	324	76	179	311	113	296	110	290	96	278	119	321	156	322	132	337	149	319				
68	208	325	77	185	314	117	297	112	303	97	285	120	323	159	327	135	342	150	325				
69	209	329	78	186	315	118	299	114	307	100	292	128	324	162	338	136	351	151	332				
70	211	330	79	187	317	119	300	116	308	101	293	133	329	164	341	142	355	153	335				
71	212	331	83	188	318	123	301	122	310	102	294	140	330	166	344	143	356	157	336				
74	214	334	84	189	320	125	304	130	312	107	295	147	343	170	346	154	359	160	339				
75	219	335	87	192	322	127	305	140	313	108	298	148	345	171	357	155	360	165	340				
80	220	339	88	193	326	131	311	142	314	111	302	152	348	179	358	167	361	168	347				
81	221	342	89	194	327	134	319	146	315	115	306	158	349	184	362	194	365	169	350				
82	222	343	91	195	328	135	326	148	316	120	309	161	353	187	363	195	366	172	352				
85	224	344	93	197	332	139	331	150	320	121	317	163	364	189	367	205	369	174	354				
86	226	345	94	199	333	149	332	157	325	124	318	173	370	192	372	212	371	178	368				
90	229	346	96	206	336	152	333	159	328	126	321	175		193		213		186					
92	233	347	97	207	337	153	336	162	335	128	322												
95	234	348	98	210	338	154	338	164	337	129	323												
99	238	349	101	213	340	163	342	175	340	132	324												
100	239	352	102	215	341	167	343	176	341	133	327												
104	243	353	103	216	350	168	344	178	348	136	329												
105	245	354	106	217	351	170	345	181	350	137	330												
107	247	357	108	218	355	172	347	183	351	138	334												
117	248	362	109	223	356	179	353	186	354	141	339												
118	249	363	110	225	358	182	355	187	356	143	346												
119	254	364	111	227	359	184	359	188	357	144	349												
120	256	366	112	228	360	185	361	190	358	145	352												
125	257	367	113	230	361	193	363	192	360	147	362												
128	258	368	114	231	365	194	367	195	365	151	364												
133	259	370	115	232	369	197	368	196	366	155	370												
134	260	371	116	235	372	205	372	198	369	156	371												

Table 4. *Results of patient allocation by randomization and random sampling*

Demographic features		Randomization into Two Groups		Randomization into Three Groups			Randomization into Four Groups				Random Sampling			
	Total N=372	I N=186	II N=186	I N=124	II N=124	III N=124	I N=93	II N=93	III N=93	IV N=93	I N=25	II N=25	III N=25	IV N=25
Male	**40%**	42%	38%	42%	36%	44%	39%	42%	38%	43%	36%	52%	28%	32%
Female	**60%**	58%	62%	58%	65%	57%	61%	58%	62%	57%	64%	48%	72%	68%
Age (yrs.)	**47 + 0.8**	46 + 1.1	48 + 1.1	45 + 1.3	48 + 1.4	48 + 1.4	43# + 1.4	48 + 1.7	49 + 1.6	47 + 1.6	50 + 3.3	40# + 2.3	49 + 3.0	46 + 2.8
Height (inches)	**67 + 0.2**	67 + 0.3	67 + 0.3	67 + 0.3	67 + 0.3	67 + 0.4	67 + 0.4	67 + 0.4	67 + 0.4	67 + 0.4	67 + 0.7	67 + 0.6	67 + 0.8	67 + 0.8
Weight (lbs.)	**180 + 2.4**	184 + 3.6	177 + 3.1	178 + 4.1	175 + 3.8	187 + 4.4	185 + 4.9	181 + 4.6	176 + 4.4	179 + 5.3	187 + 9.1	188 + 10.2	175 + 9.7	171 + 7.6
Duration of pain (months)	**102 + 2.4**	92 + 8.6	111 + 9.5	108 + 10.7	82 + 9.5	116 + 12.6	87 + 10.9	96 + 12.6	99 + 13.0	125 + 14.3	92 + 16.9	86 + 24.2	97 + 24.1	152 + 37.6
Gradual onset	**51%**	47%	55%	52%	52%	51%	41%	53%	59%*	53%	72%	40%	48%	52%
Involvement of regions														
Cervical	**47%**	43%	53%*	44%	56%	52%	47%	46%	49%	46%	48%	60%	52%	60%
Thoracic	**22%**	22%	21%	24%	20%	22%	25%	21%	16%	26%	20%	12%	20%	20%
Lumbar	**79%**	81%	77%	82%	77%	78%	79%	75%	79%	85%	64%	72%	84%	80%
Number of regions														
One region	**100%**	100%	100%	100%	100%	100%	100%	100%	100%	100%	56%	44%	44%	48%
Two regions	**56%**	54%	58%	52%	58%	58%	57%	56%	54%	58%	24%	40%	32%	36%
Three regions or more	**22%**	20%	23%	25%	18%	23%	24%	17%	17%	29%	20%	16%	24%	16%
Psychological status														
Depression	**58%**	61%	55%	61%	57%	57%	63%	53%	63%	53%	60%	44%	68%	72%
Generalized anxiety disorder	**54%**	55%	53%	58%	51%	53%	58%	45%	60%	53%	52%	44%	72%	72%
Somatization disorder	**34%**	34%	33%	40%	32%	30%	37%	24%	41%	33%	32%	20%	52%	44%
Non-physiologic features														
Non-physiologic symptoms	**15%**	14%	16%	21%	12%	11%	14%	9%	16%	20%	16%	12%	16%	20%
Non-physiologic signs	**15%**	14%	16%	21%	14%	11%	16%	11%	17%	17%	12%	8%	12%	24%
Symptom magnification	**24%**	24%	24%	34%	19%*	21%*	27%	17%	29%	26%	20%	16%	28%	32%
Clinical approach														
Interventional procedures	**74%**	73%	74%	75%	69%	77%	75%	71%	68%	81%	88%	64%	72%	80%
Non-interventional approach	**19%**	21%	18%	19%	24%	15%	22%	18%	21%	16%	12%	20%	8%	4%
Evaluation only	**7%**	6%	8%	6%	7%	8%	3%	11%	11%	3%	0%	16%	20%	16%
Dropout rate	**25%**	22%	26%	22%	26%	26%	18%#	27%	26%	27%	44%#	20%	12%	16%

* Indicates significant difference with Group I # Indicates significant difference with Total sample

compared to Group I, with randomization into three groups; 3) mean age was lower in Group I, compared to total sample, with randomization into four groups; 4) incidence of dropouts was lower in Group I, compared to total sample with randomization into four groups; 5) incidence of gradual onset of pain was higher in Group III, compared to Group I, with randomization into four groups; 6) mean age was lower in Group II, compared to total sample with random sampling; and 7) incidence of dropouts was higher in Group I, compared to total sample with random sampling.

DISCUSSION

Systematic reviews and meta-analysis offer an opportunity to test implicit assumptions about the hierarchy of research designs (8). If particular associations between exposure and outcome were studied in both randomized, controlled trials and cohort or case-controlled studies, and if these studies were then included in meta-analysis, the results could be compared according to study design, as has been done for trials with historical controls (5, 8).

In the past, comparative studies have repeatedly demonstrated no significant difference between randomized, controlled trials or observational reports. The distinction between random sampling and randomization (random allocation) also has been misunderstood. The purpose of random sampling is to choose a group that is a representative of a larger population, and random sampling is not usually employed in controlled trials. The purpose of randomization, on the other hand, is to divide a single group into groups that differ only by chance. Randomization is the only way to ensure that individuals entered into a trial are not allocated to the treatment or control groups in a biased manner. The results of this study show there are no significant differences by various types of allocation of patients into groups, except with randomization, which demonstrated differences in only one aspect in two of three samples.

The results of this study show that patients presenting to interventional pain management setting are predominantly female, with a mean age of 47 + 0.8 years, mean height of 67 + 0.2 inches, mean weight of 180 + 2 lbs., with duration of 102 + 6.4 months, with 51% of the patients with gradual onset with 29% with history of previous surgery and 69% referred by a physician.

Ninety-three percent of the patients showed involvement of spine, whereas only 7% of the patients presented with non-spinal pain. Fifty six percent of the patients presented with involvement of at least two regions, whereas, 22% of the patients presented with involvement of three or more regions. Involvement of cervical spine and lumbar spine was seen in 24%, whereas cervical spine, thoracic spine and lumbar spine was involved in 11% of the patients.

Fifty-eight percent of the patients presented with depression, compared to 54% with generalized anxiety disorder and 34% with somatization disorder. Non-physiologic symptoms and signs were seen each in 15% of the patients, whereas symptom magnification was seen in 24% of the patients.

Seventy-four percent of the patients were treated with interventional procedures compared to 19% of the patients treated without interventional procedures. Seven percent of the patients underwent evaluation only. The dropout rate was 25%. Reasons for dropout were multiple, including lack of insurance approval, lack of response, drug abuse and other miscellaneous reasons.

The results of this study show that there was only one significant difference among the groups when they were allocated by multiple means, without randomization (Table 1). Randomization also showed similarity among the groups, however; significant, differences were noted, in seven aspects (Table 4). The proponents of randomization agree that these differences may be considered the result of chance. However, the results show that allocation by other means may be superior to randomization thus avoiding numerous difficulties. This is a preliminary study demonstrating allocation to be reliable by any means as long as the physician is not involved in influencing the results. Thus, allocation by multiple means, either by serial numbers, by date of admission, by randomization into equal groups, or by random sampling into small groups, is equally effective.

Evidence-based medicine is a loose term, which has been used based not only on the necessity to present a particular view, but also based on personal philosophy, bias and conjecture. A current definition of evidence-based medicine is: the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients. Thus, evidence-based medicine is essentially what most clinicians have been trying to practice all their working lives. The practice of evidence-based medicine requires the integration of individual clinical expertise with the best available external clinical evidence from systematic research. Thus, apart from the results of randomized, controlled trials, there are a multitude of other evidence-based sources for clinical and policy decisions. All valid, relevant evidence should be considered in the decision-making process. Thus, no one sort of evidence should necessarily be the determining factor in decision-making (9). "All" implies that there should be an active search for all that is valid, relevant information and that an assessment should be made of the accuracy of information and the applicability of the evidence to the decision in question (10). Straus et al (11) described many misperceptions of evidence-based medicine. They state that rather than denigrating clinical

experience (12, 13), evidence-based medicine acknowledges expertise as the basis for all clinical practice. They also state that evidence-based medicine promotes patient values and clinician independence. It has also been suggested that the criticism of evidence-based medicine as an ivory-tower concept (14) which is not the case (15-27). Strauss et al (11) observed that it is a misperception that only randomized, controlled trials or systematic reviews constitute evidence-based medicine (14, 28). Thus, evidence-based medicine emphasizes the consideration of evidence from various types of studies appropriate to different clinical questions. The questions have been raised about the validity of evidence-based medicine when observation reports, and even unpublished observations have been excluded from consideration in a systematic review or guideline development, etc.

In spite of overwhelming evidence that evidence-based medicine includes all types of evidence, only the randomized, double-blind studiesare considered to represent the best available evidence. Randomized, double-blind trials have been considered the gold standard in judging the effectiveness of therapy. Many stumbling blocks, including the issues of ethics, feasibility, cost and reliability, pose frequently insurmountable challenges to randomized, double-blind trials in interventional pain management (29-35). Further, the value of the so-called gold standard of randomized, double-blind trials has been questioned. Benson and Hartz (36) outlined several advantages of observational studies over randomized, controlled trials, including lower costs, greater timeliness and a broader range of patients. Concato et al (8) in evaluating various types of clinical evaluations concluded that average results of observational studies were remarkably similar to those of randomized, controlled trials and that the results of well-designed observational studies do not systematically overestimate the magnitude of the effects of treatment as compared with those in randomized, controlled trials on the same topic.

In spite of a strong argument for other types of evidence, clinical research worships at the shrine of the randomized, controlled trial. The ability to assign subjects randomly to either experimental or controlled status is considered as science that is unsurpassed. However, random assignment does not confer an absolute protection against bias. It simply reduces the likelihood that such bias has occurred. Because randomized, controlled trials are complicated and difficult to conduct, they are usually restricted to very tightly targeted groups of patients. Often, the investigators are not actively concerned about how the subjects are obtained and rely on random allocation to distribute any differences equally across the two groups. As a result, randomized trials often trade internal validity (tightness of comparisons) for external validity (generalizability) (37). Hence, randomization does not provide the protective shield that some think. Further, many patients refuse to participate in the process with the belief that randomization always puts them in the control groups. Thus, it does not seem feasible to rely exclusively on randomized, controlled trials for all, or even most, of the needed empirical data linking outcomes to the process of care (8). Generally, a difference in outcome between a treatment and a control group can be due to chance, confounding, or bias due to differences between the groups, differences in handling the groups; and the true effect of intervention. Confounding and bias are avoided in the design of a trial by randomization, single-blinding or double-blinding. Thus, randomization is considered as a cornerstone to avoid bias and to maintain similarity between treatment and control groups, thus influencing the eventual outcome. Randomization by the tossing of a coin (or any equivalent method) ensures that the physician running the trial is not consciously or unconsciously allocating the certain patients to a particular group. Without randomization, trials of surgical versus medical technique are wide open to selection bias. It is assumed that low-risk cases are much more likely to be assigned to the operative group, leaving high-risk patients to be managed by the physicians. Assigning volunteers to the treatment group and those who do not volunteer to the control group is also likely to result in a biased comparison-volunteers will be quite different, in many respects, from patients who do not volunteer (38). The criticism also has been advanced against allocation to treatment or control groups based on alternate days, alternate numbers or another assigned preformed methodology. Even though, it is believed that randomization does ensure that the two groups will differ only by chance, it does not guarantee that in practice, the balance will be actually achieved through the randomization.

CONCLUSION

The results of this study show that in an interventional pain management setting, 29% of the patients have undergone previous surgery, 49% of the patients developed pain problems following an incident, female patients constituted 60%, spinal pain constituted 93% and 56% of the patients suffered with more than one region involvement. Sixty percent of the patients presenting to this interventional pain management practice presented

with one or a combination of multiple psychological disorders including depression, generalized anxiety disorder and somatization. Interventional procedures were performed in 74% of the patients with a total dropout rate of 25% from the program.

Comparison of the samples allocated by two non-randomized means, showed basically no significant differences except by chance which was demonstrated only in one parameter. However, randomization showed significant differences, in one to two parameters, in each mode of randomization or random sampling. Thus, we conclude that any systematic type of allocation will yield valid results with similar groups of patients with or without randomization. However, further studies into the validity of this concept needs to be evaluated.

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