The effectiveness of suggestive techniques in reducing post-operative side effects: a meta-analysis of randomized controlled trials

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Abstract

Background Suggestive interventions such as hypnosis and therapeutic suggestions are frequently used to alleviate surgical side effects, however the effectiveness of therapeutic suggestion intervention have not been systematically evaluated yet. The present study tested the hypotheses that 1) suggestive interventions are useful in reducing postoperative side-effects; 2) therapeutic suggestions are comparable in effectiveness to hypnosis; 3) live presentation is more effective than recordings; and that 4) suggestive interventions would be equally effective used around minor and major surgeries.

Methods We performed random effect meta-analysis with meta-regression and sensitivity analysis by moderating factors on a pool of 26 studies meeting the inclusion criteria (N = 1,890). Outcome variables were postoperative anxiety, pain intensity, pain medication requirement and nausea.

Results Suggestive interventions reduced postoperative anxiety (g = 0.40; 95% CI = 0.20, 0.59; p < .001), pain intensity (g = 0.25; 95% CI = 0.06, 0.44; p = .010) and nausea (g = 0.38; 95% CI = 0.05, 0.71; p = .026); but did not significantly affect postoperative analgesic drug consumption (g = 0.16; 95% CI = -0.08, 0.40; p = .202).Moderator analysis revealed that hypnosis was significantly more effective in decreasing anxiety than therapeutic suggestions (z = 2.51; p = .012), that live presentation was more effective in alleviating postoperative pain than recordings (z = 2.18; p = .029), while recordings reduced analgesic drug requirement more effectively (z = -2.08; p = .037). Sensitivity analyses also suggested that suggestive interventions are only effective in decreasing pain intensity during minor surgical procedures (g = 0.39; 95% CI = 0.10, 0.69; p = .009).

Conclusions Suggestive techniques are useful tools to alleviate postoperative side-effects although the size of the effect differ among outcomes. Contrary to our hypothesis therapeutic suggestions proved to be less effective than hypnosis interventions, and the moderating effect of presentation method (live vs. recorded) remain ambiguous. Our hypothesis that suggestive interventions alleviate postoperative anxiety both in minor and major procedures was supported, however they only seem to be effective in pain management in minor surgeries. For clinical purposes we advise the use of hypnosis with live presentation. Further research is needed to uncover additional moderating factors of effectiveness.

Keywords

Therapeutic suggestions; Hypnosis; Surgery; Postoperative side effects

Introduction

In the middle of the 19th century suggestive techniques were frequently used as the only analgesic procedure for surgical operations until the introduction of pharmaceutical methods[1]. Among these suggestive techniques, hypnosis is the most recognized psychological intervention in modern medicine which is demonstrated to effectively aleviate postoperative side effects. Particularly hypnosis decreases postoperative distress, pain, pain medication requirement, nausea, treatment time, and improves postoperative wellbeing and recovery[1-8]. The distinctive characeristic of hypnosis is that it includes a formal "hypnosis induction" before the application of suggestions in order to increase suggestive effects[9]. They also overtly identify the applied technique as "hypnosis".

Despite its established benefits, there is an ongoing debate whether hypnosis truly increases susceptibility to suggestions and wheter it is necessary for suggestions to be effective[10-15]. Some theories propose that patients in medical settings (e.g. being in critical condition, or waiting for an invasive operation, etc.) can experience a spontaneous trance which in itself enhances suggestibility[16-19]. Accordingly, there is evidence that suggestions given without hypnotic induction (from here on, "therapeutic suggestions") can influence perioperative outcome[1]. The meta-analysis of Schnur and colleagues[5] included six studies in which the intervention was labeled as 'suggestions' and they concluded that 'suggestions' were less effective in reducing perioperative distress than hypnosis. However this meta-analysis did not systematically search for 'suggestion' studies and they only assessed effectiveness on a single outcome variable (perioperative distress), thus the generalizability of these results is limited. Therapeutic suggestions do not require hypnotic induction, thus they are quicker and cheaper to use, they can be applied by more healthcare professionals as they do not require complex

hypnotherapy training, and the common misconceptions regarding hypnosis can also be overcomed by these methods. Therefore it is important for decision makers to know whether therapeutic suggestions are real altenatives of formal hypnosis.

The aim of the present study is to systematically investigate the effectiveness of therapeutic suggestions compared to hypnosis in alleviating postoperative side-effects. Furthermore, we want to assess how moderating factors such as the method of presentation (live or recorded) and severity of surgery (minor or major) affect the effectiveness of suggestive interventions. We hypothesized that 1) suggestive interventions significantly reduce postoperative anxiety, pain intensity, pain medication requirement and nausea; that 2) therapeutic suggestions are comparable in effectiveness to hypnosis, that 3) live suggestions are more effective than recorded ones; and that 4) suggestive interventions are equally effective used in minor and major surgeries.

Methods

Data sources and search strategy

Literature search was conducted on five online databases (PubMed, PsycINFO, CINAHL and Proquest Dissertations & Theses Database) for studies published between 1980 and 2014 on hypnosis or therapeutic suggestion interventions applied in surgery with no limitations to language or publication status. Setting a minimum publication date was necessary to improve generalizability to modern surgical, anesthesia and suggestive procedures.

The literature search was finished on February 21, 2014. We used the keywords ’hypnosis’, ’suggestion’ and ’surgery’ along with their variants and synonyms (see Appendix A in the supplementary material for exact search terms).

Selection Criteria

Randomized controlled trials (RCTs) on the effectiveness of therapeutic suggestions or hypnosis applied adjunct to routine surgical care were eligible for inclusion. Non-RCTs, observational studies, and case reports were excluded from analysis. As children are more susceptible to hypnosis and respond better to suggestive interventions in clinical settings than adults, studies conducted on a pediatric population (patients' age below 17) were also excluded[5,20,21]. For reviews on hypnosis applied during medical procedures with children, readers are advised to consult Accardi and Milling[22] or Kuttner[23]. After data extraction we decided to exclude studies in which suggestions were given under general anesthesia, mainly because the distribution of moderating factors were highly asymmetric in these studies. Specifically, when suggestions were presented under general anesthesia, they were always given without hypnosis induction and played from a recording. The effectiveness of suggestive techniques were compared to ‘regular treatment’ (no psychological intervention) or ‘attention control’ conditions.

Data extraction

Data extraction was performed by the first and second authors independently. Disagreements were resolved by consensus. The extracted data included number of participants by study group, presence or absence of formal hypnosis induction, type of presentation (live or recorded), if both

live and recorded presentation were used as part of the intervention, it was coded as live), timing of intervention (before, during, or after surgery), methodological quality (see Risk of bias assessment), and any 'special care' not related to the suggestive intervention that could have affected postoperative outcomes (see a comprehensive list in Appendix B in the supplementary material). The surgical procedure used in the study was also extracted. Two physicians independently rated the procedures as being minor or major surgery according to the definitions of McGraw-Hill Concise Dictionary of Modern Medicine[24].

Outcomes

Based on previous meta-analyses[3-5] and the frequency of occurrence in the reviewed studies four outcome measures were selected: 1) postoperative anxiety or distress, 2) postoperative pain intensity, 3) postoperative pain medication requirement, 4) postoperative nausea. For a comprehensive list of measures used in the included studies to assess the aforementioned outcomes see Appendix C (supplementary material). As we were interested in the short-term postoperative effects, only data measured until the ninth postsurgical day was extracted. To address ambiguities or the need for additional data, the corresponding authors of the papers were contacted via e-mail.

Risk of bias assessment

Methodical quality was assessed using the Cochrane Risk of Bias Assessment Tool[25]. This tool enables the evaluation of selection, performance, detection, attrition and reporting bias with several customizable assessment categories. During the process of evaluation studies were rated

as having “Low risk of bias”, “Unclear risk of bias”, or “High risk of bias” on the following attributes: a) random sequence generation, b) allocation concealment, c) blinding of personnel, d) blinding of outcome assessment, e) incomplete outcome data, and f) selective reporting. Since hypnosis – contrary to therapeutic suggestions – requires the consent and participation of the subject, the blinding of the participants is usually inappropriate[1]. Thus we did not consider lack of blinding of participants a flaw in methodical quality.

Publication bias was assessed using Begg and Mazumdar’s rank correlation[26], the random effect variant of Egger’s test[27], Duval & Tweedie’s[28] trim and fill method, and the inspection of the funnel plots[29].

Statistical Analysis

Calculating treatment effect

Corrected Hedges’ g (g) was used as a measure of effect size[30]. (On the interpretation of g values consult for example Cohen[31]). If the mean and standard deviation was not reported in the original studies, effect sizes were calculated using other statistics, using the equations by Johnson and Eagly[32], and Lipsey and Wilson[33]. If necessary, effect sizes were aggregated[34,35]. For studies which did not report any test statistics or significance values for non-significant results we imputed g = 0 (referred to as ”imprecise inference” from here on).

Statistical analysis

Statistical analysis was performed using the metafor package in R[36]. Statistical heterogeneity (I^2) yielded medium to high values, which supported the application of a random-effect approach[37-39]. Random effect meta-analysis was used to obtain the general effect size of suggestive methods on postoperative side-effects, to assess publication bias, and to have a reference point for later sensitivity analyses. meta-regression was used to investigate the risk of bias for all outcome variables including all categories from the Cochrane Risk of Bias Assessment Tool as binomial variables: 0 = Low risk of bias; 1 = Unclear or High risk of bias. A permutation-based technique[40] was used to control for multiple hypothesis testing, and sensitivity analyses were carried out to further investigate significant moderator effects by excluding studies with unclear or high risk ratings. Moderator effects of imprecise inference and special care (see data extraction) were tested as well, accompanied by appropriate sensitivity analyses.

Subsequently three meta-regressions were executed for each outcome testing the moderating effect of hypnosis induction, live vs. recorded presentation and surgery type (minor vs. major surgery). In addition, sensitivity analyses were also performed on datasets split by moderator conditions. One study[41] in the anxiety and pain datasets was omitted from the analysis of the effect of surgery type because of insufficient information to determine surgery type[41].

Results

Study selection

As Figure 1 shows, 139 records were selected for full text evaluation. 16 of these could not be retrieved (see the list in Appendix D, supplementary material) and 16 were duplicate publications. From the remaining 107 publications 56 used hypnosis, 49 used therapeutic suggestions and two used both. All non-RCTs, studies on pediatric patients, studies that did not report outcome of interest, and trials in which suggestions were given only during general anesthesia were excluded. 26 studies were retained at the end of the exclusion process incorporating a total number of 1890 patients (range: n = 12 - 346) of which 13 applied hypnosis, 11 therapeutic suggestions and 2 both in separate groups; 13 used live and 13 recorded presentation; furthermore 14 were carried out in major and 11 in minor surgical procedures (not enough information on surgery type in 1 study). Cholecystectomy (6 studies) and hysterectomy (4 studies) were the most commonly used surgical procedures. Four studies contained more than one relevant experimental conditions. See Table 1 for study characteristics.

General effects of suggestive techniques

As apparent in Table 2 and the forest plots in Figures 2 - 5, we found significant reduction in postoperative anxiety ($g = 0.40$; 95% CI = 0.20, 0.59; $p < .001$), pain intensity ($g = 0.25$; 95% CI = 0.06, 0.44; $p = .010$) and nausea ($g = 0.38$; 95% CI = 0.05, 0.71; $p = .026$); whereas no significant effect was noted for postoperative analgesic drug consumption ($g = 0.16$; 95% CI = -0.08, 0.40; $p = .202$).

Risk of bias and effects of imprecise inference and special care

Results of risk of bias assessment for each study and a summary graph is displayed in Figures 6-7 in the supplementary material. Meta-regression identified two methodological moderators as significant: random sequence generation in the anxiety dataset (z = 2.48; p = .018) and blinding of personnel in the nausea dataset (z = -3.84; p = .003, see Table 3). Running a sensitivity analysis with the exclusion of studies with unclear or high risk on random sequence generation resulted in a small, non-significant estimate for the effect on postoperative anxiety (g = 0.16; *95% CI* = -0.19; 0.50; p = .376). Exclusion of studies with high or unknown risk on blinding of personnel produced a slightly higher pooled effect size than the model without moderators (g = 0.49; *95% CI* = 0.04; 0.94; p = .032). Effect on postoperative pain and pain medication requirement was unaffected by methodical quality. Table 2 shows that there was no moderator effect of imprecise inference and that studies with special care had higher effects compared to studies with no special care.

There was no indication of publication bias based on funnel plots and asymmetry tests (see Figures 8-11 in the supplementary material). Duval & Tweedie's trim and fill method does not change our interpretation for anxiety, pain intensity and nausea. However it predicted four missing studies from the right (positive) side for the pain medication dataset, and estimated a significant effect (g = 0.31; *95% CI* = 0.06, 0.55; p = .015).

Analysis of moderators

Results of the moderator and sensitivity analyses on the main moderating factors can be found in Figures 12-15.

Hypnosis induction

Hypnosis induction had a significant moderator effect on postoperative anxiety ($z = 2.51$; $p = .012$), and although the moderating effect of hypnosis was not significant for the other outcomes, sensitivity analysis led us to different conclusions on the effects of therapeutic suggestions and hypnosis. While pooled effect size and confidence intervals show a small non-significant effect for therapeutic suggestion studies on all outcomes, hypnosis had a significant medium sized effect on postoperative anxiety and nausea, and a significant small to medium effect on postoperative pain intensity.

Presentation method

Live presentation was more effective in decreasing pain ratings than recorded presentation ($z = 2.18$; $p = .029$); however recordings are superior in reducing pain medication requirement ($z = -2.08$; $p = .037$). The sensitivity analysis showed a medium sized significant effect of live presentation on anxiety and pain intensity, while recorded presentation yielded non-significant results. On the other hand recorded interventions decreased pain medication requirement significantly with a small effect size, while live presentation did not reduce analgesic drug use.

Surgery type

Moderator analysis did not show significant moderator effect of surgery type, although sensitivity analysis led to somewhat differing conclusions for the effectiveness of suggestive interventions used in minor and major surgeries. Both interventions used in minor and major procedures reduced anxiety significantly with a medium effect size, and neither had a significant effect on pain medication requirement. However, while studies on major surgical surgeries showed negligible effect sizes in reducing pain and analgesic requirement, pooled effect sizes were medium sized for the same outcomes in minor procedures.

Discussion

The present study reviewed the results of twenty-six studies to investigate the effects of suggestive interventions in surgical settings, and to explore the factors that moderate their effectiveness. We found that suggestion interventions had a beneficial effect on postoperative anxiety, pain intensity, and nausea, and while no significant effect was found on pain medication requirement in the main analysis, trim and fill method suggests a small but significant reduction in this outcome as well. These findings are in line with previous results indicating that psychological techniques in general[3] - and hypnosis in particular[4-7] - provide effective treatment for postoperative side-effects. Furthermore our results are comparable to the small to medium effect sizes reported by previous meta-analyses[5-7].[a]

Contrary to our hypothesis but in line with the report of Schnur and colleagues[5], our findings suggests that hypnosis is better at reducing postoperative anxiety, pain and nausea than therapeutic suggestions. In fact, while hypnosis was characterized by significant medium effect sizes on these outcomes, we found no significant effects for therapeutic suggestions. The fact that the pooled effect sizes of therapeutic suggestions studies were all positive might suggest that these interventions have a small favorable effect, but our study lacked power to detect it.

The effect of presentation method showed a complex picture. Our moderator and sensitivity analyses yielded that live presentation was better at reducing postoperative anxiety and pain intensity, however we also found that recordings reduced analgesic requirement more effectively than live presentation. Previous research also reported mixed results about the effects

[a] The markedly higher intervention effects reported by Montgomery and colleagues[15] may be explained by the facts that contrary to the present meta-analysis non-RCTs were included while studies not reporting adequate statistics were excluded from their analysis, and that they used a fixed effect model.

of presentation method. While Schnur and colleagues[5] supported the superiority of live presentation in reducing postoperative distress, two other meta-analyses did not find significant difference between face-to-face and taped presentation[4,6] Although Schnur and colleagues[5] only addressed one outcome, and Montgomery and colleagues[4] used a combined effect size of several outcomes during the assessment of this moderator effect. Previous reports also point out the high correspondence between moderating factors, i.e. studies using live presentation also tend to use hypnosis instead of therapeutic suggestions and preoperative instead of intra- or postoperative presentation of the intervention. So reasons for differences in effectiveness by presentation method could lie in a third variable. For example four of the eight studies using recorded presentation in the pain medication dataset used the same suggestion script devised by Enqvist and colleagues[42]. Thus it is possible that results are distorted by this really effective protocol. Another possibility is that pain management techniques taught in suggestive interventions need to be rehearsed several times to be effective, which is more easily achieved with recordings.

In line with previous reports, no significant moderator effect was found for surgery type[6] Suggestive interventions had the same effectiveness in decreasing anxiety and nausea in minor and major surgeries. However according to the sensitivity analysis suggestions were only effective in managing pain in minor procedures. Major surgeries involve more effective analgesics compared to minor surgeries because they inflict more post-operative pain[43]. Thus it is possible that effects in major procedures are masked by the rigorous analgesic protocols. It is also possible that pain management techniques used in suggestive interventions are less effective in cases of severe pain.

Limitations

The present study has a number of limitations. A large portion of the studies did not report baseline statistics for the outcome measures, thus only between group comparisons were used in the analysis. Access to within-subjects data could have led to more accurate estimation of effect sizes. The meta-regressions also indicated that effects on anxiety might be biased by inappropriate random sequence generation. Because of the overlap between moderator conditions (e.g. studies with hypnosis induction were typically presented live, while therapeutic suggestions were mostly presented from recordings) the effects of live presentation and formal hypnosis are hard to distinguish. The majority of the included studies used single blind design (no blinding of participants) and passive control condition (i.e. regular treatment) which might have resulted in a bias favoring the intervention because of expectancy effects. Furthermore, 16 of the 139 studies selected for detailed full text assessment could not be retrieved. We also have to keep in mind that our results only apply to the selected outcomes and cannot be generalized. Clinically relevant outcome measures differ from procedure to procedure, and there is a possibility, that some of the suggestive interventions were tailored to address these specific issues (e.g. the main aim of the intervention in the study of Szeverényi and colleagues[44] is to reduce bleeding during orthopedic surgery).

Conclusion

The novelty of the present study is that it included a systematic search for both therapeutic suggestion interventions and hypnosis, this way we were able to draw conclusions on suggestive interventions in general, and address the difference between hypnosis and therapeutic suggestions in particular. Overall our results indicate that suggestive interventions can help surgical patients

to cope with postoperative side effects. For therapeutic purposes we suggest the use of suggestions with hypnosis induction and face-to-face presentation to alleviate postoperative side-effects. However, despite the lower effect sizes, the use of suggestions in the perioperative period should not be discarded just yet. Lower treatment effects compared to hypnosis might be offset by lower costs and wider applicability.

To get a clearer picture of the presently assessed moderators, studies with rare combinations of moderator factors (e.g. recorded hypnosis, live suggestions during and after surgery, and during general anesthesia etc.) are needed. Future studies should also focus on other factors that might moderate effectiveness, like the repetition of suggestions, positive versus negative phrasing of suggestions, customization of suggestion scripts to the individual patients, susceptibility to suggestions, or the experience level of the surgeon and the hypnotherapist. However the evaluation of these moderating factors is only possible if the authors publish the necessary information, including full suggestion scripts and protocols. We encourage all researchers to provide such scripts in full lengths, and journals to publish them either as an appendix or an online supplement.

Declaration of interests

Two of the papers[44,45] included in the review is a work of the first and the third authors (KZ and VK)

Author's Contribution

Z. K.: study design, literature search, data extraction and analysis, and writing up the manuscript

T. N.: study design, data extraction, and writing up the manuscript

K. V.: providing theoretical background and writing up the manuscript

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Tables

Table 1. Study characteristics

Study	n	Induction	Presentation	Timing	Outcome	Surgical procedure	Type of surgery
Ashton, et al., 1997[46]	32	hypnosis	live	a, c	anx, pme	coronary artery bypass surgery	ma
Blankfield, et al., 1995[47]	63	suggestion	recorded	b, c	anx, pme	coronary artery bypass surgery	ma
Cruise, et al., 1997[48]	60	suggestion	recorded	b	anx	cataract surgery	mi
de Klerk, et al., 2004[49]	50	hypnosis	live	a, c	anx	coronary artery bypass surgery	ma
Enqvist, et al., 1997a[50]	69	hypnosis	recorded	a	pai, pme	removal of third mandibular molars	mi
Enqvist, et al., 1997b[42]	48	hypnosis	recorded	a	pai, pme, nau	elective breast reduction surgery	ma
Ghoneim, et al., 2000[51]	60	hypnosis	recorded	a	anx, pai, pme, nau	removal of third mandibular molars	mi
Ginandes, et al., 2003[52]	12	hypnosis	live	a, c	pai	elective breast reduction surgery	ma
Hart, 1980[53]	40	hypnosis	recorded	a	anx	cardiopulmonary bypass surgery	ma
Holden, 1985[54]	24	suggestion	recorded	a, c	anx	cholecystectomy	ma
Jakubovits, et al., 1998a*[55]	26	suggestion	recorded	a	anx, pai	abdominal total extirpation,	ma

						adnexectomy, cholecystectomy	
Jakubovits, et al., 1998b*[55]	26	suggestion	recorded	a, b	anx, pai	abdominal total extirpation, adnexectomy, cholecystectomy	ma
John , et al., 1983[56]	59	suggestion	live	a	anx, pai	radial keratotomy (eye surgery)	mi
Kekecs, et al., 2014[57]	82	suggestion	recorded	a	anx	cataract surgery	mi
Lauder, et al., 1995[58]	190	suggestion	live	a	nau	total abdominal hysterectomy	ma
Marc, et al., 2007[59]	29	hypnosis	live	a, b	anx, pai	first-trimester surgical abortion	mi
Marc, et al., 2008[60]	346	hypnosis	live	a, b	anx, pai	first-trimester surgical abortion	mi
Massarini, et al., 2005[41]	42	hypnosis	live	a	anx, pai	not specified, but patients were recruited from the Surgery and Orthopeadics ward	
Migály, et al., 1991[61]	30	hypnosis	live	a, c	anx	obstetric/gynecological surgery: dilatation and curettage or only curettage	mi
Montgomery, et al., 2002[4]	20	hypnosis	live	a	anx, pai	excisional breast biopsy	mi
Montgomery, et al., 2007[62]	200	hypnosis	live	a	anx, pai, pme, nau	excisional breast biopsy or lumpectomy	mi

Nilsson, et al., 2003[63]	120	suggestion	recorded	c	anx, pai, pme, nau	varicose vein or open inguinal hernia repair	mi
Shulimson, 1987a*[64]	30	suggestion	recorded	c	anx, pai, pme	cholecystectomy	ma
Shulimson, 1987b*[64]	30	hypnosis	live	a	anx, pai, pme	cholecystectomy	ma
Shulimson, 1987c*[64]	30	suggestion	recorded	a	anx, pai, pme	cholecystectomy	ma
Szeverényi, et al., 2012[44]	64	suggestion	live	a, b	pme	hip or knee prosthesis implantation	ma
Taenzer, 1983a*[65]	20	hypnosis	live	a	anx, pai, pme	elective gallbladder surgery	ma
Taenzer, 1983b*[65]	20	suggestion	live	a	anx, pai, pme	elective gallbladder surgery	ma
van der Laan, et al., 1996[66]	40	suggestion	recorded	a	anx, pai, pme, nau	hysterectomy, myomectomy, or gynecologic laparotomy.	ma
Woo, et al., 1987a*[67]	14	suggestion	recorded	a, b	pme	abdominal hysterectomy	ma
Woo, et al., 1987b*[67]	14	suggestion	recorded	a, b	pme	abdominal hysterectomy	ma

*Note: * data extracted for multiple intervention groups; intervention: suggestion refers to therapeutic suggestions; timing: a - before surgery; b - during surgery; c - after surgery; outcome: anx - anxiety; pai - pain; pme - pain medication; nau - nausea; type of surgery: ma – major; mi - minor*

Table 2. General effects of suggestive interventions and effects of risk of bias, imprecise inference and special care

	Pooled effect size, Lower and upper bounds and Z test							Heterogeneity		Moderator effect	
Database involved	Mean g	SE	z	p	95%CI lower	95%CI upper	k	I^2	H^2	z	p
Anxiety (all studies)	0.40	0.10	3.90	<.001*	0.20	0.59	24	66.64%	3.00		
Anxiety (with trim and fill)	0.31	0.10	3.06	.002*	0.11	0.52	27	12.59%	3.32		
Anxiety (without imprecise inference)	0.43	0.11	4.02	<.001*	0.22	0.64	22	67.92%	3.12	-1.19	.235
Anxiety (without special care)	0.45	0.14	3.29	.001*	0.18	0.72	15	66.99%	3.03	-0.65	.518
Pain intensity (all studies)	0.25	0.10	2.57	.010*	0.06	0.44	19	52.39%	2.10		
Pain intensity (with trim and fill)	0.32	0.10	3.33	<.001*	0.13	0.51	22	60.01%	2.25		
Pain intensity (without imprecise inference)	0.32	0.12	2.73	.006*	0.09	0.55	15	57.66%	2.36	-0.65	.518
Pain intensity (without special care)	0.24	0.10	2.39	.017*	0.04	0.43	11	14.37%	1.17	0.11	.910
Pain medication (all studies)	0.16	0.12	1.28	.202	-0.08	0.40	16	62.63%	2.68		
Pain medication (with trim and fill)	0.31	0.13	2.43	.015*	0.06	0.55	20	78.40%	3.30		
Pain medication (without imprecise inference)											
Pain medication (without special care)	0.21	0.18	1.14	.256	-0.15	0.56	10	73.40%	3.76	-0.60	.545

Nausea (all studies)	0.38	0.17	2.23	.026*	0.05	0.71	6	74.55%	3.93		
Nausea (with trim and fill)	0.38	0.17	2.23	.026*	0.05	0.71	6	78.62%	3.93		
Nausea (without imprecise inference)	0.45	0.19	2.39	.017*	0.08	0.81	5	76.47%	4.25	-0.94	.349
Nausea (without special care)	0.23	0.13	1.82	.068	-0.02	0.47	5	34.81%	1.53	2.58	.010*

Note. * $p < .05$

Table 3. Meta-regressions with risk of bias factors as moderators

Model component	estimate	SE	z	p	95%CI lower	95%CI upper
Anxiety						
Intercept	0.41	0.33	1.22	.828	-0.25	1.06
Random sequence generation	0.69	0.28	2.48	.018*	0.14	1.23
Allocation concealment	0.51	0.35	1.45	.154	-0.18	1.20
Blinding personnel	-0.62	0.33	-1.88	.058	-1.26	0.03
Blinding outcome assessment	0.13	0.32	0.39	.642	-0.50	0.75
Incomplete outcome data	-0.27	0.27	-1.02	.304	-0.81	0.26
Selective reporting	-0.40	0.33	-1.19	.240	-1.05	0.26
Pain						
Intercept	0.02	0.69	0.03	>.999	-1.32	1.37
Random sequence generation	0.13	0.36	0.36	.678	-0.58	0.85
Allocation concealment	0.11	0.42	0.26	.856	-0.72	0.93
Blinding personnel	-0.12	0.32	-0.38	.698	-0.74	0.50
Blinding outcome assessment	0.15	0.40	0.38	.688	-0.63	0.93
Incomplete outcome data	-0.24	0.38	-0.64	.528	-0.98	0.49
Selective reporting	0.09	0.47	0.18	>.999	-0.83	1.00
Pain medication[a]						
Intercept	-0.32	0.68	-0.47	.490	-1.66	1.01
Random sequence generation	0.12	0.31	0.40	.684	-0.48	0.72
Allocation concealment	0.26	0.42	0.62	.472	-0.57	1.09
Blinding personnel	-0.43	0.32	-1.31	.230	-1.06	0.21

Blinding outcome assessment	0.60	0.49	1.24	.204	-0.35	1.56
Incomplete outcome data	-0.27	0.46	-0.59	.596	-1.18	0.63
Nausea[b]						
Intercept	0.18	0.43	0.41	>.999	-0.66	1.01
Random sequence generation	0.77	0.29	2.61	.150	0.19	1.34
Allocation concealment	0.74	0.43	1.70	.378	-0.11	1.58
Blinding personnel	-0.91	0.24	-3.84	.003*	-1.38	-0.45
Incomplete outcome data	-0.69	0.18	-3.74	.061	-1.05	-0.33

*Note. * $p < .05$; a – All of the studies in the Pain medication dataset had Unclear risk of bias rating on Selective reporting; b – All of the studies in the Nausea dataset had Unclear risk of bias rating on Blinding of outcome assessement and Selective reporting.*

Figure legends

Figure legends for Figures 6-11 are contained in a separate file: 'supplementary material.docx'

Figure 1. Flow diagram

Figure 2. Effects of suggestive techniques on postoperative anxiety

The effect is expressed as corrected Hedges g with associated 95% confidence intervals (CI). Black squares show the point estimates of the effect of individual studies with horizontal lines corresponding to 95% CIs. The filled diamond (RE Model) represent the pooled estimates and 95% CIs. The sample sizes of the suggestion (N sg) and control groups (N cg) of each study is also displayed.

Figure 3. Effects of suggestive techniques on postoperative pain intensity

The effect is expressed as corrected Hedges g with associated 95% confidence intervals (CI). Black squares show the point estimates of the effect of individual studies with horizontal lines corresponding to 95% CIs. The filled diamond (RE Model) represent the pooled estimates and 95% CIs. The sample sizes of the suggestion (N sg) and control groups (N cg) of each study is also displayed.

Figure 4. Effects of suggestive techniques on postoperative pain medication requirement

The effect is expressed as corrected Hedges g with associated 95% confidence intervals (CI). Black squares show the point estimates of the effect of individual studies with horizontal lines corresponding to 95% CIs. The filled diamond (RE Model) represent the pooled estimates and 95% CIs. The sample sizes of the suggestion (N sg) and control groups (N cg) of each study is also displayed.

Figure 5. Effects of suggestive techniques on postoperative nausea

The effect is expressed as corrected Hedges g with associated 95% confidence intervals (CI). Black squares show the point estimates of the effect of individual studies with horizontal lines corresponding to 95% CIs. The filled diamond (RE Model) represent the pooled estimates and 95% CIs. The sample sizes of the suggestion (N sg) and control groups (N cg) of each study is also displayed.

Figure 12. Moderator and sensitivity analysis for postoperative anxiety

The effect is expressed as corrected Hedges g with associated 95% confidence intervals (CI). Black squares (Therapeutic suggestions or Hypnosis), discs (Recorded or Live presentation) and triangles (Minor or Major surgery) show the point estimates of the pooled effects of studies with the same moderating factor with horizontal lines corresponding to 95% CIs.

Figure 13. Moderator effects on postoperative pain intensity

The effect is expressed as corrected Hedges g with associated 95% confidence intervals (CI). Black squares (Therapeutic suggestions or Hypnosis), discs (Recorded or Live presentation) and triangles (Minor or Major surgery) show the point estimates of the pooled effects of studies with the same moderating factor with horizontal lines corresponding to 95% CIs.

Figure 14. Moderator effects on postoperative pain medication requirement

The effect is expressed as corrected Hedges g with associated 95% confidence intervals (CI). Black squares (Therapeutic suggestions or Hypnosis), discs (Recorded or Live presentation) and

triangles (Minor or Major surgery) show the point estimates of the pooled effects of studies with the same moderating factor with horizontal lines corresponding to 95% CIs.

Figure 15. Moderator effects on postoperative nausea

The effect is expressed as corrected Hedges g with associated 95% confidence intervals (CI). Black squares (Therapeutic suggestions or Hypnosis), discs (Recorded or Live presentation) and triangles (Minor or Major surgery) show the point estimates of the pooled effects of studies with the same moderating factor with horizontal lines corresponding to 95% CIs.

Appendices

Appendices A-D are contained in a separate file: 'supplementary material.docx'

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