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A COMPARATIVE STUDY OF TWO DIFFERENT ROUTES OF DEXMEDETOMIDINE ADMINISTRATION ON THE EFFICACY OF SUBARACHNOID BLOCK

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Abstract

Background: Dexmedetomidine has emerged as a wonder drug in regional anesthesia practice owing to its co-analgesic properties. However, there is a lack of literature for comparison of intrathecal with intravenous routes of dexmedetomidine administration on the effectiveness of subarachnoid block.

Methods: Prospective, randomized, double-blind study was carried out in 40 patients aged 18-60 years with ASA I and ASA II physical status scheduled for elective infraumbilical surgery under subarachnoid block. Participants were randomly divided into two groups. Subarachnoid block was administered with 3ml of hyperbaric Bupivacaine in both groups. Patients in Group 1 received intrathecal 5µg dexmedetomidine and intravenous infusion of normal saline during surgery. Patients in Group 2 received intravenous bolus dexmedetomidine infusion of 0.5 µg /kg followed by maintenance infusion of 0.5 µg/kg/hr. Block characteristics, Ramsay Sedation score and hemodynamic variables were recorded for all patients.

Results: The duration of motor block, the dermatomal level achieved and duration of analgesia was higher in group 1 compared to group 2. The groups were similar with respect to onset time of sensory and motor block, sedation score and hemodynamic variables. There were no significant side effects in either of the groups.

Conclusions: Dexmedetomidine by either intrathecal or intravenous route is an attractive adjuvant for infraumbilical surgical procedures performed under subarachnoid block. In cases where the requirement is to prolong duration of intraoperative anesthesia and postoperative analgesia intrathecal route is desirable. Whereas, in daycare surgeries where the requirement is only to intensify the block in the intraoperative period with early postoperative ambulation intravenous route is preferable.

Keywords: Dexmedetomidine, adjuvant, spinal anesthesia, drug administration routes, block characteristics, hemodynamics, Ramsay sedation score

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Background

Subarachnoid block (SAB)/spinal anesthesia is the mainstay of anesthesia for lower abdominal surgeries as it has the advantage of being easy to perform, economical, provides excellent operating conditions with a decent safety efficacy profile. But the key limitation of the method is its short duration of action which may necessitate conversion to general anesthesia if surgical duration is prolonged beyond 2.5 hours or need for early analgesic intervention in the postoperative period if SAB is administered using only local anesthetic drugs. To combat this, there has been an eternal search to bring out the best possible adjuvants to local anesthetic drugs in SAB which when added provide the benefit of intensifying the block causing reduction in the dose of local anesthetics required and prolong the duration of postoperative analgesia hence curtailing the cost of other analgesics.

In the evolution of local anesthetic adjuvant drugs, Dexmedetomidine has emerged as a wonder drug in today's world of modern anesthesia practice and has become the frequently used drug in anesthetic armamentarium in the perioperative setting. It is a highly selective α2-adrenoreceptor agonist and a popular co-analgesic drug with SAB owing to its hypnotic, sedative, anxiolytic, sympatholytic, opioid-sparing, analgesic, neuroprotective, cardioprotective and reno-protective properties without producing significant respiratory depression [1].

Studies conducted so far have used dexmedetomidine in intrathecal route in doses ranging from 3 µg to 15 µg along with bupivacaine and have observed a dose related prolongation of duration of motor blockade along with increase in the prevalence of side impacts of dexmedetomidine. They concluded that 5 µg is a safe and effective dose compared to higher doses without severe adverse effects [2]. Based on these studies, it was hypothesized that intrathecal 5 µg dexmedetomidine would produce more analgesic effect with hyperbaric bupivacaine in spinal anesthesia with minimal side effects. Studies performed using intravenous (IV) infusions of dexmedetomidine given before spinal anesthesia as premedication [3], as loading dose alone [4], as a loading dose followed by continuous infusion during surgery [5, 6] have found prolonged duration of sensory blockade of bupivacaine induced spinal anesthesia with additional advantages of sedation and analgesia [3].

However, there is no clear consensus on the effectiveness of different routes of dexmedetomidine administration used in conjunction with hyperbaric bupivacaine in SAB. Hence, there exists an increased demand for the application of an ideal cost-effective technique by which analgesia can be prolonged to encourage early ambulation of patients thus reducing the incidence of postoperative thromboembolic events, with reduced hospital stay hence decreased incidence of morbidity and mortality. Keeping this in mind, this study was formulated to compare the block characteristics using dexmedetomidine as an adjuvant to local anesthetics SAB by intrathecal route with intravenous route. We also aimed to evaluate the effect of the drug on hemodynamic parameters and adverse effects if any.

Methods

After obtaining institutional ethical committee approval this prospective, randomized, double blinded clinical trial was performed in teaching institution during May 2019 to November 2020. The study was carried out in accordance with the Declaration of Helsinki. It was performed in 40 patients belonging to ASA 1 physical status of either gender, between 18-60 years age group, of height 150-170 cm, scheduled for elective infraumbilical general surgical

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procedures. Randomization was done using simple random sampling method, Concealment by sealed opaque envelop method performed by an anesthesiologist involved in the study and the study participants were allocated to either Group 1 or Group 2. The procedure and recording were performed by another investigator who was unaware of the group allocation thus ensuring double blinding. Patients with preexisting cardiovascular, respiratory, neurological, psychological, renal or hepatic disease, patients on adrenergic blocking drugs, calcium channel blockers or with history of alcohol, opioid, sedative drug abuse and those with any contraindication to SAB were all excluded from the study.

Written informed consent was obtained from all the participants considered for the study. After confirming for 6 hours of Nil Oral status, an 18 G intravenous cannula was secured and preloading was done with 15 ml/kg of Ringer's lactate over 20 minutes duration. After the patient was taken on operation table, multipara monitors were connected and baseline parameters recorded. The technique of SAB was standardized in both the groups by positioning patient in sitting position for SAB administration, by choosing L3-L4 interspace standard midline approach using a 25G Quincke's needle for the technique, following duration of intrathecal drug administration over 10 seconds and immediately after completion of injection all the patients were made to lie supine.

Patients in Group 1 received intrathecal hyperbaric Bupivacaine (0.5%) 3ml with 5µg undiluted dexmedetomidine (total volume 3.2 ml) as an adjuvant. Immediately after positioning supine, intravenous (IV) infusion of 100 ml normal saline over 20minutes, followed by 0.5 ml/kg was administered.

Patients in Group 2 received intrathecal hyperbaric Bupivacaine (0.5%) 3ml with normal saline 0.2ml (total volume 3.2 ml). Immediately after positioning supine, IV dexmedetomidine infusion at 0.5 µg/kg diluted in 100ml normal saline over 20 minutes as bolus infusion, followed by maintenance infusion of 0.5 µg/kg/hour diluted in 0.5 ml/kg volume of normal saline was administered.

The IV infusion used in both the groups was discontinued once the surgeon began the skin suturing.

All patients received IV fluid as per calculation and oxygen supplementation was given if the SPO_2 falls below 95% on room air. Patients who had failure of SAB and converted to General anesthesia (GA) were all excluded from the study.

Sensory blockade was assessed by pinprick sensation method using 23 G hypodermic needle along the midclavicular line bilaterally. The highest level of sensory block attained was noted and the time taken to attain was considered as the onset time for sensory blockade. Recovery time for sensory blockade was defined as two dermatome regression of sensory (TDSR) anesthesia from the maximal level. Motor block was assessed using Modified Bromage Scale and time taken to attain Bromage 3 from the time of SAB drug injection was considered as the motor block onset time [7]. Duration of motor block (DMB) was the time taken for motor block to regress to Bromage scale 0 from the time of drug injection in SAB. Sensory and motor block were assessed every 1min for the first 20 minutes subsequently every 15 min till the end of surgery. Rescue analgesia was administered when the VAS score was ≥3 and the time from administration of SAB to VAS score 3 was considered that as the duration of analgesia. Paracetamol 1gm IV infusion was administered as rescue analgesic which was repeated every eight hourly thereafter. IV infusion of Diclofenac 75mg was chosen as the second line drug if there was no response to the initial rescue analgesic. Modified Ramsay sedation score (RSS) was used to evaluate sedation levels and was assessed every 15 minutes intraoperatively till the end of surgery. Intraoperative hemodynamic parameters (heart rate,

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systolic blood pressure, diastolic blood pressure, mean arterial pressure), respiratory rate and oxygen saturation were initially measured at 3 minutes interval for 30 min followed by every 5 min till the end of surgery. Postoperatively, hemodynamic parameters were monitored every hourly for 6 hours and sedation scores were not monitored as the scores reached normal within 15 minutes of stopping the drug. Occurrence of any side effects in the study participants were noted and treated accordingly. Bradycardia defined as HR<15% of baseline values, was treated with IV atropine 0.6mg injection. Hypotension defined as BP<15% of baseline values was treated with IV fluids or IV ephedrine 6mg bolus injections. Postoperative nausea and vomiting treated with IV Ondansetron 4mg injection. Shivering was treated with warming blankets and oxygen supplementation.

Statistical analysis

Considering a difference in means between two groups of 30 minutes in postop analgesia based on study by Songir S *et al*., a sample of 18 was considered adequate for the study, keeping ∝-error at 0.05 and power of the study at 80%. However, we took 20 patients in each group considering dropouts. Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented as Mean ± SD and results on categorical measurements are presented as numbers (%). Significance is assessed at 5% level of significance. Independent t test has been applied to determine the significance of difference between two groups. Chi-square test has been applied to determine the association between qualitative variables. P value of less than or equal to 0.05 was considered statistically significant. The data was entered in MS Excel and analysis was carried out using Statistical Software SPSS v.20.The results presented as descriptive and inferential statistics.

Results

A prospective, randomized study consisting of 40 patients with 20 patients each in group 1and group 2. Subarachnoid block was successful in all participants and all the participants completed the study (Figure 1). Both the groups were comparable with regard to demographic characteristics, ASA physical status, duration of surgery and intraoperative intravenous fluids administered (Table 1 and 2).

There were no significant differences between the two groups with regard to the onset time of motor block which was 2.25±0.44 minutes in group 1 and 2.40±0.50 minutes in group 2 with a P value of 0.324. Whereas, the duration of motor block was significantly higher in group 1 with 327.75±35.78 minutes than in group 2 with 280.00±24.92 minutes (P value of 0.0001). There was no significant difference in the time taken to reach highest dermatomal level which was 10.05 ± 1.67 minutes in group1 as compared to group 2 which was 9.55 ±2.21 minutes with P value of 0.425 as seen in Table 3. However, the highest dermatomal level of sensory block achieved was significantly higher in group 1 with 4.85 ± 0.99 than in group 2 with 5.70 ±0.87 with a P value of 0.006 (Table 3). The duration of sensory block (TDSR) was similar in both the groups which was 120 min in group 1 as compared to 119 in group 2 with a P value of 0.789. Duration of analgesia was significantly higher in group 1 with 235.75±19.69 minutes as compared to group 2 which was 215.50±27.24 minutes (P value of 0.010) as seen in Table 3.

The Mean Ramsay sedation score (RSS) was 2 in both the groups (with 1 patient in group 1and 2 patients in group 2 had RSS of 3) and there was no statistically significant difference

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among the groups (Table 3).

Intraoperative and postoperative hemodynamic parameters were not substantially different among both the groups (Table 4 and 5).

There was no statistically significant difference among the groups with regard to the occurrence of side effects (Table 6).

Thus, onset time of sensory and motor block was found to be similar in both the groups however the duration of motor block, the dermatomal level achieved and duration of analgesia was higher in group 1 as compared to group 2 with a P value of < 0.05.

Table 1: Gender and ASA Physical status distribution of study participants

	Group 1 (n=20)	Group 2 (n=20)	Total
Gender distribution-Male: Female (%)	25/75	65/35	45/55
ASA Physical Status-I/II (%)	75/25	55/45	65/35

ASA-American Society of Anesthesiologists.

Table 2: Demographic characteristics

Characteristics	Group 1(n=20)	Group 2(n=20)	P Value*
Age in years	43.70±6.28	48.95±7.08	0.180
Weight in Kg	62.30±4.67	62.55±5.15	0.873
Height in Cms	157.65±3.65	156.85±3.35	0.474
Duration of Surgery (minutes)	105.00±25.55	114.75±30.02	0.276
Intra operative IVF (ml)	1347.50±343.54	1467.50±432.64	0.337

Values expressed as Mean ± SD.

*P value < 0.05 considered statistically significant.

Table 3: Block characteristics

Study parameters	Group 1(n=20)	Group 2(n=20)	P Value
Onset of motor block (minutes)	2.25±0.44	2.40±0.50	0.324
Duration of motor block(minutes)	327.75±35.78	280.00±24.92	0.0001
Onset of sensory block (minutes)	10.05±1.67	9.55±2.21	0.425
Highest level of sensory block attained*	4.85±0.99	5.70±0.87	0.006
Duration of sensory block(minutes)	120.50±13.85	119.0±20.622	0.789
Duration of analgesia (minutes)	235.75±19.69	215.50±27.24	0.010
Ramsay sedation score	2.01±0.02	2.02±0.04	0.304

*Highest level of sensory block corresponds to thoracic dermatome level.

Table 4: Hemodynamic parameters-Intraoperative

Study parameters	Group 1(n=20)	Group 2(n=20)	P Value
Heart rate (beats/minute)	77.53±9.99	76.98±10.22	0.866
Systolic blood pressure (mm of hg)	114.05±6.69	114.69±8.79	0.796
Diastolic blood pressure (mm of hg)	69.77±5.36	71.30±7.42	0.460
Mean arterial pressure (mm of hg)	85.86±23.30	86.92±23.56	0.887

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Respiratory rate (per min)	11.91±0.45	11.78±0.41	0.350
SPO2 (%)	97.99±0.99	98.37±0.99	0.231

Table 5: Hemodynamic parameters-Postoperative

Characteristics	Group 1(n=20)	Group 2(n=20)	P Value
Heart rate	71.53±6.86	72.00±8.21	0.841
Systolic blood pressure (mm of hg)	121.86±7.59	123.90±6.21	0.090
Diastolic blood pressure (mm of hg)	70.76±6.19	72.83±7.23	0.336
Mean arterial pressure (mm of hg)	86.85±7.19	88.94±6.30	0.522
Respiratory rate (per min)	11.49±0.87	12.37±0.62	0.01

Table 6: Side effects

	Group 1(n=20)	Group 2(n=20)	P Value
Bradycardia	03(15.0)	02(10.0)	0.633
Hypotension	01(5.0)	01(5.0)	1.000
PONV*	02(10)	01(5.0)	0.548
Shivering	03(15.0)	0(0.0)	0.231

*PONV-Postoperative nausea and vomiting.

Discussion

Pain is inherent to all surgeries causing significant morbidity. Perioperative pain management has been a major challenge for anesthesiologists and there has been a constant struggle to bring out the best possible analgesic method with least side effects. Even though subarachnoid block remains as the method of first choice for infraumbilical surgical procedures, the rate of conversion to general anesthesia if surgical duration is prolonged and the necessity for early parenteral analgesic intervention in the postoperative period for pain control is a main limitation of the method if local anesthetics alone are utilized in SAB.

Thus, there has been a progressive research with regard to the adjuvants to Bupivacaine SAB so as to intensify the block and to prolong the analgesic effect with additional advantage of reduction in the dose of local anesthetics used [8].

Over years dexmedetomidine an S-enantiomer of medetomidine with a highly selective α 2-adrenoreceptor agonistic activity has gained popularity over opioids as a co-analgesic with local anesthetic SAB primarily because of the avoidance of opioid associated side effects.

Arati Rai *et al*. (2017) in their study using two different doses of dexmedetomidine as adjuvant to Bupivacaine SAB by intrathecal route have observed that used in a dose of 5 µg as an additive to spinal anesthesia, maximal beneficial effect of dexmedetomidine can be obtained without any side effects [9]. Hence in our study, dexmedetomidine dose of 5 µg was selected for intrathecal route.

Shaikh *et al*. (2014) in their Study using intrathecal dexmedetomidine as adjuvant to hyperbaric bupivacaine in infraumbilical procedures have found dose dependent favourable effect on the onset and regression of sensory and motor block.[10] A similar finding of prolonged duration of motor block and analgesia was observed in group where intrathecal dexmedetomidine was administered in our study.

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In literature review, A similar finding of prolonged analgesic effect without increasing the incidence of untoward effects was found when Dexmedetomidine was used in the perioperative period by intravenous route to bupivacaine SAB with the additional advantage of providing sedation and analgesia [3, 4].

However, as there is a paucity of literature for comparison of intrathecal with intravenous routes of dexmedetomidine administration on the efficacy of subarachnoid block this prospective, randomized, doubleblind study was conducted. Based on the results from our study, the best route of dexmedetomidine administration as an adjuvant to bupivacaine SAB can be assessed and adapted for infraumbilical surgical procedures under SAB where prolonged duration of postoperative analgesia with preserved hemodynamic stability and an adequate intraoperative sedation to be maintained without requiring an additional sedative drug. By intensifying the block and increasing the duration of postoperative analgesia, GA conversion rates can be minimized, increased patient comfort with minimal additional analgesics in the perioperative period can be achieved thus, decreasing additional cost and expenditure to the patient.

A systematic review conducted by Al Nobani MK *et al*. (2020) have evaluated the effects of intravenous loading dose of 1 µg/kg with 0.5 µg/kg of dexmedetomidine on the sensory and motor blockade duration of a single shot spinal anesthetic and the incidence of any associated side effects and concluded that the administration of larger loading doses of dexmedetomidine was associated with a larger side-effect profile with minimal beneficial changes when compared to lower loading doses [11]. It is also recommended to administer dexmedetomidine over no <10 min, as rapid administration might produce tachycardia, bradycardia and hypertension [12]. Furthermore, an evaluation of the analgesic effect of different doses of intravenous dexmedetomidine (0.25, 0.5, 1 µg/kg) on ischemic pain in healthy volunteers demonstrated moderate analgesia with a ceiling effect at 0.5 µg/kg [13]. With this in mind, loading dose of dexmedetomidine 0.5 µg/kg administered over 20 min duration was chosen in our study.

SS Harsoor *et al*. (2013) conducted a study to assess the effects of IV dexmedetomidine 0.5 µg/kg as loading dose followed by maintenance infusion of 0.5 µg /kg/hr on subarachnoid block. They have observed that it hastens the onset of sensory block and prolongs the duration of sensory and motor block with satisfactory arousable sedation [14]. In our study also, the same doses were chosen in group where IV dexmedetomidine administration was designed. The stable hemodynamic parameters with mean sedation score of 2 noticed in our study was in concordance with the above studies.

Synergistic interaction between dexmedetomidine and local anesthetics has been observed in previous studies [15, 16, 17] But the proposed mechanism of action of dexmedetomidine is found to vary in different routes. When administered intrathecally, it gets rapidly absorbed into CSF owing to its highly lipophilic nature and binds to the presynaptic C-fibers on the superficial dorsal horn in lamina II, thus inhibiting the release of pronociceptive transmitters namely substance-P and glutamate and also causes hyperpolarization of postsynaptic dorsal horn neurons [18, 19] by G-protein mediated activation of potassium channels which is responsible for its sympatholytic effect. When dexmedetomidine is administered through intravenous route, the anesthetic and analgesic action is provided through its supraspinal action by producing a differential blockade of myelinated A α-fibres involved in sensory conduction over unmyelinated C-fibres [20] involved in motor conduction. It suppresses neuronal firing in locus coeruleus by hyperpolarization of noradrenergic neurons thus inhibiting noradrenaline release and inhibiting activity in descending medullospinal noradrenergic pathways.[21] Thus,

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our study was designed to evaluate the block characteristics of bupivacaine SAB when different routes of dexmedetomidine administration were chosen.

Both the groups considered for study were similar in terms of patient characteristics, duration of surgery and intraoperative IV fluids administered. The variation in the treatment modalities was primarily based on the different routes of administration of the adjuvant. This helped us to evaluate the efficacy of different routes of administration of the adjuvant to bupivacaine SAB.

In our study the factors that would have contributed to prolonged block duration was administration of both loading and maintenance dose of IV dexmedetomidine similar to the study by SS Harsoor *et al*. as in most of the studies only loading dose has been used. The factors which could have contributed to stable hemodynamic parameters is preloading of 15 ml/kg of IV fluids and administration of loading and maintenance drug or placebo infusions diluted in normal saline throughout the surgical procedure in all the study participants. The factors which could have contributed to PONV are female gender and surgical procedures with bowel handling like appendicectomy.

Limitations: Our study comprised of small sample size hence inclusion of a control group using bupivacaine only for SAB would have added greater power to the study and the total analgesic consumption in 24 hours was not assessed in our study.

Conclusion

1) It is concluded within the constraints of the present design that dexmedetomidine by either intrathecal or intravenous route is an attractive adjuvant for long duration infraumbilical surgical procedures performed under SAB.
2) Dexmedetomidine as an adjuvant to bupivacaine SAB by intrathecal route provides prolonged duration of analgesia and motor blockade as compared to intravenous route. Thus, in daycare surgeries where early ambulation with good analgesia is desirable intravenous route is preferable.

Abbreviations: Not applicable.

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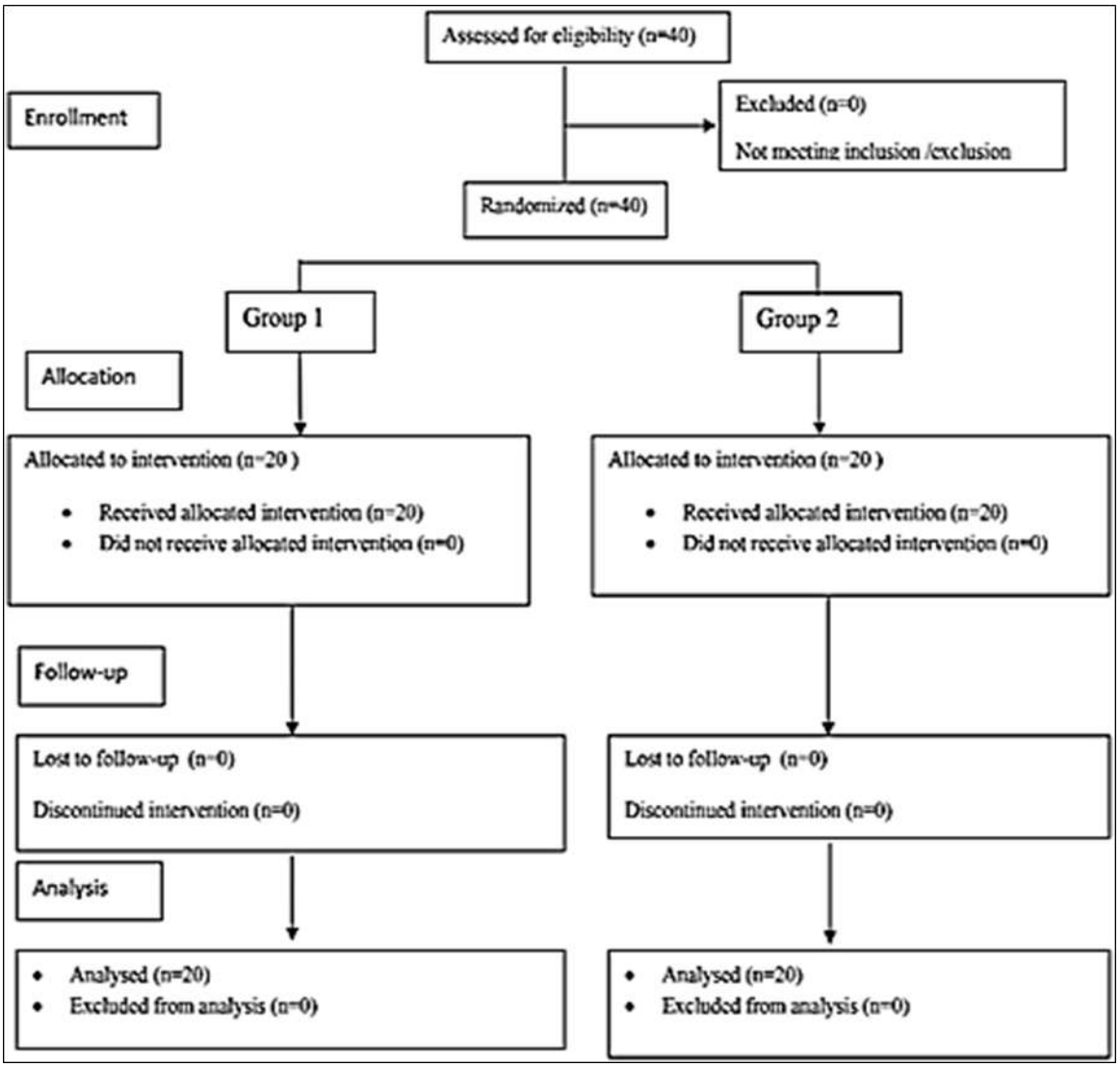

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