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A STUDY OF PRE-OPERATIVE AND INTRAOPERATIVE EVALUATION OF AUTONOMIC FUNCTIONS IN DIABETIC PATIENTS UNDERGOING NEUROSURGERY UNDER GENERAL ANAESTHESIA

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Abstract

The Autonomic nervous system (ANS) controls involuntary activities of the body outside the normal realm of consciousness. Cardiovascular autonomic neuropathy is frequently observed in patients with diabetes mellitus. As anaesthesia has a marked effect on peri-operative autonomic function, the interplay between diabetic neuropathy and anaesthesia may result in unexpected haemodynamic instability during surgery. The objective of this literature review was to examine the association of cardiovascular autonomic neuropathy with peri-operative cardiovascular complications. Depending on the type of anaesthesia, the presence of cardiovascular autonomic neuropathy in surgical patients can markedly affect peri-operative haemodynamics and postoperative recovery. Pre-operative testing of the extent of autonomic dysfunction in particular

populations, like diabetics, may contribute to a reduction in haemodynamic instability and cardiovascular complications.

Key words: Autonomic, nervous, anaesthesia, diabetic

Introduction

The ANS consists of a somatic afferent pathway, a central nervoussystem with brain and spinal cord, and two efferent limbs, the sympathetic andparasympathetic nervous systems, these together execute the autonomicresponse and thereby help in maintaining optimal homeostasis. Norepinephrine is the primary chemical neurotransmitter at sympathetic nerve endings,whereas acetylcholine is the primary chemical neurotransmitter atparasympathetic nerve endings. Since the ANS innervates all organs of thebody, autonomic neuropathy too will result in a multisystem disorder.Surgery and the co-administration of anaesthesia will disrupthomeostasis in patients despite having a proper functioning ANS. Hence, athorough understanding of the ANS is required for safe administration ofanaesthetic care.[1]Dysautonomia means to an abnormality of function of the ANS.Dysautonomia may be seen in patients having autoimmune neuropathies (GullianBarre syndrome, Rheumatoid arthritis, Myasthenia gravis),Amyloidosis, Diabetes mellitus, metabolic diseases(Fabry's disease),Parkinson's syndrome, Shy-Dager syndrome, Familial dysautonomia(RileyDay syndrome); in patients taking antidepressants, antihypertensives and inalcoholics.[2]Diabetic autonomic neuropathy is the most common form of autonomicneuropathy in both insulin dependent and non-insulin dependent patients.[3]Diabetic patients usually tend to develop parasympathetic autonomicneuropathy than sympathetic neuropathy. The symptoms associated withdiabetic autonomic neuropathy will lead to an increased risk during anaesthesia and surgery by direct or secondary mechanisms.Diabetic patients with autonomic neuropathy may be at additional risk during general anaesthesia. A significant decline in blood pressure and greaterneed for vasopressors may be seen in diabetics with autonomic dysfunctionwhen compared to diabetics without autonomic dysfunction.[4]Anaesthesiologists may need to do a group of pre-operative autonomic tests asaprognostic tool for identifying diabetic patients with autonomic neuropathyand thereby, predicting the mortality and perioperative risks.[5]Direct laryngoscopy and tracheal intubation play an integral part ingeneral anaesthesia, associated with hemodynamic responses that cause an increase in blood pressure and heart rate. Laryngoscopy and passage ofendotracheal tube throughlarynx acts as a powerful stimulus which normallyproduces an abnormal hemodynamic

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response. It has been claimed thatstimulation of the supraglottic region by the laryngoscopy blade is mainlyresponsible for this response (sympatho-adrenal). Placement of endotracheal tube provides additional stimulation.[6] In patients with diabetes mellitus bothattenuated and enhanced pressor response to intubation has been reported.[7,8]Measurement of plasma concentration of adrenaline in diabetic patients showsboth a normal and a reduced response. ANS dysfunction in patients withdiabetes mellitus may significantly alter the normal cardiovascular responsesthat occur during general anaesthesia and thereby, increasing the risk ofcardiovascular morbidity in these patients. The present study is undertaken tocompare the changes in systolic (SBP), diastolic blood pressures (DBP), meanblood pressures (MBP) and heart rate responses to induction of anaesthesia andtracheal intubation, in both diabetic and non-diabetic patients.Therefore, we intend to undertake this study to assess and compare the degree of autonomic dysfunction in patients with Diabetes Mellitus (Type 1 and II)and in controls peri-operatively and its effect on induction of anaesthesia, if itexists. The aim of the study is to compare various autonomic tests preoperatively& after induction of general anesthesia .

PRIMARY OBJECTIVE-

 To detect changes in autonomic function of Diabetes Mellitus patients & compare with control patients pre operatively.

SECONDARY OBJECTIVE-

 Effects of autonomic dysfunction on hemodynamics of Diabetes Mellitus Patients & compare with control patients intra-operatively

Materials and method

SOURCES OF DATA:

This study was approved by the Institutional Ethics Committee,Cuttack, Regdno ECR/84. Eligible patients aged between 25-70 years, ASA grade I-II,scheduled for elective surgeries under anaesthesia in SCB,Medical college &hospital, between December 2020 and October 2022.

STUDY DESIGN: Prospective randomized comparative study.

METHODS OF COLLECTION OF DATA: Fifty adult surgical patients aged between 25-70 years scheduled for electivesurgeries requiring anaesthesia in SCB,MCH, Odisha, were included in thestudy. After explaining the procedure, written informed consent was obtainedfrom each of

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the patients. Pre-anaesthetic evaluation for all patients was doneand patients were divided into two groups (Group I and Group II) of 25patients each. Group 1 comprised of 25 diabetic patients (cases), while Group 2included 25 non diabetic patients (controls), of either sex.Group I (Cases): 25 Diabetes mellitus patients• Group II (Controls): 25 non diabetic patients

SELECTION CRITERIA:

A] Inclusion Criteria:

1. Patients belonging to ASA grade I or II.
2. Patients posted for elective surgeries under general anaesthesia.
3. Patients of either sex, between the age group 25-70 years.

B] Exclusion criteria:

1. Patients belonging to ASA grade III /IV
2. Patient refusal.
3. Patients with severe cardiac disease
4. Patients on Cardiovascular medication like beta blockers.
5. Anticipated difficult intubation
6. Unable to stand
7. Extreme frailty
8. Emergency procedures
9. Patients with Body mass index more than 1.5 times normal.
10. Patient age greater than 70 years and less than 25 years.

SAMPLE SIZE ESTIMATION:

To demonstrate a mean difference of 10 mm Hg of systolic blood pressurebetween diabetes and non-diabetes, after induction of general anaesthesia (witha SD of 10 mm Hg for each group). We require minimum of 20 subjects ineach group (with α error of 0.05 and power 80%). Assuming 10% of our totalestimated subjects may be lost to follow up , we included 25 patients in eachgroup for final analysis.

METHODOLOGY:

Each patient scheduled for surgery, underwent detailed pre-anaestheticexamination and were acquainted to the autonomic function tests that wereperformed on the day prior to the surgery.

Appropriate laboratoryinvestigations were done. The data is shown in proforma.The bed side autonomic tests are briefed as below:

The tests are described as:

a) HR response to Valsalva manoeuvre:

 Valsalva ratio > 1.21 is considered as normal, any deviation fromthis value was taken as positive test.

b) HR response to standing:Ratio >1.04 is normal value; Any deviation from this value was taken aspositive test. **HR response to deep breathing**:

 Expiratory – inspiratory ratio (i.e., ratio of longest RR interval and
shortest RR interval) was calculated.

Mean difference >15 beats per minute or E:I ratio of 1.17 is
normal; any deviation from this value was taken as positive test.

c) BP response to standing:

 . **A difference of <10 mmHg was taken as normal value**.

 Fall in SBP >20 mmHg was taken as positive test.

d) BP response to sustained handgrip:

 The difference between initial DBP and final DBP just beforerelease was calculated

 A difference >16 mmHg is normal, any reading less than this willbe considered as positive test.

The tests were performed in a pre-operative ward, a day prior to surgery.

The tools used to obtain these are:

a) Handgrip tocodynamometer (figure 1)

b) Pressure gauge containing mouth piece with readings in water column and mmHg. (figure 2)

c) Multipara monitor with print record of ECG, non-invasive BP (NIBP). A positive response to any of the two above autonomic tests was considered as“positive” implying a sign for the presence of autonomic neuropathy.Patients were premedicated with tablet ranitidine, 150mg, orally, on the nightprior to surgery. Baseline values of non-invasive blood pressure, heart rate withlead II Electrocardiogram and oxygen saturation were taken using multiparaECG printrecord monitor on the pre-operative day. Insulin or oral antidiabeticmedications were withheld on the day of surgery.On the day of scheduled surgery, patient was shifted to the operation theatre and made to lie in supine position on the OT table. After connecting to NonInvasive Blood Pressure

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(NIBP), five lead Electrocardiogram and saturationprobe, baseline vitals were recorded. 18 gauge intravenous access was securedin each patient on upper arm under local anaesthesia. An infusion of ringerlactate or 0.9% normal saline was connected prior to administration of generalor spinal anaesthesia. Patient"s blood pressures (SBP, DBP, MABP) wasrecorded at intervals of 2 minutes each for a period of 10 minutes following intubation and at intervals of 5 minutes thereafter till the end of procedure.SPO2 and HR monitoring was done continuously throughout the procedure.

PROCEDURE FOR GENERAL ANESTHESIA:

All subjects were preoxygenated for a period of three minutes using a prechecked anaesthetic machine before induction of general anaesthesia. Inj. Glycopyrrolate 0.005mg/kg, Midazolam 0.05mg/kg, Fentanyl 1-2 mcg/kg, wasgiven as premedication prior to induction. For induction, Inj. Thiopentone sodium 4-5 mg/kg was given over 30-45 seconds and titrated till the loss of eyelash reflex as an end point. Inj. Rocuronium 0.9mg/kg was given tofacilitate tracheal intubation. After three minutes of manual ventilation,patients were intubated using size 3 or 4 Macintosh blade for laryngoscopy and polyvinyl chloride tracheal tube of internal diameter 7.0 mm for females and8.0 mm for males. After confirmation by end tidal carbon dioxide (ETCO2), Sevoflurane 1.2 MAC level along with 33% oxygen and 66% nitrous oxide was kept to maintain adequate depth of anaesthesia. Towards the end of the procedure, the inhalational agent and nitrous oxide was discontinued and lungsventilated with 100% oxygen.For analgesia Paracetamol 1gm I.V. given. The neuromuscular blockade was pharmacologically antagonised using Inj.Neostigmine 0.05 mg/kg and Inj. Glycopyrrolate 0.08mg/kg. Once the patient resumed regular spontaneous breathing pattern and opened eyes to command,the patient was extubated after deflating the endotracheal tube cuff. Patients were monitored and hemodynamic data (HR, SBP, DBP, MABP) were recorded throughout the procedure. Any adverse hemodynamic event was noted and treated accordingly using medications. Patient was kept normocarbia during the entire procedure and temperature was maintained using forced warm air devices. Blood loss and urine output were watched upon.

STATISTICAL ANALYSIS:

All the parameters measured as mentioned above were subjected to statistical analysis and interpreted. Statistical Analysis was done by using SPSS (Statistical prgramme for social science) version 28.0, for group of 2 and total of 50 subjects. The data were checked for its

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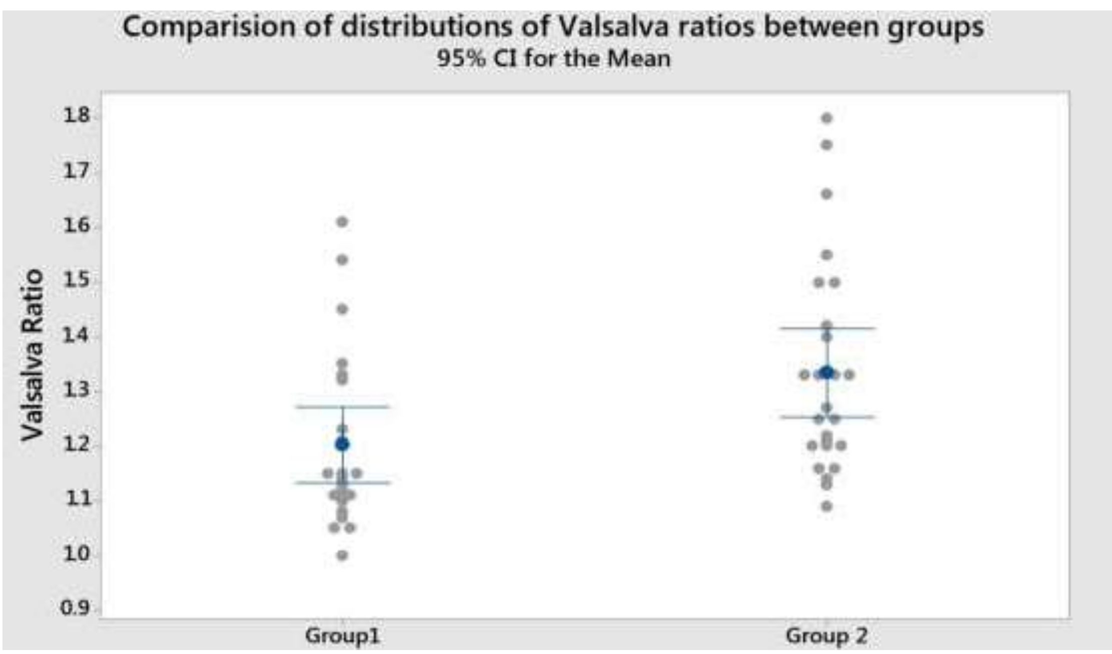
normality of distribution using Shapiro Wilk test. For parametric data, numerical data were analysed using student t test for two groups comparisons and for repeated measures, analysis of variance (repeated measures of ANOVA) was used. For non-parametric continuous numerical variables MannWhitney U test was used. For repeated measures, if they were found to be nonparametric, a Kruskal Wallis ANOVA was used. Categorical data were presented as proportions and percentages. All the numerical values were presented as mean with standard deviation (SD) or median with Inter Quartile Ranges. These included age, weight, duration of illness and were compared using student t test.

Results

In group 1, there were 19 males (55.88%) and females were 6(37.50%) whereas, in group 2 number of males were 15 (44.12%) and females10 (62.50%). Distribution of sex in both the groups was comparable with Pvalue of 0.225 analysed using chi-square test.Heart rate variability ratio during valsalva test showedsignificant difference between the two groups with P value of 0.0044 analysed using MannWhitney U test.(fig 1)

Figure 1:



Heart rate variability ratio during change of posture (supine to

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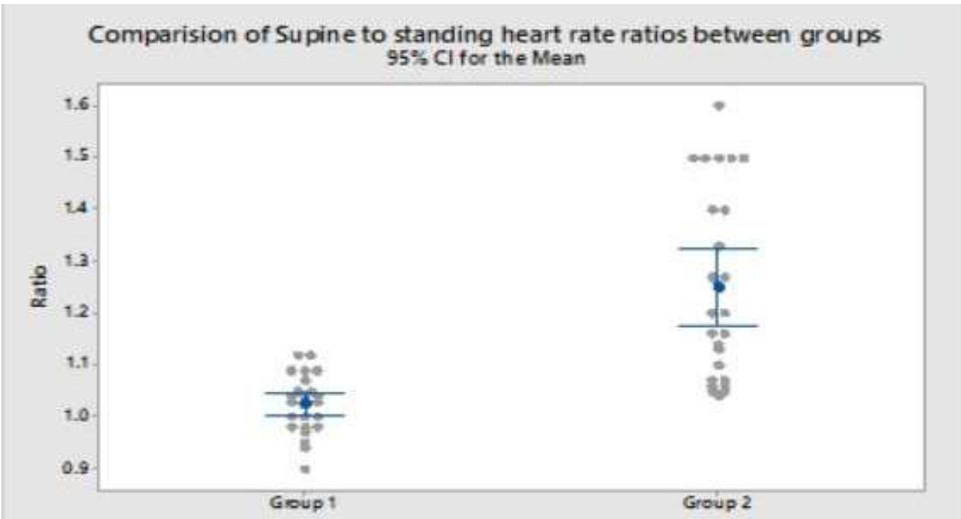
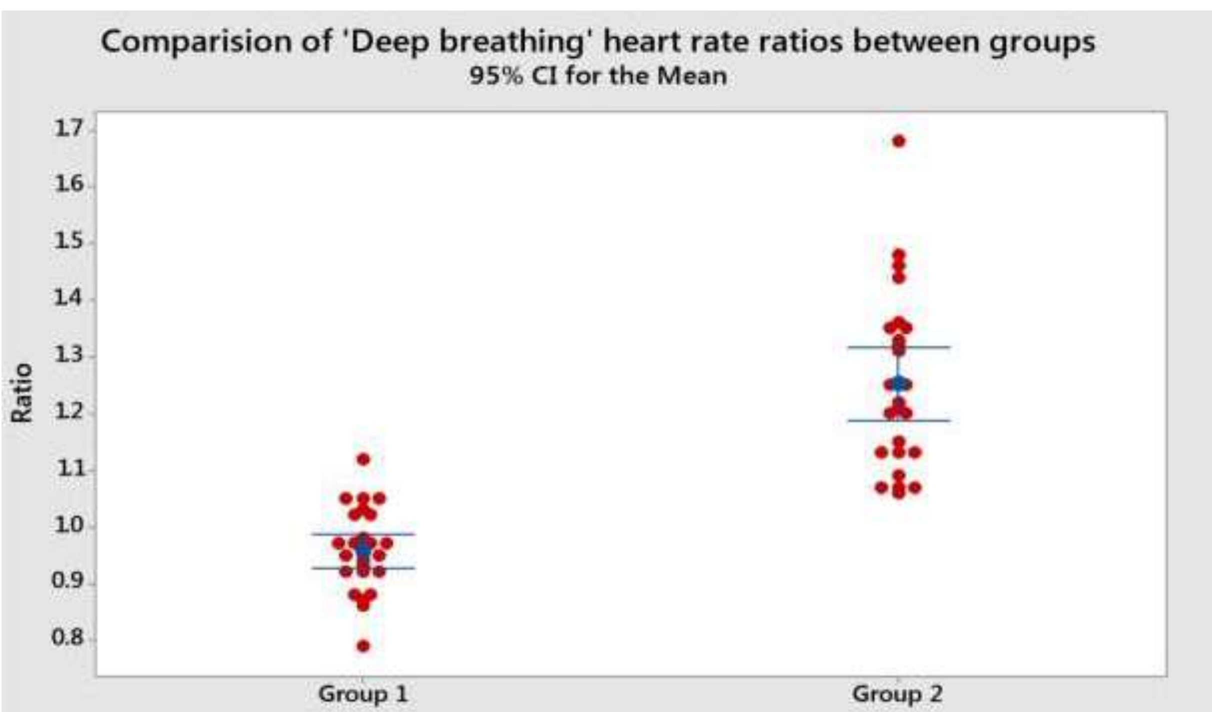
standing) test showed significant difference between the two groups, P value < 0.0001 analysed using Mann-Whitney test.(fig 2)

Figure 2:



Comparison of heart rate variability ratio during Deep breathing test between the two groups [inter group variation]. The values are represented as median. MannWhitney U test used.(fig 3)

Figure 3:



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Discussion

A total fifty patients who were undergoing elective surgery under General Anaesthesia were divided in to two groups according to presence of Diabetes Mellitus.The comparision of various autonomic test in pre anaesthetic check up room & intra operative room were observed. The demographic profile in both the groups in terms of AGE,SEX showed no stastically significant.The comparision of heart rate variability ratio during valsalva in group 1was more than group 2& p value came significant.The patients in Group 1 had a mean E: I ratio less than 1.17 thus implying reduced vagal activity. The Valsalva ratio, E: I ratio and 30:15 ratio revealed areduced vagal activity in diabetic individuals when compared to normal subjectsas per the present study.

SYSTOLIC BLOOD PRESSURE : PRE OPERATIVELY)

In our study, SBP values expressed in mm of Hg from baseline to various intervals of time for a duration of 5 minutes were compared within the groups [intra group comparison]. In Group 1, we saw a significant decline in SBP on change in posture during each interval of time. The fall in SBP was greater in Group 1 (diabetes) than in Group 2 (controls) owing to altered baroreceptor reflex mechanism in long standing diabetes. The overall group mean fall of SBP however was lesser in magnitude and it was up to 14mm of Hg (average) in Group 1 subjects. This is lesser than the 20 mm of Hg fall. This is because the average was considered from all diabetics who had negative test of supine to standing SBP measurement. It is very much true that the positive test individual would demonstrate a mean of more than 20 mm of Hg in study group subjectsThe overall incidence of orthostatic hypotension was 41.67% in diabetic group which was more than that seen in normal subjects.

DIASTOLIC BLOOD PRESSURE: (PRE OPERATIVELY)

We observed no significant elevation of DBP during isometric sustained hand grip exercise testing in diabetics. The magnitude of mean elevations in diabetics were only about 4mm of Hg in contrast to the normal individuals were these were defined actually up to 16mm of Hg. However, we observe in our control subjects this magnitude as 12mm of hg which are much more than our study subjects. The control subjects had little less than expected values. The patients of control subjects were at a times complained of fatigue during the test and the true isometric exercise might have not possible to elevate the blood pressures and thus affecting the

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readings. In this study the prevalence of sympathetic dysfunction during sustained hand grip was found to be significantly higher in the diabetic group (77.8%) than normal subjects.

VALSALVA TEST :

The valsalva ratio, 30:15 ratio and E: I ratio in our present study showed significant lower values than the normal ratios in the diabetic group when compared to normal indicating parasympathetic cardiovascular reflex .[7] Although this incidence of our study may not reflect the true incidence of autonomic dysfunction of overall population, we noticed a little higher incidence because of following reasons; a) The study subjects had long duration of diabetes. b) The study subjects were not considered for the study in a consecutive manner, however randomly selected by author. c) Study subject who were coming for operative procedure only were included. Subjects who undergo surgery generally are with comorbid conditions which are likely to developed because of their diabetes and its complications; i.e., autonomic involvement, peripheral neuropathy etc.[8] Overall population subjects will havemuch lower hospital admissions and surgical incidences compared to our subjects thus influencing the results of our study.Valsalva ratio, 30:15 ratio, BP response from supine to standing each of thesewhen analysed separately, and clearly showed no association with any of thepredictors such as age, sex, duration of diabetes, use of insulin, use of OHA andpresence of any co-existing illness.[9] In contrast to this, the test for BP responseto sustained hand grip was associated with use of insulin (P = 0.029). thisimplies, that the insulin, duration of diabetes, age etc. were unable to predict thepositive tests but hand grip tests were likely to be positive with use of insulin.[10,11]This can be explained by the very fact that the insulin use is many a times is associated with longer duration of diabetes or in persons who are resistant tooral hypoglycaemic agents or a poor control of diabetes and a autonomicdysfunction is likely to develop in such individuals.[12]

SYSTLOIC BLOOD PRESSURE : (INTRA OPERATIVELY)

SBP was studied immediately after induction for duration of 10 minutes with intervals of 2 minutes. We observed a greater fall in SBP after induction inGroup 1 subjects compared to other. The magnitude was significant compared to base line and there was less fall in controls. Thus, we considered the vasopressor requirements in each group to obtain valid data. We noticed higher usage of vasopressors after induction of anaesthesia in diabetics suggesting the correlations of DAN positives with incidences of hypotension episodes very well.

DIASTOLIC BLOOD PRESSURE : (INTRA OPERATIVELY)

DBP was also studied immediately after induction for duration of 10 minutesbwith intervals of 2 minutes. We observed that a slight fall from base line in group 1 compared to group 2. So accordingly need of vasopressure was more compared to group 1.

Conclusion

From our study it can be concluded that non-invasive bedside tests can be performed using the available, inexpensive resources in the hospital to detect the hidden autonomic dysfunction reliably for making a diagnosis of autonomic dysfunction in the preoperative subjects. Thus indicating feasibility of these bedside autonomic function tests in routine practice**.**

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