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Abstract

Objectives: Post-operative delirium (POD) is a relatively common occurrence particularly in the elderly, especially after prolonged surgery. This study aimed to determine the incidence of post-operative delirium at the Port of Spain General Hospital, Trinidad, West Indies.

Methods: After obtaining consent, elderly patients (≥ 65 years of age) were prospectively screened using the 4AT questionnaire pre and post-operatively. Post-operative assessment was done on day 0, 1 and 2 between the hours of 18:00 and 22:00. Demographic and clinical data were recorded.

Results: Sixty-one (61) patients were recruited. After exclusion, a total of 42 were included for the study. The incidence of POD in elderly patients at the Port-of-Spain General Hospital in Trinidad was 21.4%. Overall, eighteen (43%) patients displayed cognitive impairment post-operatively. The factors associated with development of POD were duration of anaesthesia, with surgery lasting >120 min having a 17% incidence. Delirium occurred more frequently after general anaesthesia (27%) compared to regional anaesthesia (8%). Vasopressor use and malignancy was also associated with a higher incidence of POD (33%).

Conclusion: Elderly patients had a higher risk of developing postoperative delirium following general anaesthesia compared to regional anaesthesia, and where the surgical duration exceeded 2 hours. Other factors included hypotension requiring vasopressor use and gynaecological malignancy. The 4AT is a useful tool in detecting postoperative delirium in our setting.

Introduction

The word ‘delirium’ is derived from the Latin root ‘delirare’, translated as ‘being out of one’s furrow’. Delirium is a neuropsychiatric condition characterized by a reduced state of awareness, and a fluctuating course, usually triggered by a precipitating medical condition, including surgery. The newest update to the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) has the following definitions for delirium:

1. Disturbance in attention (i.e. reduced ability to direct, focus, sustain, and shift attention] and awareness [reduced orientation to the environment).
2. The disturbance develops over a short period of time (usually hours to a few days), represents an acute change from baseline attention and awareness, and tends to fluctuate in severity during the course of a day.
3. An additional disturbance in cognition (e.g. memory deficit, disorientation, language, visuospatial ability, or perception.
4. The disturbances in Criteria A and C are not better explained by a pre-existing, established or evolving neurocognitive disorder and do not occur in the context of a severely reduced level of arousal such as coma.

5. There is evidence from the history, physical examination or laboratory findings that the disturbance is a direct physiological consequence of another medical condition, substance intoxication or withdrawal (i.e. due to a drug of abuse or to a medication), or exposure to a toxin, or is due to multiple aetiologies

Delirium manifesting in the postoperative period affects a significant proportion of patients. It is more common in the elderly (> 65 y age), affecting from 5-50% of this subset of patients [1-3]. Other major risk factors include intraoperative hypotension [4, 5], presence of infection or sepsis [6-8]. It manifests usually within 1-3 days of surgery [9].

Postoperative delirium has also been linked to delayed mobilization after surgery, and increased time to hospital discharge [2]. It has also been associated with inability to achieve a good overall functional outcome, a higher incidence of long-term institutionalization, with increased transfer to elderly care homes [10]. There has also been an observed increased risk of anxiety disorders and major depression in patients who have suffered POD [10].

Recent guidelines from the National Institute for Clinical Excellence (NICE), UK enlists the major risk factors for developing POD. These include age greater than 65 years, pre-existing cognitive decline or dementia, poor vision or hearing, presence of infection, and severe illness [11]. Raats *et al* found that a history of pre-existing delirium, an American Society of Anesthesiology [ASA] score ≥ 3 and daily alcohol use to be predictors of POD [3]. Poor functional autonomy, as measured by Activities of Daily Living scores such as the Katz score has been shown to be associated with POD [3, 12]. Poor nutritional status, as measured by scoring systems such as the Short Nutritional Assessment Questionnaire (SNAQ) is also linked to POD [3, 13, 14].

The overall incidence of POD is widely variable with published incidence in the range of 4 – 65%; the highest incidence has been reported after hip surgery [1, 6, 15]. Part of the difficulty of assessing the incidence of POD is that there has been no single standard screening tool for POD.

A well validated screening tool applied is the Confusion Assessment Method score (CAM) [16]. The CAM questionnaire, while brief (taking about 5 min) relies on nine operationalized criteria taken from the DSM-III-R handbook. This requires some training for its effective use by non-psychiatrists or nurses without a background in psychiatry. The CAM also requires a cooperative patient and thus may pose some challenges to administer on the busy surgical wards.

A retrospective literature review of 239 published articles on the CAM by Wei *et al* found that the CAM had an overall sensitivity and specificity of 94% and 89% respectively [17].

There was a need for a newer screening tool for delirium that was brief, simple for use on busy general wards, easy to understand and interpret, and provide early warning that delirium was a potential problem. In 2011, researchers in the UK devised such a newer, simplified screening tool for delirium. This became known as the 4AT assessment test [18]. The advantages of the 4AT tool include its simplicity, brevity (it usually takes < 2 min to complete) and that formal training in its administration is kept to a minimum [18-20]. It does not require responses to instructions such as drawing or copying figures, and it allows for the assessment of patients previously considered "untestable" such as those with severe agitation or drowsiness [19].

This tool underwent validation in several subsequent trials [19-21]. Authors have recommended 4AT to be used as a brief screening tool to detect delirium on the geriatric wards [20]. The 4AT tool was also investigated and validated in other countries. The application of the 4AT tool in an elderly population of a predominantly non-

English speaking inpatients in a Thai university hospital showed that even among non-native English speakers with differing cultural influences, the 4AT test can perform with a good discriminatory power [21].

A previous study by Ramroop *et al* from Trinidad & Tobago investigated the factors associated with 'Emergence Delirium' [ED] in the Post Anaesthesia Care Unit (PACU) of a tertiary level teaching hospital, which was found to be 11.8% [22]. Factors associated with ED were ethnicity, (twice the incidence in Afro-Trinidadians, emergency surgery, length of surgery and number of attempts for endotracheal intubation [22].

With this background, the current study was designed to determine the incidence of postoperative delirium as well as the various perioperative risk factors. The difference between the study by Ramroop *et al* [22] and the current study is that the former studied only 'Emergence' delirium in all adult patients following sevoflurane anaesthesia, while the current study included assessment of elderly patients followed up for a longer period of time in the postoperative period. A greater understanding of the clinical manifestation and the consequences of postoperative cognitive decline in the elderly may lead to improved diagnosis and early treatment in this group of patients.

Methods

This was designed as a prospective observational study of elderly patients who underwent general or regional anaesthesia [with sedation] lasting more than 1 hour at the Port of Spain General Hospital (POSGH), Trinidad, West Indies.

Approvals were obtained from the North West Regional Health Authority as well as the University of the West Indies.

Data were collected over a 6-month period.

Inclusion Criteria:

1. Patients over 65 years of age
2. Patients undergoing general anaesthesia or regional anaesthesia (with or without IV sedation) for elective and urgent surgery
3. Operations expected to last more than 1 hour
4. Post-operative hospitalization expected to be 3 or more days

Exclusion Criteria:

1. Patients under 18 years of age
2. Those undergoing intracranial surgery
3. Pregnant patients
4. Surgery expected to last less than 1 hour
5. Pre-existing history of cognitive impairment, stroke or psychiatric disorders

The sample size was determined by using the online sample size calculator (Clincalc™) using a 30% population incidence and a 15% study group incidence, α-error of 0.05 and power of 80%. The sample size was calculated to be 64. Patients were selected by scrutinizing the published operating lists of the operating theatres of the POSGH, and by consultation with the surgical teams on the estimated duration of surgery. Written, informed consent was obtained for each patient, either by the researcher or other members of the Anaesthetic

Department.

At the preoperative visit when informed consent was obtained, the preoperative baseline 4AT questionnaire was administered. The 4AT test was then administered on the evening of surgery (day 0), and the successive 2 evenings (day 1 and 2 post op). The postoperative questionnaires were all performed between 18.00 h and 22.00 h, or until the patient was discharged from hospital.

All perioperative decisions concerning the type of anaesthesia including drug selection appropriate for each patient, was undertaken by the specialist anaesthetist or registrar responsible for the operating list. The intra-operative anaesthetic management of each patient conformed to the standard policies of the Anaesthetic Department, POSGH. The researchers did not influence the type of anaesthetic administered, or in drug selection for the patients' management.

The patients' demographic data were recorded, as well as their preoperative use of any drug known to be linked to delirium. The type of operation, anaesthetic induction drugs for general anaesthesia (where performed) and the duration of anaesthesia were documented. The presence and duration of any episodes of intraoperative hypotension (systolic BP < 90 mmHg) and/or hypoxia (SpO_2 < 88%) were also recorded. The use of any intraoperative vasopressors or inotrope infusions were noted. Postoperative factors charted were the presence of postoperative pyrexia, postoperative hypoxia and the duration of such hypoxia.

Data were analysed using the Statistical Package for the Social Sciences (IBM) version 24. Pearson's Chi-squared test (χ^2) for categorical nominal data, and Fisher's exact test [where applicable] were performed to determine the presence or absence of POD, and to determine statistically significant association between the above variables and POD.

Results

A total of sixty-one (61) patients were recruited into the study. Nineteen (19) were cancelled and did not undergo surgery. Finally, forty-two (42) patients had surgery and underwent pre-and post-operative 4AT screening. Fifteen (15, 36%) were male and twenty-seven (27, 64%) were female. Ages ranged from 49 – 84 years with a median of 68 years.

Fig 1: Age Distribution of the study population

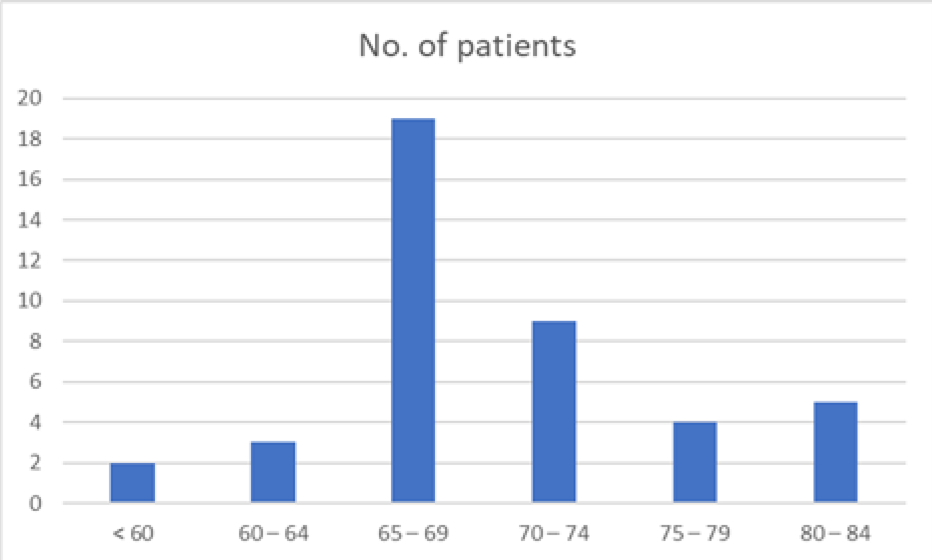

Figure 1 shows the distribution of the age-groups in the study. There were 2 deaths in the postoperative period, after the data collection period. They were included in the group of 42 patients who underwent successful surgery and postoperative screening. The overall incidence of POD in this study was 21.4%.

Thirty (30) cases were performed under general anaesthesia, seven (7) under regional anaesthesia without sedation and five (5) under regional anaesthesia with midazolam sedation.

Fig 2: Distribution of Surgical Specialties

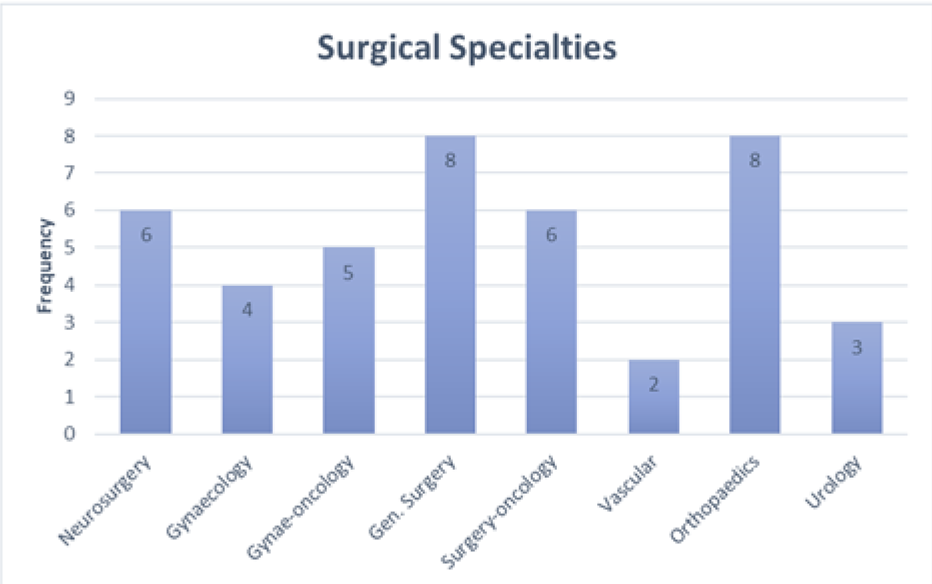

Figure 2 shows the distribution of specialties of the patients in the study. During the period of data collection, the majority of cases belonged to General Surgery and Gynaecology, especially Gynaecological Oncology.

Table 1: Overall 4AT scores

	Frequency	Percent [%]
4AT score 0 & 1	33	78.6
4AT score >2	9	21.4
Total	42	100

Table 1 depicts the distribution of the patients' 4AT scores in order to diagnose the presence of postoperative delirium.

Table 2: Distribution of preoperative 4AT score abnormalities

Pre-op Component of 4AT score Abnormality	Frequency
Alertness	0/61 [0.0%]
AMT4	7/61 [11.4%]
Attention	17/61 [27.8%]
Acute change/fluctuating course	0/61 [0.0%]

Table 2 shows the distribution of preoperative 4AT score abnormalities in all the patients. This is for comparison with the postoperative score.

Table 3: Type of anaesthesia and POD

Type of Anaesthesia	Cognitive Impairment [4AT score 0 & 1]	Delirium [4AT score >2]	Total
General	22	8	30
Regional + sedation	5	1	6
Regional, no sedation	6	0	6
Total	33	9	42

Table 3 suggests that general anaesthesia (GA) was more strongly linked to cognitive impairment and delirium, with 22 cases of possible cognitive impairment and 8 cases of possible delirium occurring after GA. Five (5) cases of possible cognitive impairment and 1 of possible delirium occurred after regional anaesthesia (RA) with sedation (midazolam). Six (6) cases of cognitive impairment occurred after RA without no sedation. Of note no cases of possible delirium occurred after RA without sedation.

The duration of anaesthesia was also analysed to see if there was a link with the development of POD. The duration of anaesthesia was subdivided into 2 categories for analysis purposes – duration < 120 min and > 120 min. Also intraoperative vasopressors were used in 27 and of these 6 had 4AT scores suggesting POD (14%). The remaining 21 patients had scores indicating possible cognitive impairment (50%). In the cases where no vasopressors were used 3 of these had scores suggesting possible delirium (7% and 12 had scores indicating that possible cognitive impairment was present (28%).

Table 4: Duration of anaesthesia, vasopressor use and POD

	Cognitive Impairment [4AT = 0&1]	Delirium [4AT = >2]	Total
Duration < 120 min	14	5	19
Duration > 120 min	19	4	23
Vasopressors used	21	6	27
No vasopressors used	12	3	15

Table 4 shows the comparison of incidence of POD with respect to duration of surgery and vasopressor use. However, all comparisons using Chi-squared analysis, and Fisher's Exact Test as appropriate did not reach statistical significance thus indicating poor association of the factors with the occurrence of postoperative delirium.

The study showed that gynaecological oncology patients had the highest incidence of POD (33.3%), while the gynaecological-oncology subset (40%) had possible cognitive impairment. The next highest number (22.2%) was found in general surgical patients (without malignancy). The subset of general surgery-oncology, however had 14% patients with possible cognitive impairment postoperatively. Surprisingly only one orthopaedic patient scored possible POD, but 87.5% of this subset scored possible cognitive impairment.

Discussion

This study documented the incidence of postoperative delirium (POD) to be 21% in an elderly population at the Port of Spain General Hospital, Trinidad. This incidence of postoperative delirium is comparable to international reports. Other authors have reported incidences between 5-50% in elderly patients [1-3]. The highest incidence has been reported after hip surgery varying from 35-65% [2, 5, 6]. The wide range of incidence is partly attributable to the variety of screening tools which may be utilised at differing times of a patient's hospital stay to screen for POD. Tools such as the CAM, NEECHAM scale, NuDESC, with inherently varying sensitivities and specificities have been used [17, 22, 23]. Variations in protocols may also account for the large differences noted in the incidence of POD.

At present, the role of anaesthesia in precipitating delirium is undefined. While induction drugs and benzodiazepines can possibly induce cognitive changes in brain tissue their exact role remains unclear and warrants further investigation [1]. There have been suggestions that inhalational anaesthetic agents alter the electrical activity in neurons and are also linked to amyloid deposition and cellular apoptosis [1, 24]. Animal studies have suggested that the combination of anaesthesia and surgery can trigger the inflammatory state, seemingly responsible for POD, rather than anaesthesia *per se* [14, 25]. Other researchers have reported that general anaesthesia was not an independent risk factor for developing POD [3, 12].

But researchers have noted a reduced incidence of POD after regional anaesthesia. A Cochrane database review indicated in their review of 22 trials involving 2567 patients, that regional anaesthesia had lesser incidence [26]. Other authors caution that drugs such as opioids and benzodiazepines may be linked to POD, and hence techniques that reduce these in the perioperative period might reasonably be expected to reduce the risk of POD [14].

The results of the present study are in keeping with these published findings. Of all the patients who showed POD, 89% had general anaesthesia and 11% had regional anaesthesia with sedation, although this difference did not reach a statistical significance.

The role of sedation during regional anaesthesia (RA) and the link with POD also remains contentious. Some researchers have suggested that sedation leads to an increased risk of POD [1, 14, 27]. Elderly (>65) patients undergoing spinal anaesthesia for hip surgery were randomised to receive Bispectral Index (BIS) targeted propofol sedation [28]. Either moderate sedation [BIS 50] or light sedation (BIS >80) was used. They noted that the incidence of POD was lower in the light sedation group (11/57, 19%) vs. 23/57 (40%) in the moderate sedation group [28]. A study by Radtke *et al* in which they randomised patients (>60 years) to receive guided BIS monitoring under general anaesthesia, compared to patients not receiving BIS monitoring of depth of anaesthesia, reported 16.7% POD in the monitored group versus 21.4% in the non-BIS monitored group [29].

The present study did not specifically monitor patients for depth of anaesthesia. A minority of patients (14.2%) received midazolam intraoperatively. Only 7% of these had 4AT scores suggestive of possible delirium. Paradoxically a higher proportion (36%) was noted to be delirious, despite not having received benzodiazepines intraoperatively. It must be noted that the range of drugs available for intraoperative sedation is limited at the study hospital. Intravenous midazolam is most commonly employed while intravenous opioids (fentanyl) are used far less frequently. Anxiety during surgery under regional anaesthesia should be managed by counselling, reassurance and perhaps use of distractions such as reading [where this will not unduly interfere with monitoring], watching television or videos via the patients' smartphone (when such is available) or listening to calming music via headphones.

Advanced age has been reported as a significant risk factor for developing POD by many authors [29-31]. There was a weak, non-significant association between use of intraoperative vasopressors and POD. The use of vasopressors implies that the patient was hypotensive to a significant degree. There is however no fixed algorithm for the management of intraoperative hypotension, and the decision to use vasopressors has significant inter-individual variability at the study institution. Hence there are marked differences in the treatment of hypotension.

There is dispute about the role of intraoperative hypotension in the development of POD. Although the NICE guidelines do not indicate that it is an isolated factor, Wang *et al*'s study has linked the average mean arterial pressure during surgery (MAP) to the incidence of POD, with MAP < 80 mmHg being associated with higher risk of developing POD [32]. It was however noted in the "Best Practice Statement from the American Geriatrics Society" that there was insufficient published evidence to guide intraoperative blood pressure monitoring as a measure to prevent POD [33]. Hirsch *et al* also found that large intraoperative variations in BP (as measured by the variance) was statistically linked to POD [4].

The present study showed that gynaecological oncology patients had the highest incidence of possible POD (33.3%), while the gynaecological oncology subset (40%) had possible cognitive impairment. However published studies have not associated malignancy as a predisposing factor for POD. Most authors did not find malignancy as a major risk factor for POD [34-36].

In conclusion, postoperative delirium is a major cause for concern especially in the elderly under general and regional anaesthesia. Modifiable risk factors such as duration of surgery and intraoperative hypotension may be addressed to minimise the risk of its development.

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