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ORIGINAL ARTICLE

Evaluating the Impact of Opium Poppy Toxicity on Pediatric Patients: Clinical, Laboratory, and Outcome Analysis

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ABSTRACT

Traditionally, the opium poppy plant, *Papaver somniferum* L., has been used for a variety of therapeutic uses, such as pain treatment and cough suppression. Hippocrates once described the herb as hypnotic, cathartic, and styptic. The current study was conducted at the Tertiary Care Hospitals in Peshawar, KPK, Pakistan, from August 2022 to August 2023. It examined the clinical and laboratory profiles of newborns and children admitted to a tertiary care hospital with poppy intake and compared the profiles between those who survived and those who died. All infants and kids who showed up for the research period exhibiting meiosis, respiratory depression, and decreased consciousness all indications of opium poppy intoxication as well as a verified history of poppy administration at home, were included in the study. There were admittedly 65 cases of opium poppy intoxication. The patients' ages varied from one month to twenty-three months, with an average age of 7.22 ± 5.43 months. 35 (53.85%) of these infants and children died, while 30 (46.15%) survived ($p<0.001$). Those who survived had a considerably shorter period from poppy intake to hospital admission (6.0 ± 2.56 hours versus 12.47 ± 4.14 hours, $p<0.001$) than those who died. Children who were administered poppy powder mixed with water had a considerably higher mortality rate 13 out of 17 cases (76.47%) resulted in death ($p<0.001$). There was a strong correlation between increased mortality and low respiratory rate, decreased oxygen saturation, aspiration pneumonia, apneic episodes, cyanosis, and leukocytosis >15,000/mm³. For newborns, opium poppy poses a serious risk because it can cause a coma, impair breathing, and even be lethal. The selling of poppies in shops and supermarkets must be outlawed, and public education is essential to ending this destructive activity.

Keywords: *Opium Poppy, Toxicity, Infants and Children, Meiosis, Respiratory Depression.*

INTRODUCTION

The opium poppy (*Papaver et al.*) was described by Hippocrates over 350 years BC for its properties as a hypnotic, cathartic, and styptic agent[1]. Historically, poppy plants have been used to produce various medicinal products, including pain relievers, antimalarials, and cough suppressants, as well as items like baby rattles and culinary additives[2]. This plant contains several alkaloids such as morphine, codeine, narcotine, papaverine, thebaine, narcotoline, and narceine. Most of these alkaloids are concentrated in opium, which is obtained from the milky latex that oozes from incisions made in the unripe poppy heads[3]. Opium has been traditionally employed to alleviate pain and suppress coughs. In Pakistan, poppy seeds are frequently used in cooking, although they usually contain minimal alkaloid levels. Nonetheless, issues such as pest infestations or improper harvesting can lead to contamination with opium alkaloids[4].

Morphine pharmacokinetics are similar in adults and children; however, neonates and infants exhibit distinct pharmacokinetic profiles, including a prolonged half-life, increased volume of distribution, reduced plasma clearance, and lower protein binding[5]. These differences, combined with an immature blood-brain barrier in younger patients, result in higher brain concentrations of morphine and an increased risk of adverse effects. By the age of one, the pharmacokinetics of morphine in infants generally align with those observed in adults[6,7]. Consequently, the risk of morphine toxicity is heightened in younger populations.

In response to these concerns, many countries have implemented regulations to control alkaloid levels in food-grade poppy plants, including setting maximum limits or outright bans[8]. Health authorities are advocating for harmonized regulations to address this, necessitating a comprehensive understanding of toxin exposure[9]. While existing research has predominantly focused on morphine, it is crucial to consider all opium alkaloids present in poppy seeds[10]. Limited research has been conducted on these food matrices, highlighting the need to develop and validate new analytical methods for accurate quantification. Recent advances have shifted interest towards innovative sample treatment techniques, moving beyond conventional extraction methods that utilize biologically hazardous solvents.

Chronic use of morphine in pediatric patients, particularly for more than three months, poses significant risks, including respiratory depression and seizures[11]. Codeine, another alkaloid found in poppies, presents similar risks due to its metabolism into morphine, with symptoms including respiratory depression, drowsiness, and pulmonary oedema[10,12]. In some regions, misuse of poppy products for treating coughs and discomfort in infants can lead to severe toxicity and even death.

This research aims to evaluate the clinical and laboratory profiles of infants and children admitted to tertiary care hospitals due to poppy intake and to compare outcomes between those who survived and those who did not.

METHODOLOGY

The study was carried out in Tertiary Care Hospitals in Peshawar, KPK, Pakistan, from August 2022 to August 2023 with permission from the local Ethical Committee. All participants' parents provided their informed consent. Sixty-five babies and kids with a verified history of opium poppy consumption at home and one or more clinical signs of opium toxicity, such as meiosis, low breathing rate, decreased level of consciousness, convulsions, or vomiting, were included in the study. The study did not include infants whose mothers were taking opioid analgesics or children who were given opioids (such as morphine).

Age, gender, clinical presentation, rationale for providing opium poppy, preparation and delivery technique, parents' educational backgrounds, work position, socioeconomic situation, number of siblings, hospital admission time following intake, and patient outcomes were among the information gathered. There

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were three categories for socioeconomic status: poor/lower class, middle class, or high class/wealthy; also, there were two categories for employment: unemployed and employed. Mothers were classified as either housewives or working adults. After a thorough history, examination, and assessment, cases involving encephalitis, septic shock, convulsions, drug overdose, and related illnesses were excluded.

The data analysis software used was SPSS version 23. Frequencies were expressed as percentages and subjected to the Chi-square test to analyse qualitative variables. The quantitative data, expressed as mean and standard deviation, was studied using the independent t-test. Less than 0.05 was the threshold for statistical significance. The Kolmogorov-Smirnov and Shapiro-Wilk tests were used to determine the normality of all quantitative variables, and normally distributed variables were studied.

RESULTS

A total of 65 cases of opium poppy toxicity were included in the study, with the age of the patients ranging from 1 month to 23 months (mean age: 7.45 ± 5.38 months). Among these cases, 30 (46.15%) were male and 35 (53.85%) were female. Out of all the cases, 30 (46.15%) infants and children survived, while 35 (53.85%) died.

In every case, poppies were given as a traditional home treatment for various illnesses. Excessive coughing and crying (25 cases) were the most common reason for providing poppy, followed by excessive weeping alone (18 cases), coughing (15 cases), and fever with cough (7 cases). The poppy was either given as a powder, made by pulverising poppy seeds and combining them with a tiny amount of water (30 cases) or as a liquid, made by boiling it in water and giving it to the young patients (35 cases).

The average period from poppy intake to hospital admission was 9.58 ± 4.95 hours, while the range was 2 to 20 hours. The cases had an average temperature of 37.55 ± 0.65°C and an average oxygen saturation of 86.8 ± 6.02%. Meiosis (constriction of the pupils) and modified sensorium were evident in every patient. Aspiration pneumonia was observed in 32 instances, apneic episodes in 33 cases, and seizures in 35 cases.

Laboratory findings included anaemia, leukocytosis, electrolyte imbalances, and elevated levels of urea and creatine phosphokinase (CPK). Tables I and II present specific clinical and analytical results. Out of the 48 instances, 47 belonged to the lower socioeconomic class, 17 to the middle class, and none to the upper socioeconomic class. Table III lists the parents' career and educational backgrounds along with the size of the family.

The majority of the infants in critical condition also displayed other severe clinical scenarios, as previously indicated, and all showed abnormal sensorium and meiosis. All cases involved the administration of naloxone, an antidote for opium poisoning, which reversed the effects of the poppy's morphine alkaloids. The usual naloxone dosage was 0.1 mg/kg, and in certain situations, it was given again to keep the reversal going.

Tables II and III evaluated the effects of several factors on outcomes (survival versus death). Infants and children in Group A (survived) had a mean age of 7.92 ± 4.88 months, whereas those in Group B (died) had a mean age of 7.02 ± 5.70 months; however, this difference was not statistically significant (p=0.580). Group A's gender distribution revealed 13 men and 17 women, while Group B's revealed 17 men and 18 women (p=0.290).

There was a strong association between the reason for administering the poppy and the outcome (death or survival). Of the 25 cases where the reason was coughing and excessive crying, 22 resulted in death and 3 in survival (p=0.003). Other complaints, such as coughing (9 survived, 6 died), excessive crying (11 survived, 7 died), and fever with cough (4 survived, 3 died), had better survival rates.

Children who were given poppy powder combined with water had a much greater mortality rate—26 out of 30 instances resulted in death, compared to 4 survivors. In contrast, the results were better for those who received boiling water from poppy pods (26 lived, nine died; p<0.001).

The time to hospital admission was another critical factor; children who survived reached the hospital in a mean time of 6.1 ± 2.64 hours, compared to 12.54 ± 4.20 hours for those who died (p<0.001).

Table II illustrates the clinical characteristics that were substantially linked to increased mortality: cyanosis, aspiration pneumonia, low respiratory rate, decreased oxygen saturation, and apneic episodes. Leukocytosis (>15,000/mm³) also correlated with increased mortality (p=0.004). However, other laboratory findings, such as anaemia, electrolyte imbalances, raised serum urea, and elevated CPK levels, were not significantly associated with outcomes.

While altered sensorium and meiosis were observed in all cases, making statistical comparison for these factors irrelevant, other factors such as parental education, job status, and socioeconomic status showed no significant association with mortality. However, a high number of siblings (four or more) was significantly associated with higher mortality rates; 33 out of 34 children with more than four siblings died (p<0.001), as shown in Table III.

Table I: Clinical and Laboratory Characteristics of Poppy Poisoning Cases (n = 65)

Profile		Result
Age (in months)	Mean	7.22 ± 5.43 months
	Min-Max	1 month to 23 months
Outcome	Survived	30 cases (46.15%)
	Died	35 cases (53.85%)
Gender	Males	28 (43.1%)
	Females	37 (56.9%)
Main reason for giving poppy	Fever and cough	8 cases (12.3%)
	Cough	14 cases (21.5%)
	Excessive cry	18 cases (27.7%)
	Excessive cry and cough	25 cases (38.5%)
Form of giving poppy	Powder form mixed in water	30 cases (46.2%)
	Poppy pods boiled in water	35 cases (53.8%)
Time duration (hours) from intake of poppy to hospital	Mean	9.44 ± 4.75 hours
	Min-Max	2 hours to 19 hours
Clinical findings	Temperature °C:	37.50 ± 0.60°C
	Min-Max:	36.5°C, 39.1°C
	Oxygen saturation:	Mean = 87.3 ± 5.82%
	Min-Max:	76%, 95%
	Meiosis:	65 cases (100%)
	Low respiratory rate:	55 cases (84.6%)
	Seizures:	39 cases (60%)
	Altered sensorium:	65 cases (100%)
	Apneic spells:	37 cases (56.9%)
	Aspiration pneumonia:	35 cases (53.8%)
Laboratory findings	Hemoglobin ≤9 gm%:	41 cases (63.1%)
	Leucocytosis ≥15000/ml:	43 cases (66.2%)
	Hypernatremia ≥150 mEq/L:	8 cases (12.3%)
	Hyponatremia ≤135 mEq/L:	2 cases (3.1%)
	Hyperkalemia >5 mEq/L:	10 cases (15.4%)
	Hypokalemia <3.5 mEq/L:	4 cases (6.2%)
Education status	Mother Uneducated:	47 cases (72.3%)
	Mother Educated:	18 cases (27.7%)
	Father Uneducated:	41 cases (63.1%)
	Father Educated:	24 cases (36.9%)
Socioeconomic status	Poor class:	49 cases (75.4%)
	Middle class:	16 cases (24.6%)
Father job status	Jobless:	10 cases (15.4%)
	Employed:	55 cases (84.6%)
Mother job status	Housewife:	57 cases (87.7%)
	Employed:	8 cases (12.3%)
Number of siblings in the family	Four or more:	35 cases (53.8%)
	Less than four:	30 cases (46.2%)

Table II: Impact of Various Factors on Outcomes in Poppy Poisoning Cases

Factor	Total (N=65)	Group A (Survived) N=30	Group B (Died) N=35	p-value
Age (in months)	Mean ± SD: 7.22 ± 5.43	7.77 ± 4.94	6.74 ± 5.92	P=0.600
Gender	Male: 28 (43.1%)	10 (33.3%)	18 (51.4%)	P=0.308
	Females: 37 (56.9%)	20 (66.7%)	17 (48.6%)	
Main reason for giving poppy	Cough: 14 (21.5%)	12 (40.0%)	2 (5.7%)	P=0.005
	Excessive cry: 18 (27.7%)	12 (40.0%)	6 (17.1%)	
	Cough & excessive cry: 25 (38.5%)	2 (6.7%)	23 (65.7%)	
	Fever and cough: 8 (12.3%)	4 (13.3%)	4 (11.4%)	
Form of giving poppy	Poppy pods boiled in water: 35 (53.8%)	26 (86.7%)	9 (25.7%)	p<0.001
	Poppy powder mixed in water: 30 (46.2%)	4 (13.3%)	26 (74.3%)	
Time duration (hours) from intake of poppy to hospital	9.44 ± 4.75 hours	6.00 ± 2.56 hours	12.47 ± 4.14 hours	p<0.001
Clinical findings				
Temperature °C	37.50 ± 0.60	37.49 ± 0.59°C	37.51 ± 0.63°C	
Oxygen saturation	87.3% ± 5.82	92.47 ± 1.81%	82.82 ± 4.07%	p<0.001
Meiosis	65 (100%)	30 (100%)	35 (100%)	
Respiratory depression	Yes: 55 (84.6%)	20 (66.7%)	35 (100%)	P=0.015
	No: 10 (15.4%)	10 (33.3%)	0 (0%)	
Seizures	Present: 39 (60%)	16 (53.3%)	23 (65.7%)	
	Absent: 26 (40%)	14 (46.7%)	12 (34.3%)	
Altered sensorium	65 (100%)	30 (100%)	35 (100%)	
Apneic spells	Present: 37 (56.9%)	10 (33.3%)	27 (77.1%)	P=0.031
	Absent: 28 (43.1%)	20 (66.7%)	8 (22.9%)	
Aspiration pneumonia	Present: 35 (53.8%)	6 (20%)	29 (82.9%)	P=0.001
	Absent: 30 (46.2%)	24 (80%)	6 (17.1%)	
Cyanosis	Yes: 35 (53.8%)	4 (13.3%)	31 (88.6%)	p<0.001
	No: 30 (46.2%)	26 (86.7%)	4 (11.4%)	
Hemoglobin ≤9 gm%	41 (63.1%)	18 (60%)	23 (65.7%)	
		12 (40%)	12 (34.3%)	
Leucocytosis ≥15000/ml	43 (66.2%)	12 (40%)	31 (88.6%)	P=0.008
		18 (60%)	4 (11.4%)	
Hypernatremia ≥150 mEq/L	8 (12.3%)	4 (13.3%)	4 (11.4%)	
		26 (86.7%)	31 (88.6%)	
Hyponatremia ≤135 mEq/L	2 (3.1%)	0 (0%)	2 (5.7%)	
		30 (100%)	33 (94.3%)	
Hyperkalemia >5 mEq/L	10 (15.4%)	2 (6.7%)	8 (22.9%)	
		28 (93.3%)	27 (77.1%)	
Hypokalemia <3.5 mEq/L	4 (6.2%)	4 (13.3%)	0 (0%)	
		26 (86.7%)	35 (100%)	
Serum urea >40 mg%	8 (12.3%)	6 (20%)	2 (5.7%)	
		24 (80%)	33 (94.3%)	
Serum CPK ≥500 u/L	12 (18.5%)	6 (20%)	6 (17.1%)	

Table III: Additional Factors Influencing the Outcomes of Poppy Poisoning Cases

Factor	Total (N=65)	Group A (Survived) N=30	Group B (Died) N=35	p-value
Education (Mother)				
Uneducated	46 (70.77%)	22 (73.33%)	24 (68.57%)	P=0.778
Educated	19 (29.23%)	8 (26.67%)	11 (31.43%)	
Education (Father)				
Uneducated	39 (60.00%)	19 (63.33%)	20 (57.14%)	P=0.645
Educated	26 (40.00%)	11 (36.67%)	15 (42.86%)	
Mother Job				
Housewife	57 (87.69%)	26 (86.67%)	31 (88.57%)	P=1.00
Employed	8 (12.31%)	4 (13.33%)	4 (11.43%)	
Father Job				
Jobless	10 (15.38%)	4 (13.33%)	6 (17.14%)	P=0.742
Employed	55 (84.62%)	26 (86.67%)	29 (82.86%)	
Socioeconomic Status				
Poor	50 (76.92%)	26 (86.67%)	24 (68.57%)	P=0.094
Middle class	15 (23.08%)	4 (13.33%)	11 (31.43%)	
Siblings				
Number of siblings >4	35 (53.85%)	2 (6.67%)	33 (94.29%)	P<0.001
Number of siblings ≤4	30 (46.15%)	28 (93.33%)	2 (5.71%)	

DISCUSSION

The widespread availability and traditional use of opium poppy in our region have contributed to a significant public health challenge, particularly regarding its toxicity in infants and children. Often administered by parents to treat common ailments such as colds, coughs, crying, and abdominal colics, opium can easily lead to overdose and severe toxicity, potentially resulting in death[13,14]. In our study, which involved 65 cases of opium poppy toxicity, the mortality rate was 50.77%. This high mortality rate highlights the critical and life-threatening nature of opium poisoning in children, underscoring the urgent need for timely medical intervention.

The most frequent reasons for opium administration were to manage excessive crying and cough, accounting for 35.38% of the cases. In most cases, poppy pods were boiled in water to deliver opium, or the powdered poppy was mixed with water in 46.15 per cent of cases. These results align with those of other research

projects carried out in comparable environments. Allameh et al., for example, documented 31 cases of opium poisoning in Iran, where the drug was prescribed for ailments like cough, diarrhoea, colic, and restlessness[15]. Similarly, Rostam-Abadi et al. documented 310 children admitted to Loghman Hakim Hospital in Iran between 2001 and 2009 due to opium toxicity, with the majority of cases involving infants and toddlers who had been given opium as a folk remedy for minor complaints[16]. In the local context, Safdar et al. highlighted the issue of opium poisoning in Pakistan, reporting 22 cases of infant poisoning at Lady Reading Hospital, Peshawar, in 1979. The symptoms observed in these cases, such as drowsiness, cyanosis, and seizures, align with the clinical presentations in our study[17]. While some reports suggest that the frequency of opium intoxication in infants has decreased over time, our findings indicate that it remains a significant problem in certain regions[18,19].

Interestingly, our study did not find a significant correlation between the educational status of parents and the outcome of opium poisoning. However, families with more than four children exhibited significantly higher mortality rates, suggesting that larger family size may be a risk factor, possibly due to divided attention and care. Moreover, the potential for water source contamination near poppy fields presents an additional risk of accidental exposure to opium, highlighting the need for community education on the dangers of using opium for medicinal purposes. Management of opium poisoning typically involves the use of naloxone, an opioid antagonist. However, there is no standardized consensus on the optimal dosage, with existing guidelines varying significantly. Complications during treatment, such as hypertension, opioid redistribution from adipose tissue, gastrointestinal motility dysfunction, and rhabdomyolysis, further complicate the development of dosing algorithms[20]. For example, a study by Vitzthum found that symptoms of opioid toxicity might persist or recur even after prolonged naloxone infusion, emphasizing the challenges in managing these cases[21]. Methadone, another opioid, has been identified as a common cause of poisoning in children. Studies by Baldo and Rose have shown that methadone is a leading cause of pediatric poisoning, which complicates the broader issue of opioid toxicity in pediatric patients[22]. Authorities should implement and enforce regulations to limit the availability of opium poppy and prevent its misuse. Additionally, further research is needed to establish standardized treatment protocols for managing opioid toxicity in children, including the development of optimized naloxone dosing strategies. Addressing the socioeconomic factors that contribute to the misuse of opium, such as poverty and lack of access to healthcare, will also be crucial in reducing the incidence of pediatric opioid poisoning.

CONCLUSION

The opium poppy is commonly administered to infants and children by parents as a remedy for common ailments such as colds, coughs, crying, and restlessness. However, our study of 65 cases of opium toxicity highlights the severe dangers associated with this practice. Opium ingestion can lead to respiratory depression, coma, and potentially fatal outcomes. The high mortality rate observed in our study (50.77%) underscores the critical need for public education on the risks of using opium as a home remedy. Efforts should be made to curtail the sale and use of opium poppy by implementing stricter regulations and raising awareness about its hazards. In addition, promoting proper hygiene and family planning can significantly reduce the incidence of opium poisoning and improve the overall health outcomes in pediatric populations. Enhanced community education and robust public health strategies are essential to mitigate the dangers associated with opium poppy and protect vulnerable children from its toxic effects.

Ethical Approval: Approval for this study was granted by the Ethical Review Board of the hospital before commencing the research.

Informed Consent: Informed consent was secured from the parents or guardians of all participants for the publication of their case data.

Conflict of Interest: The authors declare that there are no conflicts of interest related to this study.

REFERENCES

1. Agrawal, N., S. Kumar, and N. Gupta, *Pharmacological Benefits of Papaver somniferum L.: Nutritional and Medicinal Aspects of Opium Poppy*, in *Pharmacological Benefits of Natural Agents*. 2023, IGI Global. p. 298-317.
2. Kwiecień-Obara, E., et al., *Morphine (obtained from poppy seeds) and dextrometorfan poisoning–a case report.* Przeglad Lekarski, 2016. **73**(8): p. 596-598.
3. Duthel, H., *Illegal drug trade-The War on Drugs: Drug trade generated an estimated US $531.6 billion in 2013*. 2015: BoD–Books on Demand.
4. Akram, S., M. Fazil, and K. Ullah, *Poppy intoxication in infants and children: hazards of a folk remedy*. Journal of the College of Physicians and Surgeons--Pakistan: JCPSP, 2021. **30**(5): p. 576-581.
5. Kesavan, K., *Neurodevelopmental implications of neonatal pain and morphine exposure.* Pediatric annals, 2015. **44**(11): p. e260-e264.
6. Lyon, C. and D.B. Njoku, *Anesthetic pharmacology: physiologic states, pathophysiologic states, and adverse effects.* Essentials of Pediatric Anesthesiology, 2015: p. 27-37.
7. Oakes, V. and C. Domene, *Capturing the molecular mechanism of anesthetic action by simulation methods.* Chemical reviews, 2018. **119**(9): p. 5998-6014.
8. O'Neil, D.S., *Fix the Pumps: The History of the Soda Fountain*. 2010: Darcy O'Neil.
9. Vo Van Regnault, G., et al., *The need for European harmonization of nutrivigilance in a public health perspective: A comprehensive review.* Critical Reviews in Food Science and Nutrition, 2022. **62**(29): p. 8230-8246.
10. Chain, E.P.o.C.i.t.F., et al., *Update of the scientific opinion on opium alkaloids in poppy seeds.* EFSA Journal, 2018. **16**(5): p. e05243.
11. Knipper, E., C.J. Banta-Green, and N. Jimenez, *Opioid use disorder and misuse: A review of the epidemiology and medical implications for pediatric anesthesiologists.* Pediatric Anesthesia, 2017. **27**(11): p. 1070-1076.
12. Hauer, J., et al., *Pain assessment and treatment in children with significant impairment of the central nervous system.* Pediatrics, 2017. **139**(6): p. e20171002.
13. Martínez, M.A. and S. Ballesteros, *Opium poisoning in modern times. An overview.* Forensic science international, 2019. **302**: p. 109848.
14. Vearrier, D. and O. Grundmann, *Clinical pharmacology, toxicity, and abuse potential of opioids.* The Journal of Clinical Pharmacology, 2021. **61**: p. S70-S88.
15. Allameh, Y., et al., *Methadone poisoning in children: a systematic review and meta-analysis in Iran.* Journal of Pediatrics Review, 2017. **5**(2): p. 1-8.
16. Rostam-Abadi, Y., et al., *Public health risks associated with methadone in Iran: A systematic review and meta-analysis.* International Journal of Drug Policy, 2022. **100**: p. 103529.
17. Safdar, M., et al., *Suicide by poisoning in Pakistan: review of regional trends, toxicity and management of commonly used agents in the past three decades.* BJPsych open, 2021. **7**(4): p. e114.
18. Obladen, M., *Lethal lullabies: a history of opium use in infants.* Journal of Human Lactation, 2016. **32**(1): p. 75-85.
19. Zamani, N., H. Sanaei-Zadeh, and B. Mostafazadeh, *Hallmarks of opium poisoning in infants and toddlers.* Tropical doctor, 2010. **40**(4): p. 220-222.
20. Wijdicks, E.F. and S.L. Clark, *Neurocritical Care Pharmacotherapy: A Clinician's Manual*. 2018: Oxford University Press.
21. Vitzthum, L.K., et al., *Predicting persistent opioid use, abuse, and toxicity among cancer survivors.* JNCI: Journal of the National Cancer Institute, 2020. **112**(7): p. 720-727.
22. Baldo, B.A. and M.A. Rose, *The anaesthetist, opioid analgesic drugs, and serotonin toxicity: a mechanistic and clinical review.* British journal of anaesthesia, 2020. **124**(1): p. 44-62.

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