Letters to the Editor

[The Editor is not responsible for the views expressed by the correspondents]

Mirtazapine Induced Acute Pancreatitis with Hypertriglyceridemia — a case report

Sir, — Acute pancreatitis has numerous aetiologies – commonest being gall stones, second most common being alcohol, while other etiological agents include post ERCP, hypertriglyceridemia, drugs, anatomical abnormalities like pancreas divisum or periampullary diverticulum, renal failure, hypercalcemia, trauma, post-operative, genetic mutations such as SPINK-1, PRSS1, CFTR genes etc.[1] Amongst more than 100 drugs causing acute pancreatitis, the common ones include valproate, 5-aminosalicylic acid, azathioprine, 6-mercaptopurine, sulphonamides, oestrogens, steroids, etc.[2] Mirtazapine, an atypical antidepressant, is found to cause hypertriglyceridemia in rare instances, which, in rarer conditions, can get highly elevated to cause acute pancreatitis.[3]

This report discusses a case of acute pancreatitis in a 52-year-old male, taking mirtazapine regularly for more than 3 years. At presentation, he had acute severe pancreatitis along with hypertriglyceridemia, and his triglyceride levels came back to near-normal after 2 weeks of cessation of mirtazapine during the course of hospital stay; he was retrospectively diagnosed to have had mirtazapine induced acute pancreatitis.

Case Report

A 52-year-old non-alcoholic male patient presented with acute epigastric pain radiating to the back along with vomiting for 2 days preceding admission. There was no history of similar episode in the past. He was taking paroxetine 20 mg/day and mirtazapine 15 mg/day for last 3 years for depression as prescribed by psychiatrist. On examination, his pulse rate was 128/ minute, regular; blood pressure was 80/40 mm of Hg; respiratory rate was 30/ minute; epigastric tenderness was present; auscultation of both the lung fields was normal.

Laboratory investigations showed Hb 14.0 g/dL, TLC – 7600/ mm^3, platelets 152000/mm^3, serum amylase 878 U/L, lipase 526 U/L, urea 202 mg/dL, creatinine 6 mg/dL, Na^+ 139 mEq/L, K^+ 4.8 mEq/L, ionised Ca^{2+} 1.10 mmol/L, total cholesterol 214 mg/dL, triglyceride 807 mg/dL, HDL 19 mg/dL, LDL 42 mg/dL. Arterial blood gas analysis showed pH 7.22, HCO_3^- 11.6 mmol/L, pCO_2 26 mmol/L, PaO_2 92 mm of Hg. He was thus diagnosed to have acute pancreatitis with acute kidney injury and metabolic acidosis probably due to hypertriglyceridemia. He was shifted to the intensive care unit where he was given conservative management for acute pancreatitis along with bicarbonate infusion and 4 rounds of hemodialysis was done over a period of 7 days after which renal function and metabolic acidosis improved. All his previous medications were discontinued. An Ultrasonography of the abdomen was done the following day which revealed bulky non-homogenous pancreas, normal main pancreatic duct. Both kidneys were normal in size & corticomedullary differentiation was mildly altered bilaterally. Non-contrast CT abdomen was done on the 4th day of admission which confirmed the diagnosis of acute pancreatitis (Fig 1).

His pain subsided and his appetite returned from about the 6th day when he was initiated on liquid diet which was later titrated to fat restricted diet with pancreatic lipase supplementation. On 14th day his lipid profile was repeated which revealed total cholesterol of 110 mg/dL, triglycerides 270 mg/dL, LDL 38 mg/dL, HDL 20 mg/dL. No lipid lowering agent had been administered in those 14 days.

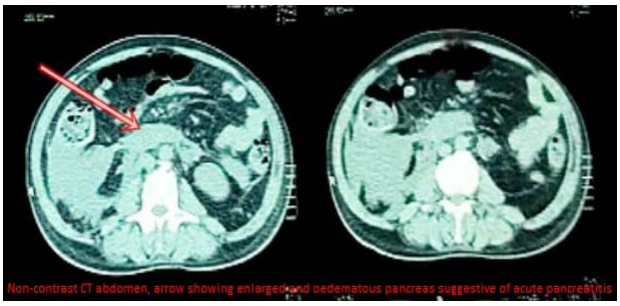

Fig 1 — Non-contrast CT abdomen, arrow showing enlarged and oedematous pancreas suggestive of acute pancreatitis

Discussion

Pancreatitis can have multiple aetiologies, of which drug induced pancreatitis is believed to account for less than 5% of the cases.[4] The pathophysiology varies according to the medication responsible. Mirtazapine, an atypical antidepressant, is being frequently prescribed for major depressive disorder and anorexia. The incidence of hypertriglyceridemia in patients taking mirtazapine is less than 10%, and in very rare instances it can cause very high level of hypertriglyceridemia and consequently may lead to acute pancreatitis.[5] The improvement in the lipid profile after cessation of one of those offending drugs lead to the possibility of mirtazapine induced acute pancreatitis in our patient as paroxetine is not known to be associated with such a high triglyceride level. Physicians must be aware of this association of mirtazapine with hypertriglyceridemia, so that lipid profile is being monitored in those patients who are being given mirtazapine. Also, a quick diagnosis based on the association can prompt cessation of the drug, which will help in reducing morbidity and mortality.

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Department of General Medicine,
Calcutta National Medical College,
Kolkata 700014
[1]MD, Assistant Professor
[2]MBBS, Postgraduate Trainee
[3]MD, Assistant Professor
[4]MD, Professor

Tuhin Santra[1],
Anustup Mukherjee[2],
Parinita Ranjit[3],
Partha Pratim Mukherjee[4]

Constitutional Ends Through Unconstitutional Means : A Doctor's View on Rajasthan Right to Health Care Act 2023

Sir, — The Rajasthan Right to Health Care Act 2023 has been in the news for several controversial reasons in the recent past. As the fiasco has ended with an eight-point agreement[1] between the government and the agitating doctors, one can say thatit is a piece of ill-conceived legislation by an overenthusiastic state government to entitle its population to the right to health.In fact, the right to health is a natural extension of the right to life and liberty guaranteed to all of us under Article 21 of the Constitution of India.The current legislation derives its basis from the fundamental rights, directive principles of state policy as well as several other judgments pronounced by the supreme court of India in this regard[2].

The major flaws in the legislation have already been thoroughly researched by several legal scholars so far and are mentioned here just for the sake of convenience. Primarily, the act has no explicit provision which covers the reimbursement of costs incurred by private healthcare establishments which violates their right to free and fair-trade practices under Article 19 (1)(g). This also, in turn, amounts to an act of hyper-regulating the private healthcare sector and impinging upon the professional rights of healthcare providers. Secondly, the act failed to contemplate privacy concerns regarding the collection, possession, transfer, and use of sensitive health information of patients. Lastly, implementing such enormous welfarist legislation involves a huge financial burden on the state which has not been properly looked into[3].

The major issue at the helm was projected as the unwillingness of the doctors working in private healthcareestablishments to cater their services to the needy by the mainstream media. The serious protests by the medical community in Rajasthan are not unfounded for any reason as alleged by a lot of armchair policy experts and pseudo-socialists. Similarly, this conflict between the parties is not a legal conundrum of *Article 21 versus Article 19* of the Constitution of India. The noble intention of the state in upholding the right to health of citizens is a welcome move but the means adopted by the state are outrightly unconstitutional because they would make private healthcare establishments commercially unviable.

This question of regulating the private healthcare sector in the interest of the upholding constitutional rights of citizens will surface in other Indian states as well in due course.It won't take long duration for this debate on*the right to health*to become a national political issue that could influence the outcome of general elections.The task at hand is not to take sides but find a harmonious and conducive way forward to achieve constitutional goals through constitutional means.

Before implementing a right to free emergency medicare, the first and foremost action desired from governments is the establishment of a statutory body with unbridled authority to reimburse healthcare institutions for all costs incurred. However, this seems like a perfect daydream under the present budgetary allocations to health by several states and the union government. Moreover, the quality of care provided at each private clinical establishment in our country is glaringly different. Healthcare establishments are a heterogeneous group that cannot be treated as a single unit for any purpose. Hence, the amount to be reimbursed to each institution for each particular procedure or healthcare service needs to be established beforehand by constituting a statutory commission for this purpose. Only after these things are done, and after due deliberations and consultations in this regard, can the state attempt to pass legislation of this sort. This may attract vast resistance from commercial establishments in the healthcare industry because it is extremely difficult to legally define and medically confirm when an individual has attained a stable medical state and is out of the need for emergency care. The practical dilemmas of shifting a patient to another center after providing emergency care may be betternot reduced to black and white. This can sometimes cause serious repercussions for patients and ethical dilemmas for medical practitioners. There is a strong necessity for developing a standard operating system for the referral of patients between institutions beforehand. This requires a scientific evaluation of existing resources on both infrastructure and human resources fronts. The state has a bound responsibility to address the refurbishment of these resources in both public and private sectors before opening the doors of all hospitals for claiming health care services as a matter of right. All in all, any legislation with public health ramifications requires thorough groundwork before trying to bring forward a gargantuan change.

The governments of the day should also attain a moral authority over and above the existing constitutional authority to persuade the medical community to prioritize public health needs. This canpartly be achieved by incentivizing medical practitioners in establishing clinics (securing lands, loans, and licenses to initiate practice), reducing the operational costs of organizations, giving tax breaks to individual practitioners, framing laws to prevent violence against doctors, using existing machinery to eliminate quackery in the hinterland, etc. A strong policy-based approach should be initiated in this regard separately towards both the individual practitioners running small nursing homes and big corporate companies running chains of hospitals.

On a personal note, the public needs to abandon the age-old perception of doctors as money-hungry individuals. The healthcare sector has evolved into a health industry driven by market forces, and doctors have become pawns in the chessboard of supply and demand. The private sector has brought about a revolutionary change in the Indian healthcare domain, which cannot be disregarded entirely in the light of its lion's share contribution during the COVID-19 pandemic. The simple principle that we would like to emphasize is that we should not try to stifle the private sector's growth at this moment, as it is destined to make healthcare more affordable in the long term due to economies of scale in a country like India.

Nevertheless, the persisting demand for upgrading public health infrastructure and human resources is something we would also like to emphasize once again. It is not just a matter of numbers and mere presence; the credibility of public health services has to take a rocket leap from current standards for the larger good of society. The public and private health insurance models in the country also require a strong revisit at this crucial moment of overhauling the healthcare sector.

In conclusion, the recent incident in Rajasthan is just the beginning of a trend towards increased state control over doctors in the private sector and the healthcare industry. All stakeholders in the private sector must make a more concerted effort to strike a balance between their public responsibilities and their legal rights, while also upholding the constitutional rights of citizens. Running away from these responsibilities is not a viable option. Instead, we must work towards finding a proper middle ground that benefits all parties involved.

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Ananth Rupesh Kattamreddy[1]
Jitendra Durga Kanna Allu[2]
[1]MD, Assistant Professor, Department of Forensic Medicine and Toxicology, ACSR Government Medical College, Nellore, Andhra Pradesh 524004
[2]MBBS, Junior Resident, Department of Forensic Medicine and Toxicology, Andhra Medical College, Visakhapatnam, Andhra Pradesh 530002

Fostering Competent Medical Graduates : The Imperative of Medically Trained Teachers in Medical Education, Inspired by Dr Frances Oldham Kelsey

Sir, — Frances Oldham Kelsey, an extraordinary individual, embarked on a remarkable journey driven by her passion for Medicine and Science. Born in Cobble Hill, Vancouver Island, British Columbia, she nurtured an early fascination with the World of Science. Her academic pursuits led her to attain a Bachelor of Science from McGill University in 1934, followed by a Master of Science in pharmacology in the subsequent year. Driven by her determination to become a competent physician, she pursued further studies in Pharmacology at the University of Chicago, where she achieved both a PhD in 1938 and an MD in 1950. Dr Kelsey's dedication to medical knowledge and patient care led her to teach pharmacology at the University of South Dakota, while also practicing general medicine starting in 1954. Her zeal to make a meaningful impact on the medical field and safeguard the well-being of the public eventually led her to accept a position with the Food and Drug Administration (FDA). As one of the few medical officials at the FDA, Dr Kelsey faced a crucial responsibility: reviewing new drug applications to ensure their safety for public use. In this pivotal role, she was assigned one of the earliest applications for thalidomide, a drug already available in numerous countries. Despite immense pressure from the drug's manufacturer, Dr Kelsey staunchly refused to authorize the application due to the lack of sufficient evidence on its safety. With an unwavering commitment to scientific rigor and her duty to protect potential patients, Dr Kelsey emphasized the importance of thorough and reliable evidence before allowing any drug to be sold on the market. Her insistence on stringent evaluation procedures proved to be a crucial decision. Approximately a year later, researchers in Germany and Australia uncovered thalidomide's devastating link to severe and rare birth defects, impacting thousands of babies who were born with hands and feet projecting directly from their shoulders and hips.Thanks to Dr Kelsey's foresight and unwavering dedication, thalidomide was never marketed in the United States. Her exemplary actions played a vital role in the passage of the 1962 Drug Amendments, a transformative bill that revolutionized drug regulation, prioritizing patient safety and scientific evidence[1]. Dr Frances Oldham Kelsey's legacy remains an enduring testament to the significance of a well-trained physician's keen judgment and steadfast commitment to patient well-being and public health. Her contributions have saved countless lives, making her an exemplary role model for medical professionals Worldwide.

Dr Frances Oldham Kelsey[1], a distinguished pharmacologist, demonstrated the importance of medical training in shaping a well-rounded and clinically oriented approach in the field of medicine. Despite earning her PhD in non-medical pharmacology in 1938, she recognized the significance of medical education and pursued an MD degree in 1950. This historical context becomes particularly relevant in the current debates surrounding non-medical teachers in MBBS and MD curricula.

In the present context, India's National Medical Commission (NMC) is emphasizing competency-based medical education, underlining the necessity of clinical orientation in subjects like Anatomy, Physiology, Biochemistry, Pathology, Pharmacology, Microbiology and others[2, 3]. Dr Kelsey's life serves as an interesting example, illustrating how a distinguished Pharmacologist came to understand the value of medical training in improving clinical judgment.

The ongoing discussions urge the exclusion of non-medical teachers from medical courses. It is essential to acknowledge the expertise of MSc Postgraduates and PhD non-medical teachers in their respective subject domains. They can be effectively utilized in areas such as research and development, conducting laboratory work and contributing to various research activities.

However, the focus should be on providing medical students with the highest level of efficient training, considering the significant responsibility they carry in providing appropriate care for a population of over 130 crores. Drawing lessons from Dr Frances Oldham Kelsey's life, it becomes evident that clinical training is indispensable in upholding the best practices for both patient care and drug development.

In light of this, it is crucial for regulators and the Government to deliberate on appropriate guidelines for the future. Strengthening drug regulatory procedures requires a balanced representation of both medically trained professionals and non-medical professionals. Collaborative decision-making, incorporating insights from both domains, can enhance drug regulations in India and contribute to the overall well-being of society.

In summary, Dr Kelsey's extraordinary journey underscores the importance of medical training in shaping competent medical professionals. As the medical education landscape evolves, maintaining a clinically oriented approach becomes paramount to ensure the best possible care for patients and the advancement of drug development. A thoughtful and inclusive approach to regulatory procedures can further strengthen healthcare practices and ultimately benefit society at large.

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Shambo S Samajdar[1]
Santanu Munshi[2]
School of Tropical Medicine, Kolkata 700073
[1]MD, DM, Clinical Pharmacologist,
[2]MD, DM, Professor and Head,
Department of Clinical & Experimental Pharmacology