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Prolactin monitoring in the acute psychiatry setting

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ABSTRACT

Hyperprolactinaemia is a common side effect associated with psychotropic medication. Limited guidance on its monitoring and management results in inconsistency in practice due to individual clinical variability. A retrospective service evaluation study was conducted on all patients admitted to an acute psychiatric assessment unit in South Wales, United Kingdom, over one calendar year ($n=524$), to assess the prevalence and possible causes of hyperprolactinaemia, correlation with symptomatology and monitoring and management by clinicians. The prevalence of hyperprolactinaemia in this population ($n=67$, 13%) was higher than in the general population. The most common association was medication ($n=39$, 58%), particularly Risperidone ($n=19$). Illicit substance use ($n=10$, 15%), and physical conditions ($n=12$, 18%) may also have contributed. However, only 44 (66%) received follow-up for their hyperprolactinaemia. There was a statistically significant difference in the sample means of those that did receive follow-up and those who did not, suggesting a degree of bias in patients selected to receive follow-up. These findings suggest that hyperprolactinaemia is relatively common in patients with mental illness, and that comprehensive guidelines need to be established for the monitoring and management thereof.

1. Introduction

Hyperprolactinaemia is a relatively common endocrinological disorder, with a prevalence documented at around 0.4% in the general population (Biller et al., 1999). There are many known causes, both physiological and pathological, such as prolactinoma, chronic kidney disease, hypothyroidism, illicit substance use and pregnancy (Mancini et al., 2008). It is also a side effect of many medications including antipsychotics.

Antipsychotics are regularly prescribed for patients with a range of psychiatric disorders, including schizophrenia, bipolar disorder, delusional disorder and increasingly also non-delusional disorders (Pakpoor and Agius, 2014). Ever since the accidental but revolutionising discovery of Thorazine in the 1950's, psychiatrists have contended with troublesome side effects as reported by their patients. Early first-generation antipsychotics were noted for their potentially debilitating extra-pyramidal effects. Clozapine, still arguably the most efficacious antipsychotic, is prescribed cautiously due to the risk of potentially fatal blood dyscrasias, and the newer 'second-generation' antipsychotics can cause a wide variety of cardiovascular and metabolic side-effects (Rummel-Kluge et al., 2010).

Consequently, guidelines published by the National Institute for Health and Clinical Excellence (NICE) emphasize the importance of monitoring and managing cardiovascular risk factors in patients taking antipsychotic medication (NICE 2009). There are however no formal recommendations with regard to monitoring other side effects associated with these drugs, including hyperprolactinaemia.

Typical antipsychotics have been shown to raise prolactin levels mere minutes after administration in both healthy individuals and patients with schizophrenia. Meltzer et al., 1974 reported that administration of a typical antipsychotic to 27 newly admitted patients with schizophrenia caused a mean 3.2-fold (men) and 3.8-fold (women) increase in serum prolactin, which did not dissipate over a three-month study period, suggesting that tolerance does not develop. Furthermore, a study on 67 patients with schizophrenia that had been stable on the same antipsychotic medication for at least two years found a significant correlation between drug doses and plasma prolactin levels (Smith et al., 2002). Research on patients with first-episode psychosis has also provided an insight into the role of hyperprolactinaemia in patients with mental illness. Riecher-Rössler et al., 2013 found that 39% of

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antipsychotic-naïve patients displayed raised prolactin levels not attributable to other causes. The study raised the possibility of 'mental-stress' as an independent risk factor for hyperprolactinaemia, and that stress in its own right may also trigger psychosis (Riecher-Rössler et al., 2013).

Hyperprolactinaemia may present with galactorrhoea, disturbance of the menstrual cycle (oligomenorrhoea or amenorrhoea), may affect sexual wellbeing by causing decreased libido in both sexes and cause decreased potency in men (Chahal and Schlechte, 2008). In addition, patients may experience symptoms consistent with oestrogen and androgen deficiency (Peveler et al., 2008; Peuskens et al., 2014). Furthermore, there is an increased risk for low bone density and osteoporosis in patients on long-term therapy with antipsychotics when there is associated prolactin elevation (Meaney et al., 2004; Peveler et al., 2008; Peuskens et al., 2014). Hyperprolactinaemia and its effects may also be asymptomatic, and possible consequent osteoporosis therefore has the potential to be severe by the time it is detected (Meaney et al., 2004). Moreover, while the severe downstream effects of hyperprolactinaemia are uncommon, even the more common described side effects are amongst the most important reasons quoted by patients for non-compliance (Zadrozna-Sliwka et al., 2007; Stubbs, 2009; Novick et al., 2009; Maggi et al., 2013).

The Maudsley Prescribing Guidelines in Psychiatry recommend that patients with schizophrenia should have a baseline prolactin level measured prior to commencing antipsychotic medication, followed by repeat measurements six months into treatment and then annually once the treatment dose has been stabilised (Taylor, 2012). It is also recommended that the antipsychotic agent should be switched, or that Aripiprazole be added, should a patient develop symptomatic hyperprolactinaemia, since Aripiprazole is known to attenuate serum prolactin levels (Peuskens et al., 2014). The guidelines also recommend that patients are asked proactively about symptoms possibly related to hyperprolactinaemia at three months. They also note that the severity of the symptomatology may not correlate with the levels of prolactin. The guidelines do not however, prescribe recommendations for the monitoring of asymptomatic hyperprolactinaemia, which may be important in managing the risk of osteoporosis or osteopenia. Furthermore, there are no recommendations on how to monitor a patient with a raised prolactin level at baseline. It can therefore be challenging to both interpret and act upon moderately elevated results, especially as there is limited evidence as to when an elevated prolactin level attains clinical significance.

American Psychiatric Association guidelines recommend that patients are asked about symptoms consistent with possible hyperprolactinaemia prior to starting an antipsychotic and that a baseline serum prolactin level should be measured depending on the clinical history. They recommend screening for symptoms of hyperprolactinaemia at each follow-up appointment until the patient is stable and annually from then onwards. Again, whether or not to measure plasma prolactin levels on a follow up basis is left to the discretion of the individual clinician (Citrome, 2008).

It would appear that national supporting guidance is lacking, and clinical decisions around the monitoring and management of hyperprolactinaemia in the psychiatric population fall to the individual clinician. The authors believe this is far from ideal, and warrants further work into establishing national guidelines that are more robust.

1.1. Aims and objectives

The aim of the study was to analyse prolactin levels in a psychiatric population admitted in an acute setting over one calendar year, and to observe how these were managed and monitored by clinicians. The objectives were to establish the prevalence of hyperprolactinaemia in the above cohort of patients, explore the possible causes, to assess how often patients presented with symptomatology, the nature of those symptoms, and how patients with hyperprolactinaemia were managed and followed up. The psychiatric diagnoses and the investigations performed and onward referrals initiated in the context of hyperprolactinaemia were also examined.

2. Methodology

2.1. Study location and local policy

Retrospective data was collected from all patients admitted to the acute psychiatric assessment unit at the Royal Glamorgan Hospital, a 570-bed medium sized district general hospital in South Wales, United Kingdom, between 1 Jan 2013 and 31 Dec 2013. The model of care adopted by the Health Board is relevant in the context of prolactin monitoring and involves the operation of a 14-bedded Acute Assessment Unit (AAU) and a six-bedded Psychiatric Intensive Care Unit (PICU) for a catchment population of approximately 320,000. All acute psychiatric admissions for the entire Health Board come through either of these units. Once patients are stabilised over a short period of time (one to three weeks), they are discharged from the AAU/PICU either back to the community or alternatively to less acute 'treatment wards', to the care of the sector/community teams who are best placed to undertake their continued care.

As part of a battery of tests requested for all patients admitted to the AAU/PICU (Fig. 1), local guidelines dictate that serum prolactin levels are checked for patients deemed 'at-risk' for hyperprolactinaemia.

Specifically, this includes patients on, or likely to be prescribed psychotropic medication at the time of admission.

Assessment / Investigations on Admission to the AAU
· Full Psychiatric Assessment · Complete Physical History and Examination Full Medication History confirmed by GP · Haematology (Full Blood Count) · Biochemistry (Urea & Electrolytes, C-Reactive Protein, Liver Function, Bone Profile, Thyroid Function, Prolactin, Vitamin B12, Folate · Urine Drug Screen (UDS) · ECG · Imaging (as appropriate) including: Chest X-Ray, CT / MRI Head

Fig. 1. Assessment/Investigations on Admission to the AAU.