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Clinical and scientific letters

OVERVIEW

Letters not directly related to articles published in *Clinical Medicine* and presenting unpublished original data should be submitted for publication in this section. Clinical and scientific letters should not exceed 500 words and may include one table and up to five references.

Clinical stories are necessary for drug safety

Post-marketing reports of suspected adverse drug reactions (ADRs) are key elements to prevent patients being harmed by drugs. In addition to the data collected on pre-specified fields, descriptive free-text case stories (narratives) might be crucial when interpreting these reports, which can add to the knowledge of adverse effects and are the basis for regulatory decisions.

Narratives occur in only 11% of the reports in VigiBase,[1] the WHO Global Individual Case Safety Report database.[2] Usually only minimum information about the drugs and ADRs are listed in the structured data fields. The citation below is a fragment from a published case report for a 13-year-old boy with olanzapine-induced rhabdomyolysis with concomitant lithium-induced electrocardiogram changes.

> *On day 1 (8 weeks prior to hospitalization) the patient had been admitted to a psychiatric residential care controlled environment facility because of a behavioural disorder and was placed on olanzapine 2.5 mg/d. On day 6, he reported weakness, sore throat, abdominal cramping, myalgias, and diaphoresis, which appeared to be consistent with influenza. On day 14, he experienced increasing weakness and failed to participate in organized activities, which was misinterpreted by the residential care faculty as manifestation of disobedient and oppositional behaviour. Sertraline 100 mg every morning and lithium sustained release 300 mg twice a day were added to olanzapine. On day 27, he fell several times while trying to get out of bed. He was transferred to an outside institution where he was noted to have an elevated creatine phosphokinase, leukocytosis and T-wave inversion of his precordial leads.*[3]

The same case is reported in VigiBase, but the standard report fields only mention patient age and gender, olanzapine and lithium and the ADRs myocardial infarction and rhabdomyolysis. The description of the course of the events provided in the narrative was essential to complete a causality assessment and provided a greater understanding of the clinical picture for rhabdomyolysis in this teenager. Information found exclusively in VigiBase narratives[1] includes ADR severity and site, intervention, patient ethnicity and specifications of the underlying disease. Variables having assigned standard fields, regardless of how they are reported exclusively in free-text, are: drug indication, concomitant drugs, dose, onset date of ADR and laboratory findings. Information on withdrawal of drug treatment (dechallenge) or the re-introduction of drug treatment after withdrawal (rechallenge) can also appear exclusively in the narratives.[1]

Methods

A random sample of 50 reports from VigiBase was evaluated by an expert physician, without access to previously recorded causality assessments. Each narrative was categorised as: (1) crucial to causality assessment of suspected ADRs; (2) considerably affecting the understanding of the clinical course of the reported events; or (3) adding no useful information to the standard report fields.

The length distribution of narratives within the randomised sample ranged from 20 to 3,395 characters, reflecting the general narrative length distribution of reports in VigiBase. In parallel, we also studied longer outlier narratives in VigiBase (defined as reports ranging from 10,000 to 20,000 characters); 50 such reports were evaluated according to the same categorisation.

Results

Within the sample of narratives with general-length distribution, 22% (n=11) contained information that was crucial to the causality assessment. An additional 26% (n=13) considerably affected the understanding of the clinical course of the cases (Table 1). When applying the same categorisation on the sample of 50 long outlier narratives, the proportion of information that was crucial to causality assessment increased to 32% (n=16) and the proportion considerably affecting the clinical understanding to 42% (n=21).

Among 50 reports with narratives of general length, the causality or clinical assessment of almost every second report (48%) was affected when taking the narrative into

Table 1. Narratives affecting outcomes of causality or clinical assessment for each studied sample.

Narratives	1 Affecting causality assessment n (%)	2 Affecting clinical assessment n (%)	3 Not affecting causality or clinical assessment n (%)
Random sample of 20–3,395 characters (n=50)	11 (22)	13 (26)	26 (52)
Random sample of 10,000–20,000 characters (n=50)	16 (32)	21 (42)	13 (26)

consideration. The assessment of 50 reports with long narratives (10,000–20,000 characters) was affected in 74% of cases.

Discussion

Our evaluation of two international samples of randomly selected reported clinical stories highlights the importance of detailed descriptions of circumstances under which suspected ADRs occur. Without the case story, crucial misinterpretation of case reports could lead to wrong regulatory decisions and deny clinically useful information to healthcare practitioners. ■

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2 Lindquist M. Vigibase, the WHO Global ICSR Database System: basic facts. *Drug Inf J* 2008;42:409–19.
3 Rosebraugh CJ, Flockhart DA, Yasuda SU, Woosley RL. Olanzapine-induced rhabdomyolysis. *Ann Pharmacother* 2001;35:1020–3.

How frequently are bedside glucose levels measured in hospital inpatients on glucocorticoid treatment?

Glucocorticoids are widely used in many medical specialties for their anti-inflammatory and immunosuppressive qualities. The majority of glucocorticoid use occurs in the outpatient setting. Long-term glucocorticoid use is associated with several side effects, including the development of hyperglycaemia. Observational data for many, if not most, medical and surgical conditions requiring hospitalisation suggest that the additional presence of hyperglycaemia or diabetes is associated with poorer outcomes.[1,2] Despite this association there are no data on the prevalence of glucocorticoid use in hospitalised inpatients.

We conducted a single centre prevalence study carried out over two consecutive days in January 2014, assessing every adult bed (n=940) in our institution, excluding the accident and emergency department, coronary care, and intensive care units. Our aim was to look at the number of patients on glucocorticoids and to see how many had their glucose levels measured.

We found that 120 patients (12.8%) were being treated with glucocorticoids; 99 of these (82.5%) were on prednisolone. The mean daily dose (MDD) for prednisolone was 25.0 mg ± 12.5 (range 0.5–60). Sixteen patients (13.3%) were receiving dexamethasone with a MDD of 9.2 mg ± 6.5 (range 0.5–20). The remaining four patients (3.3%) were being treated with hydrocortisone either intravenously or orally, with a MDD of 107.5 mg ± 106.9 (range 20–200). Sixty-four (53.3%) of patients who were being treated with glucocorticoids had been receiving their treatment for longer than 10 days at the time the data was collected.

Table 2. Baseline characteristics and steroid use of patient cohort (n=120).

Variable	Category	n (%)
Age (years)*		74.7±14.3
Gender (Male:Female)		52:68 (43.3:56.7)
Previous diagnosis of diabetes (Yes:No)		16:104 (13.3:86.7)
Steroid type	Prednisolone	99 (82.5)
	Dexamethasone	16 (13.3)
	Hydrocortisone	4 (3.3)
Indication for steroids	Respiratory	76 (63.3)
	Musculoskeletal	14 (11.7)
	Vasculitis	7 (5.8)
	Oncology	12 (10.0)
	Other	11 (9.2)
Duration of course	>10 days	64 (53.3)
	<10 days	56 (46.7)
Glucose monitoring	No monitoring	95 (79.2)
	Glucose levels monitored	25 (20.8)

*Mean ± standard deviation.

Of the 120 patients receiving glucocorticoids, only 25 (20.8%) had their blood glucose levels measured during their time as inpatients. Of these, 13 had pre-existing diabetes. There were three patients who had diabetes and were receiving glucocorticoids but had no regular blood glucose measurements. Compared to those without diabetes, patients with pre-existing diabetes were more likely to have their glucose levels measured ($p<0.001$). Of the patients without diabetes, only 12 patients (11.5%) were having their blood sugars measured while on glucocorticoids.

This study has highlighted the need for continued improvement to the care of hospitalised inpatients. Despite the knowledge that glucocorticoids cause hyperglycaemia and that high levels of glucose are associated with harm, very few patients in this study were having their glucose levels measured.

We suggest that all hospitalised patients being treated with glucocorticoid doses greater than an equivalent of 7.5 mg of prednisolone must have their blood glucose levels measured regularly. Initially this should be postprandially once or twice per day, and if the glucose level is found to be >12 mmol/l during any 24-hour period then testing should be before meals and before bedtime. If glucose levels remain >12 mmol/l then treatment (initially with sulfonylureas) should be started. A new guideline produced by the Joint British Diabetes Societies Inpatient Care group addresses glucocorticoid associated hyperglycaemia and is freely available at www.diabetologists-abcd.org.uk/JBDS/JBDS.htm. ■