

BACKGROUND

When intravenous (IV) pegaspargase began to replace the intramuscular (IM) injection as the predominant route of administration, there were reports of a suspected greater rate of hypersensitivity reactions (HSRs) with the IV route. Such reactions warrant therapeutic changes for acute lymphoblastic leukemia. We reviewed 8 reports on this issue.

RESULTS

- For grade 3-4 HSRs, the rates are comparable with IV and IM administration.
- Grade 2 HSRs appear to be more likely with IV than IM administration but the validity of the difference is uncertain.
- None of the HSRs were grade 4 by either IV or IM administration, one-third were grade 3, and two-thirds were grade 2 (no grade 1 HSRs were reported). There was no difference in grade 3 HSR rates at any of the 5 institution-specific sites that included individual grade levels in their reports
- Multiple factors confound the analyses, including the historically controlled nature of the comparisons and the increased likelihood of reporting adverse reactions with IV administration.

CONCLUSIONS

The reports are inconsistent to conclude that the IV HSR rate is more problematic than with IM injection. The most significant problem is the implementation of CTCAEv4.0 during the years covered by the retrospective chart reviews that not only resulted in lower grade HSRs being reported at higher grades but also increased the likelihood of an HSR being reported. Grade 2 HSRs appear to be more likely with IV than IM administration but the validity of the difference based on these studies is uncertain.

METHODS

A PubMed search using appropriate terms identified 8 peer-reviewed reports comparing IV to IM pegaspargase. Included were abstract presentations at national meetings. These 8 reports were examined based on number of patients evaluated, the grading of hypersensitivity reactions, and which Common Terminology Criteria for Adverse Events (CTCAE) version was used.

Report In order of Publication/Presentation Date			No. of Patients	IM HSRs	No. of Patients	IV HSRs	$\chi^2$ p-value
1	Children’s Minnesota, Minneapolis, Minnesota	2005-2010	186	20 (9%)	10	4 (40%)	0.01
2	Aflac Cancer Center and Blood Disorders Service of Children’s Healthcare of Atlanta, Georgia	2006-2008	27	3 (11%)	16	2 (12%)	1
3	Aflac Cancer Center and Blood Disorders Service of Children’s Healthcare of Atlanta, Georgia	2006-2011	159	17 (11%)	159	31 (20%)	0.03
4	The Hospital for Sick Children, Toronto, Ontario	2010-2012	69	8 (12%)	40	14 (35%)	0.005
5	IWK Health Centre, Halifax, Nova Scotia	2005-2011	77	2 (3%)	51	7 (14%)	0.03
6	Women and Children’s Hospital of Buffalo and Roswell Park Cancer Institute, Buffalo	2003-2012	60	8 (13%)	31	10 (32%)	0.03
7	Children’s Oncology Group (US and Canada) Study AALL0331 and AALL0932 *only two doses of asparaginase in regimen*	2005-2015	1380	I – 0.2% DI – 0.5%	2851	I – 0.3% DI – 1.8%	0.84 <0.001
8	Children’s Oncology Group (US and Canada) Study AALL0232 and AALL1131	2005-2015	2771	I – 0.54% C – 14.4% DI – 2.1%	1797	I – 0.22% C – 12.6% DI – 1.0%	0.10 0.18 0.07

IM – intramuscular; IV – intravenous; HSR – hypersensitivity reactions; I – Induction phase; C – Consolidation phase; DI – Delayed Intensification

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