Treatment For The Suprachoroidal Haemorrhage With Intraocular Alteplase: A Case Report

Co-authors


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Background

Suprachoroidal haemorrhage (SCH) is one of the complications associated with intraocular surgery; it can happen both at the intra and postoperative period. It comes up in its severest form with the expulsion of the intraocular content. At the beginning of the dissolution of the blood clot, passed between 10 and 14 days, it is considered the optimum moment to drain the SCH. Alteplase is a thrombolytic agent tissue-plasminogen activator (r-tPA). The intraocular inoculation of alteplase can make easier the clearance of the blood clot reducing the retinal complications in addition to be favourable in subsequent surgical procedures.

Purpose

To evaluate the effectiveness and security of the use of alteplase in a patient with massive SCH who was underwent to drainage vitrectomy.

Materials and Methods

A 50-year-old woman, diagnosed with glaucoma resistant to drug treatment, was admitted with a 50 mmHg of intraocular pressure. His medical history included risk factors as degenerative myopia, hypertension, and eye inflammation. She was underwent trabeculectomy with Mitomycin C and after the surgery she developed a expulsive SCH. To manage the SCH, ophthalmology decided to do a vitrectomy and drainage performed with intraocular inoculation of alteplase 50 mcg/0.1 mL.

A bibliographic search was conducted in PubMed (keywords: tissue plasminogen activator, suprachoroidal hemorrhage, vitrectomy) to explain the clinical use and the pharmaceutical product was made according to the standard operating procedure (SOP) established in the Pharmacy Service.

In the vertical laminar flow hood we reconstituted 20 mg of alteplase with 20 ml of sterile water injection. 1 mL of this solution was added to 1 mL of 0.9% sodium chloride. The final concentration was 500 mcg/mL. 0.1 mL of this solution was transferred to a 0.5 mL sterile insulin syringe and it was sealed with a sterile cap and labelled recommending its use immediately was added to obtain a 500 mcg/mL final concentration.

Results

16 days after the SCH presentation, a drainage surgery was achieved after a 50 mcg intraocular inoculation of alteplase in operating theatre to remove the blood clot. During the posterior afterfollow, there was evidence of a satisfactory clinical evolution, although a retinal detachment in right eye was detected and the patient needed of a posterior surgery. She was prescribed brinzolamide and timolol ophthalmic drops and five months later she showed a normal intraocular pressure and a good quality of vision.

Conclusions

The intraocular alteplase inoculation helped to dissolve the blood clot and it permitted a better drainage of the massive haemorrhage, improving the patient's vision and making easier the posterior retinal detachment surgery. There wasn't any adverse reaction referable to the intraocular inoculation of alteplase.

No conflict of interest

Keywords

Suprachoroidal Haemorrhage; Alteplase; Vitrectomy;

Authors letter

Score: 180

Remarks all reviewers:

Neef, Cees: Conclusion warranted
Conflict of interest clear

Accepted, but Author modifications

1. Modifications needed: ;

Nominee: No

This is an interesting case report, showing the added value of a hospital pharmacy

Jena, Helena: Conclusion warranted
Conflict of interest clear

Rejected

2.

Reason for reject: ;

This preapration is not new at all.
Background
Our centralized cytotoxic preparation unit generates over 50,000 preparations per year, of which about 4% are standardized rounded doses preparations performed manually. In order to optimize the production and to increase volume and quality of these preparations, the unit acquired the semi-automatic Repeater™ pump.

Purpose
To test the analytical performance of the pump by establishing a qualification protocol in order to integrate it in the current functioning of the unit.

Materials and Methods
The parameters assessed were linearity, precision (repeatability and reproducibility) and accuracy. To this end, transfers of solvent (5% glucose and 0.9% sodium chloride) were performed for different volumes: 1, 10, 20, 50, 100, 150, 250, 500 and 900 mL (which is the maximal used volume). Each volume was repeated six times and the reproducibility was studied on three different days. These volumes were determined by weighing. The linearity was evaluated by testing the slope, the coefficient of determination $r^2$ and the coefficient of variation (CV) of response factor. The acceptance levels of fidelity and accuracy were determined on the basis of our practices: CV less than 2% for fidelity and less than 5% for accuracy.

Results
No difference was found between the two solvents: linearity was demonstrated throughout the range of volume. Repeatability was proved from 10 to 900 ml. For 1 ml volumes, although the CV is higher than the set threshold, it remains very low (2.8% maximum). Reproducibility was satisfied on the whole range of volume. We can however notice increasing values of CV for extreme volumes: 2% for 1 ml, and 1.8% for 900 ml (versus 0.2-1.6% from 10 to 500 mL). Accuracy was validated from 20 ml to 900 ml (maximum relative bias = 3.8%). Results are not satisfied for 1 ml (CV about 15%) and 10 mL (CV about 8%) volumes but this does not impact the quality of our procedure which involved no volumes lower than 25 ml. These results should be considered in units performing transfers of volumes less than 20 ml.

Conclusions
To the set standards, the distribution of volumes with the Repeater™ pump was shown linear, repeatable, reproducible and accurate from 20 ml to 900 ml. This study guarantees the quality of our preparations with this new production process. It also opens new organizational possibilities: currently, 15 different lots (20 to 45 units/lot) are realized to achieve 10% of the total unit production activity.

No conflict of interest

Keywords
Centralized cytotoxic preparation unit; automatic; dose banding;

Authors letter
Automatisation in centralized cytotoxic preparation units become more and more important since few years. It is very important to qualify these new automates and to guaranty the quality of preparations and then patients’ health. No many studies are actually available on this topic. These study show an exemple of such qualification in a high volume production unit (more than 250 preparations/day) ans could be useful for others units.

Score: 240

Remarks all reviewers:
Neef, Cees: Conclusion warranted
Conflict of interest clear
Accepted
Nominee: No
Jenzer, Helena: Conclusion warranted
Conflict of interest clear
Accepted, but Author modifications
Nominee: No

Please state clearly that the pump does not satisfy at lowest and highest volumes. Is the pump's performance depending on the viscosity of the liquid? Ad keyword "Baxa Repeater Pump".
BAR14-0717
Microbial stability of an amikacin formulation for intrathecal use

Co-authors
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Background
Amikacin is a drug used in treatment of gram-negative meningitis at 5-50 mg/day dose. Sterility is very important for formulations by intrathecal route of administration.

Purpose
To test microbial stability of a formulation of amikacin 10 mg/mL for intrathecal injection for a period of 30 days.

Materials and Methods
We prepared 10 doses of intrathecal amikacin in laminar air flow cabinet in Pharmacy, according to the protocol of the Pharmacy Service, by taking solution of Amikacina Braun 10 mg/mL Solución para perfusión intravenosa, packed in polyethylene. We have made 10 sterile syringes of polyethylene and polypropylene (BD Discardit II, Becton Dickinson) with 5 mL of 10 mg/mL amikacin solution each and covered with a sterile Luer-Lock polypropylene cup (Baxa Ltd). We keep the syringes protected from light. 5 syringes were stored at 4ºC and other 5 syringes were stored at 25ºC. We have made the microbiological analysis at 0, 3, 7, 15 and 30 days.

Results
Microbial contamination was not observed after 30 days of storage in any of the solutions.

Conclusions
The amikacin formulation for intrathecal administration, prepared according to the protocol of our Pharmacy Service can be stored at 4ºC or 25ºC, protected from light, by a period of 30 days, without microbial growth.

No conflict of interest

Keywords
Amikacin; Intrathecal; Microbial;

Authors letter
Low grade of relevance and/or innovation to the European community of Hospital Pharmacists, medium impact on the future of hospital pharmacy practice and medium relevance regarding practice changes due to the investigated intervention.

Score: 220

Remarks all reviewers:
Neef, Cees: Conclusion warranted
Conflict of interest clear
Accepted, but Author modifications
5.
Modifications needed: ;
Nominee: No

this study is neither a validation study, nor an adequate microbial stability study. 30 samples is far to few to estimate sterility. An aseptic validation procedure should have been done with broth samples. This must be included in the study
Jenzer, Helena: Conclusion warranted
Conflict of interest clear
Accepted
Nominee: No

BAR14-0721
Costs saving impacts of biological drugs reuse after opening

Co-authors
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Background
As happens with other cytotoxic medications, biological drugs such as bevacizumab (Avastin®), cetuximab (Erbitux®), trastuzumab (Herceptin®), panitumumab (Vectibix®) and rituximab product’s information do not incite the keeping and reusing of the leftover volume in the preparation of a cytotoxic solution. Economic constraints have forced Hospital Pharmacies to adopt more rigorous budgets and in the Faro’s Hospital Central Unit for Cytotoxic Manipulation (UCMC PROFARO) there is now a tradition of
This study intends to demonstrate the final cost saving obtained during one year (2012) regarding the use of the above mentioned biological drugs.

**Purpose**

To determine the total volume of bevacizumab, cetuximab, trastuzumab, panitumumab and rituximab used during one year in CHA’s Faro Unit. The software used (GHAF) allows for the determination of the total volume considering both discarding and reusing the initial unused volumes. Final comparison of the costs resulting from both approaches.

**Materials and Methods**

The total volume of bortezomib per day and per patient can be easily extracted from the software program used by the Pharmacy Services (GHAF) and daily records are kept by the Cytotoxic Unit regarding reuse of unused volumes from open vials. This is done to assure rastreability of each preparation and is useful to perform economic impact studies such as this.

**Results**

In 2012, the leftover volume reuse approach allowed a total saving of 100000€. Individually, there was a 4% saving for rituximab, 5% for bevacizumab and cetuximab, 7% for trastuzumab and 15% for panitumumab.

**Conclusions**

A clear cost benefit is obtained from the policy adopted in the Pharmacy Cytotoxic Unit.

No increase was noted in the number of adverse reactions reported by the patients using biological drugs or health care professionals involved in the treatments. Physicians did not report changes in the expected results nor increased toxicity. The studies presented by the manufacturer are unrealistic considering the existing budget constraints but if it is possible to assure top quality for a cytotoxic preparation this reuse of open vials should be adopted always. Manufacturers would benefit with the publication of stability tests with shelf life for open reconstituted vials.

No conflict of interest

**Keywords**

biological drugs; Oncology; Cost savings;

**Authors letter**

The present submission refers to a study on the economical impact of the reuse of the leftover volumes of cytotoxic biological open vials. This procedure is not planned or mentioned in the drug’s information leaflet but literature is available to safely take this step. And if quality is assured there is no reason not to adopt this policy since it can bring great savings to Hospital Pharmacies and, therefore, Hospitals as a whole.

Score: 220

Remarks all reviewers:

Neef, Cees: Conclusion NOT warranted
Conflict of interest clear
Accepted, but Author modifications
3.5.
Modifications needed: ; ;
Nominee: No

Jenzer, Helena: Conclusion warranted
Conflict of interest clear
Accepted, but Author modifications
Nominee: No

This is a very controversial subject. In some european countries this way of saving is not allowed. That should be added to the discussion. Th text of the conclusion should be moved to the. This is more discussion than results.

Jenzer, Helena: Conclusion warranted
Conflict of interest clear
Accepted, but Author modifications
Nominee: No

New category: T8
please combine this abstract with 742!Please change the title: use "bortezomib" instead of "biological drugs". Describe the storage conditions for bortezomib residues. State if microbiological stability has been tested. What is "rastreability"? Authors letter: Is quality really assured?
Cholesterol oral suspension for Smith-Lemli-Opitz syndrome

Co-authors

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1HOSPITAL CLINICO UNIVERSITARIO VIRGEN DE LA ARRIXACA, Pharmacy, Murcia, Spain.

Background

Syndrome due to a birth defect in cholesterol synthesis and caused by mutations in the DHCR7 gene, which lead to a deficiency of the enzyme that converts 7-dehydrocholesterol to cholesterol. The management is symptomatic and most patients are treated with supplemental dietary cholesterol.

Purpose

Evaluate efficacy and safety of a formulation of cholesterol 150mg/cc for the treatment of hypocholesterolemia in a patient diagnosed with Smith-Lemli-Opitz Syndrome (SLOS).

Materials and Methods

Infant 7 months old diagnosed of SLOS and with nasogastric tube feeding. Treatment was initiated with nutritional support based on carbohydrates and cholesterol, against which quickly developed symptoms of gastric intolerance. Due to the lack of commercialization of other nutritional preparations with similar characteristics, the available literature was reviewed in order to develop a formulation that would allow exogenous cholesterol, finding several formulations all based on other centers own experience. A suspension of cholesterol 150mg/cc was proposed.

Results

A standard operating procedure for the preparation of a suspension of cholesterol in a final volume of 300cc was developed. Composition:

- Colesterol (PH.EUR quality) 45g
- OraSweet® SF 60cc
- OraPlus® 160cc

Modus operandi: Prepare the vehicle for suspension, weigh cholesterol and add it to an appropriately sized mortar, add the vehicle slowly, stirring until homogeneous. Transfer the contents to a beaker and homogenize with a magnetic stirrer. Package and label.

Sensory characteristics: flavor: strawberry, aspect: viscous, free of debris.

Stability assigned: 90 days, preserved in refrigerator and protected from light. Any problems of tolerance had not been reported during the follow-up interval of 6 months. During this period the levels of cholesterol in the patient experienced a slight increase since the last review, while still maintaining cholesterol values below recommended levels.

Conclusions

The suspension of cholesterol is a formulation easy to prepare and with good tolerance that offers a viable option in patients with SLOS who have intolerance to commercial preparation.

No conflict of interest

Keywords

Smith-Lemli-Opitz Syndrome; Cholesterol; Suspension;

Authors letter

- Formulation that offers a viable option in patients with SLOS who have intolerance to commercial preparation. - A standard operating procedure for the preparation of a suspension of cholesterol. - To evaluate the efficacy and safety of a formulation of cholesterol for the treatment of SLOS.

Score: 220

Remarks all reviewers:

Neef, Cees: Conclusion NOT warranted
Conflict of interest clear
Accepted, but Author modifications
3.5.
Modifications needed: ;
Nominee: No

the development of this formulation is very poor. Not even the particle seize and other physico-chemicl properties are measured. In the conclusion the authors mention good tolerance, but this is not mentioned how this was measured.

Jenzer, Helena: Conclusion warranted
Conflict of interest clear
Accepted
Nominee: No
Selection process for the procurement of an automated robotic solution for cytotoxic compounds

Co-authors

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2Amgros, safe, Copenhagen, Denmark.

Background

In 2012 we were granted funds for an automated robot for cytotoxics compounds, whose purpose is to ensure a more stable delivery of chemotherapeutic drugs, ensure an even higher quality level and improve the working environment for the employees. In Denmark it is a legal requirement that new equipment purchased in the public shall be offered by EU tender if the purchase price is more than approximately 67,000 euros.

Purpose

The purpose is to describe the selection process regarding the tender of an automated (robotic) solution for the preparation of cytotoxic compounds.

Materials and Methods

Based on a risk analysis a User Requirements Specification describing all the requirements for the new robot was prepared. The User Requirements Specification was divided into a number of overarching themes: Application and suitability, GMP compliance, Air quality and temperature, Safety and efficacy of the products, IT-systems, Alarms/alerts/messages, Installation requirements, Works safety, Maintenance, training and support. A total of 231 requirements were described. The requirements were categorized into A- and B-requirements. A-requirements were minimum requirements that should be met in order for the tender to be considered. Fulfilment of the B-requirements was considered positive in relation to the award criteria.

As a part of the selection criterion of the tender, the supplier had to expect an audit according to EU GMP and it should be possible to evaluate the robot by an audit at one or more reference sites.

Results

When the tendering period was done, two vendors had bid on the task. Each response to each of the 231 requirements were reviewed and evaluated according to A- and B-requirements.

Audits at the vendor and at the vendors reference sites was conducted before the final choice was made.

Conclusions

After reviewing the bids and execution of audits, our choice fell on the manufacturer of APOTECChemo robot.

No conflict of interest

Keywords

Tender; Requirements; APOTECChemo robot;

Authors letter

Score: 160

Remarks all reviewers:
Neef, Cees: Conclusion warranted
Conflict of interest clear
Accepted, but Author modifications
5.
Modifications needed: ;
Nominee: No

to few data in the results section
Jenzer, Helena: Conclusion warranted
Conflict of interest clear
Accepted, but Author modifications
3.4.5.
Modifications needed: ; ; ;
Nominee: No

It would be more important to describe the key criteria and how they were met by the vendors. Such a machine is too expensive for most hospitals, thus of moderate added value. It is not obvious why one tender is better than the other one. No evaluation is described. Please adapt the keywords.
One year experience using bortezomib within shelflife after reconstituted

Co-authors

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1Hospital de Faro E.P.E., Pharmacy Department, Faro, Portugal.

Background

As happens with other cytotoxic medications, Bortezomib(Velcade®) indications do not include guidelines for the reuse of an open reconstituted vial. Economical constraints push Hospital pharmacists towards more stringent budgets and, to save costs, the Faro Unit from the Centro Hospitalar do Algarve (CHA Faro) as initiated a policy of keeping and reusing the unused volumes of open vials. To assure quality, the risks implicated in the use of the molecule beyond its formal (Summary of Product Characteristics or SPC) indications were analyzed and taken into account.

Although not initially predicted by the manufacturers there is enough information to sustain this procedure and this study intends to demonstrate the final cost saving obtained during one year (2012) of Bortezomib (Velcade®) use.

Purpose

To determine the total bortezomib volume used during one year in CHA’s Faro Unit. The software used allows for the determination of the total volume considering both discarding and reusing the initial unused volumes.

Final comparison of the costs resulting from both approaches.

Materials and Methods

The total volume of bortezomib per day and per patient can be easily extracted from the software program used by the Pharmacy Services (GHAF) and daily records are kept by the Cytotoxic Unit regarding reuse of unused volumes from open vials. This is done to assure rastreability of each preparation and is useful to perform economic impact studies such as this.

Results

In 2012, the discarding approach would deem necessary the use of 196 Bortezomib vials to complete all prescriptions, with a total cost of 240000€. While assuring the quality of the prepared cytotoxic medication, the reuse of unused volumes from open vials resulted in less 60 vials used and an expense 30% lower (total saving of 72000€).

Conclusions

A clear cost benefit is obtained from the policy adopted in the Pharmacy Cytotoxic Unit.

Also, no increase was noted in the number of adverse reactions reported by the patients using bortezomib or health care professionals involved in the treatments. Physicians did not report changes in the expected results nor increased toxicity.

The studies presented by the manufacturer are unrealistic considering the existing budget constraints but if it's possible to assure top quality for a cytotoxic preparation this reuse of open vials should be adopted always. Manufacturers would benefit with the publication of stability tests with shelf life for open reconstituted vials.

No conflict of interest

Keywords

Bortezomib; Cost savings; Handling;

Authors letter

The present abstract refers to the submission of a study on the economical impact of not discarding open and still usable volumes of the cytotoxic drug Bortezomib but instead reuse them for other preparations. Indications on how to comply safely with this policy - now adopted by the Pharmaceutical Services of CHA Faro - are not readily available in the drug’s summary of product characteristics but there is available literature to proceed safely and guarantee top quality for the use of leftover volumes while cutting heavily on costs.

Score: 180

Remarks all reviewers:

Neef, Cees: Conclusion NOT warranted
Conflict of interest clear
Accepted, but Author modifications

Jenzer, Helena: Conclusion warranted
Conflict of interest clear
Accepted, but Author modifications

this is a similar abstract as nr 721, same story other substance. The conclusion is wrong: there are only costs surveyed and no benefit is described in the results
Conflict of interest clear
Accepted, but Author modifications

this abstract should be merged with 721! See comments there.
BAR14-0848
EFFICACY STUDY OF OMALIZUMAB IN ATOPIC DERMATITIS

Co-authors
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1HOSPITAL UNIVERSITARIO FUNDACION JIMENEZ DIAZ, pharmacy, madrid, Spain.

Background
Omalizumab is a humanised monoclonal antibody manufactured by recombinant DNA technology. This treatment should only be considered for patients with asthma mediated by IgE (immunoglobulin E). Omalizumab in atopic dermatitis is an off-label treatment.

Purpose
To check efficacy of omalizumab in atopic dermatitis (AD).

Materials and Methods
Retrospective observational study, including all patients who have received omalizumab from January 2010 to march 2013. Data were obtained from clinical history.

Results
We studied 6 patients.

- Woman, 48 years. She had received treatment with topical and oral corticosteroids, antihistamines and cyclosporine. IgE>5000 UI/ml. Omalizumab dose was 300mg/2 weeks. After fourteen months omalizumab was discontinued by non-response.

- Woman, 24 years. She had received treatment with azathioprine mycophenolate mofetil, topical and oral corticosteroids and cyclosporine. IgE=1683 UI/ml. Omalizumab dose was 300mg/2 weeks. After four months she had small lesions but less intense.

- Woman, 47 years. She had received treatment with oral and topical corticosteroids, UVB-BE and cyclosporine. IgE=387 UI/ml. Omalizumab dose was 300mg/4 weeks. After five months omalizumab was discontinued by non-response.

- Man, 33 years. He had received treatment with topical corticosteroids and antihistamines. IgE 453 UI/ml. Omalizumab dose was 150mg/2 weeks. After fifteen months omalizumab was discontinued by non-response.

- Woman, 15 years. She had received treatment with oral and topic corticoids, topical corticosteroids and tacrolimus. IgE >5000. Omalizumab dose was 450mg/2 weeks. After sixteen months she had another episode, it was recommended UVB-BE and continued with omalizumab.

- Woman, 19 years. She had received treatment with topic and oral corticoids and topic tacrolimus. IgE 723 UI/ml. Omalizumab dose was 300mg/4 weeks. After two months good answer, but after new episode omalizumab was discontinued by non-response.

Conclusions
In the most of the patients omalizumab was discontinued by inefficacy. Due to small number of patients, more studies are necessary to confirm efficacy of omalizumab in AD, dose and time of treatment.

No conflict of interest

Keywords
Omalizumab; Dermatitis; atopic;

Authors letter
Omalizumab is a relatively new drug; we think that in these drugs is important to do efficacy studies despite the small number of patients.

Score: 200

Remarks all reviewers:
Neef, Cees: Conclusion NOT warranted
Conflict of interest clear
Accepted, but Author modifications
Nominee: No

this n=6 study is on the edge of acceptability. The conclusion is not correct. To draw conclusions out of 6 patients is not very valuable. The wording of the conclusion is wrong: 4 out of 6 patients have negative results. The point is of omalizumab will turn out to be effective with more patients whereas the literature also show very weak succes rates for this drug
Jenzer, Helena: Conclusion warranted
Conflict of interest clear
Accepted
Nominee: No
New category: T3