Comparing Efficacy of Tapering Dose vs Low Dose Oral Steroid in Chronic Rhinosinusitis with Nasal Polyp

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Alhamdulillah, praise to Allah, The Almighty and The Most Beneficent.

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My gratitude also goes to all lecturers, my colleagues well as the ORL-HNS clinic staffs for their cooperation, assistance and friendly support in numerous ways in the course of my study.

I would like to dedicate my work to my parents Fauzi Ab Razak and Raziah Ab Rashid, my parent in law; Latifah Rahmat who have devoted their lives to ensure that we get the best of everything.

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ABSTRAK (BAHASA MALAYSIA)

Latar Belakang: Rhinosinusitis kronik dengan polip hidung (CRSwNP) adalah salah satu penyakit keradangan kronik yang paling biasa pada mukosa sinonasal. Tablet kortikosteroid (OCS) dianggap sebagai rawatan utama untuk penyakit ini. Walaubagaimanapun, terdapat kepelbagaian dari segi tabiat preskripsi ubat ini ke atas penyakit CRSwNP di kalangan pakar Rhinologi. Kajian ini membawa hipotesis bahawa steroid dos rendah akan menghasilkan keputusan yang baik berbanding dengan dos secara pengurangan.

Objektif: Untuk membandingkan keberkesanan antara penggunaan kortikosteroid oral secara pengurangan dos and dos rendah ke atas pesakit CRSwNP

Kaedah: Satu kajian kumpulan dua lengan dan tidak buta telah dijalankan di klinik Otorinolaringologi Hospital Universiti Sains Malaysia melibatkan 58 pesakit CRSwNP. Pesakit dipilih secara rawak dalam nisbah 1:1 untuk menerima rawatan prednisolon oral secara pengurangan dos yang bermula dari 60mg/d, atau prednisolon oral dose rendah 25mg/kg selama 2minggu. Parameter subjektif soal selidik kualiti hidup dan jumlah markah simptom hidung serta parameter objektif penemuan endoskopik hidung diukur sebelum dan selepas rawatan. Kesan buruk kedua-dua preskripsi juga direkodkan.

Keputusan: Nilai min SNOTT-22 selepas 12 minggu rawatan ialah 27.61 (SD 8.17) untuk dos secara pengurangan dan 27.75 (SD, 12.22) untuk kumpulan dos rendah.(p=0.58) Purata penurunan skor TNSS bagi kumpulan dos tirus selepas 6 minggu dan 12 minggu ialah masing –masing ,2.18 dan 2.39. Sementara itu, kumpulan dos rendah ialah 1.93 dan 2.22 (p=0.072). Purata penurunan dalam skor Lund-Kennedy daripada garis dasar kepada 12 minggu ialah 2.89 unit untuk kumpulan dos secara pengurangan dan 2.29 unit untuk kumpulan dos rendah.(p=0.517) Nilai purata penggredan polip hidung untuk 12 minggu selepas rawatan ialah 2.50 unit(SD, 1.29) dalam kumpulan dos tirus dan 2.68unit(SD, 1.41) dalam kumpulan dos rendah.(p=0.66)

Kesimpulan: Kajian ini menunjukkan peningkatan yang ketara dari segi kualiti hidup, jumlah markah simptom hidung dan penemuan endoskopik bagi kedua-dua kumpulan preskripsi. Walau bagaimanapun, tiada perbezaan hasil peningkatan yang ketara antara kedua-dua dos preskripsi.

Kata kunci: Rinosinusitis, Radang Hidung, Polip Hidung, Kortikosteroid, Steroid, Prednisolone

ABSTRACT (ENGLISH)

Background: Chronic rhinosinusitis with nasal polyp (CRSwNP) is one of the most common chronic inflammatory diseases of sinonasal mucosa. Oral corticosteroid (OCS) is considered a mainstay of treatment in the management of the disease. However, there is significant heterogeneity existed in OCS prescribing habits for this disease among the rhinologist. This study comes with the hypothesis that a low dose steroid can have a good outcome as compared to a tapering dose.

Objective: To compare the efficacy between tapering dose and low dose oral steroid in patients with CRSwNP.

Method: A balanced randomisation, two-armed, non-blinded interventional parallel-group study conducted involving 58 CRSwNP patients from Otorhinolaryngology clinic of Universiti Sains Malaysia Hospital. Patients were randomly assigned in a 1:1 ratio to receive either oral prednisolone tapering dose which the starting dose of 60mg/d, or low dose oral prednisolone of 25mg/d for 2weeks. Subjective parameter of quality of life questionnaire and total nasal symptoms score as well as objective parameter of endoscopic finding were measured before and after treatment. The adverse effects of both prescribtion were also recorded.

Result: The mean value SNOTT-22 after 12 weeks post treatment is 27.61 (SD 8.17) for tapering dose and 27.75 (SD, 12.22) for low dose group.(p=0.58) The mean decrease in TNSS score for the tapering dose group after 6weeks and 12weeks were 2.18 and 2.39, respectively; meanwhile, the low dose group was 1.93 and 2.22 (p=0.072). The mean decrease in modified Lund-Kennedy score from baseline to 12weeks was 2.89units for the tapering dose group and 2.29units for the low dose group.(p=0.517) The nasal polyp grading mean value for 12weeks post-treatment was 2.50units(SD, 1.29) in the tapering dose group and 2.68units(SD, 1.41) in the low dose group.(p=0.66)

Conclusion: This study indicates a significant improvement in terms of quality of life, total nasal symptoms score and endoscopic findings for both prescription groups. However, there are no significant improvement outcome differences between the two prescription dose.

Keywords: Rhinosinusitis, Nasal Polyp, Corticosteroid, Steroid, Prednisolone

Chapter 1:

INTRODUCTION

1.1 INTRODUCTION

According to the European Position Paper on Rhinosinusitis and Nasal Polyps (EPOS) 2012, chronic rhinosinusitis (CRS) with or without nasal polyp (NP) in adults is defined as the presence of two or more symptoms, one of which should be either nasal blockage/obstruction/ congestion or nasal discharge (anterior/posterior nasal drip), with or without facial pain/pressure, with or without reduction or loss of smell, for ≥12 weeks, with validation by telephone or interview.[1] Questions on allergic symptoms (i.e. sneezing, watery rhinorrhea, nasal itching, and itchy watery eyes) should be included. CRS with NP (CRSwNP): chronic rhinosinusitis as defined above and bilateral, endoscopically visualized polyps in the middle meatus.

There is a lack of accurate epidemiological data on CRS without NP (CRSsNP) and CRSwNP. The reported prevalence ranges widely from 5 to 15%.[2] Geographical variation plays a role, but also the differences in diagnostic criteria used in studies and grouping together of the two major phenotypes. In the non-specialist setting, where endoscopic confirmation of disease is not always possible, the prevalence may be overestimated. In a recent multinational study undertaken by the Global Allergy and Asthma European Network, the total prevalence of both CRSsNP and CRSwNP has been estimated around 10.9% and 15.5% in Europe and the USA, respectively.[3] Meanwhile, in the Asian region, the prevalence reported in Korea, China and Singapore were 7%, 8% and 2.7%, respectively.[4]

Assessment of symptoms

It is useful to quantify the severity of symptoms reported by patients, as it allows more effective monitoring of response to treatment. The simplest way is to ask patient 'how troublesome are your symptoms of rhinosinusitis', which allows categorization of each cardinal symptoms into none (score 0) mild (score 1), moderate (score 2) and severe (score 3) (Appendix 1). Total nasal symptoms score (TNSS) is the sum of the total severity of 4 cardinal symptoms (max 12). There are also several disease-specific patient-rated outcome measures (PROMs) that record the severity of several individual symptoms important to patients with CRS. Most widely used in the medical literature are the 31 items Rhinosinusitis Outcome Test (RSOM-31), the 22 items Sinonasal Outcome Test (SNOT-22), and the Chronic Sinusitis Survey (CSS). In this study, we used the 22 items sinonasal outcome test (SNOT-22) [Appendix 2] as our measure

of disease-specific health-related quality of life (HRQL). In general, TNSS is assessing CRS symptoms specifically while SNOTT-22 is assessing CRS symptoms as well as the quality of life.[5]

Management of chronic rhinosinusitis

The CRS management aims to revive the functional integrity of the inflamed mucosal lining with the relief of patient symptoms. Patient-reported outcome measures often help guide response to treatment more than objective clinical measurements. The management of CRSsNP and CRSwNP are distinct in the current EPOS guidelines due to the differences in their underlying aetiology and pathophysiology. Medical therapy remains the primary treatment modality for both pathways.[6]

However, medical treatment options for patients with CRSwNP is limited. Both topical corticosteroids and nasal saline irrigations are recommended as initial medical therapies for affected patients. Intranasal corticosteroids can decrease nasal polyp size, lessen sinonasal symptoms and improve patient quality of life.[7] Oral corticosteroids (OCS) also can reduce polyp size and improve symptoms. However, duration and dose of OCS vary from various studies. There are also no recommendations of what would be considered a "standard" dose and duration of OCS. Antibiotics may be useful in treating infectious exacerbations of CRSwNP, but clinically significant efficacy (i.e. polyp shrinkage) in large, randomized trials is lacking. Patients with significant sinonasal disease and/or those who fail medical management should be evaluated for sinus surgery. Functional endoscopic sinus surgery can improve sinonasal symptoms evidenced by improvement seen in sinus CT scan.[8]

OCS is commonly used and considered a mainstay of treatment in the management of CRSwNP. Many rhinologists considered the used of OCS is a key component of "maximal" medical therapy.[9] OCS have several adverse effects such as hyperglycemia, hypothalamic-pituitary-adrenal axis suppression, gastrointestinal disturbance, dyspepsia, insomnia, mood disturbance, headache, increased appetite, fatigue, backache, acne and oedema. Hissaria at el showed most of the side effects were infrequent and no different in those with placebo except for insomnia.[10] There is a risk of osteonecrosis after a short course of oral steroid, but this appears to be extremely rare.

Vaidyanathan et al. performed a randomized, double-blind placebo-controlled study on 60 patients meeting criteria for the diagnosis of CRSwNP as defined by the EPOS 2007. The study was done in rhinology clinic in Tayside, Scotland. Patients were randomized to receive either oral prednisolone 25 mg or placebo daily for two weeks followed by fluticasone nasal drops for eight weeks and fluticasone nasal spray for 18 weeks in both groups. The oral steroid treatment arm showed significant improvement compared to placebo at two weeks in hyposmia score report, Pocket Smell Test, TNSS score, mini-Rhinosinusitis Quality of Life Questionnaire, endoscopic assessment, peak nasal inspiratory flow, serum eosinophil derived neurotoxin, and C-reactive protein.[11]

Devyani Lal from Department of Otolaryngology-Head and Neck Surgery, Loyola University Medical Center, Maywood, Illinois had done retrospective case series on targeted medical therapy for Chronic rhinosinusitis using tapering dose steroid (60, 40, 20 and 10 mg for three days for each dose) showed 51% complete endoscopic and symptomatic resolution.[12]

David M.Poetker from Wisconsin University, US, when evaluating the use of oral steroids in patients with CRSsNP and CRSwNP, 16 articles were identified 5 of which had level-2 evidence. All the studies showed positive changes in the majority of the parameters evaluated. Analysis of the data supports the use of oral steroids in patients with CRS and with nasal polyps in the immediate and short-term period. All the studies showed benefit with very few adverse effects, and no severe adverse events were reported. The researchers made a strong recommendation for the use of oral steroids in the management of patients with both CRSsNP and CRSwNP, provided the use was short term.[13]

John R Scott et al. concluded that significant heterogeneity existed in OCS prescribing habits for rhinosinusitis among the member of American Rhinologic Society. Discrepancies were observed between survey results and evidence-based recommendations. They suggested that developing standardized OCS treatment protocols for rhinosinusitis may improve the quality of care by optimizing clinical outcomes and reducing the risk of complications.[14]

In Malaysia, the discrepancy of the OCS prescription also occur. There are many prescription habits for prescribing oral steroids in the management of CRSwNP amongst rhinologists in Hospital USM and MOH hospitals. There are different in term of dose and duration of oral

steroids prescribtion. The most common prescription habits are tapering dose and low dose (25mg or 30mg) for 2weeks duration. The heterogeneity also occurs amongst the tapering dose group, which differ in the starting dose and differ in style of tapering, such as 60mg for 4days, then a reduction of 5mg daily for a total duration of 2weeks; some give 50mg daily for 3days then tapering 10mg every 3days for a total duration of 2weeks.

Our study aims to assess the outcome of the two different OCS prescriptions and make a recommendation after analyzing the efficacy and adverse effects of both prescriptions. The two different OCS prescriptions are the tapering dose of oral prednisolone with a starting dose of 60mg/d, and low dose oral prednisolone of 25mg/d for 2weeks duration.

Rationale of the study

1. We hypothesize that low dose steroid can have a good outcome in our population. In reality, in the daily practice, there is actually no consensus in which dose of OCS used for medical treatment of CRSwNP.
2. Cost-effectiveness is better with the low dose with an almost similar outcome.
3. We can reduce the confusion of tapering dose steroid and has better compliance in our population.

Chapter 2:

OBJECTIVES

CHAPTER 2: OBJECTIVES OF THE STUDY

2.1 General objective

To compare the efficacy between tapering dose and low dose oral steroid in patients with chronic rhinosinusitis with nasal polyps (CRSwNP)

2.2 Specific objective

The specific objectives for this study were as the following:

1. To compare the symptom severity scores using the 22-Item Sino-nasal Outcome Test (SNOT-22) between tapering dose and low dose oral steroid in patients with CRSwNP.
2. To compare symptom severity scores using the Total Nasal Symptom Score (TNSS) between tapering dose and low dose oral steroid in patients with CRSwNP.
3. To compare the endoscopic findings using Lund-Kennedy score between tapering dose and low dose oral steroid in patients with CRSwNP.
4. To compare the nasal polyp grading (Meltzer et al) between tapering dose and low dose oral steroid in patients with CRSwNP.
5. To describe the adverse effects of oral steroid between tapering dose and low dose oral steroid in patients with CRSwNP.

Chapter 3:

STUDY PROTOCOL

3.1 Study protocol submitted for ethical approval

JEPeM Code: USM /JEPeM/21020149

Study Title: Comparing Efficacy of Tapering Dose vs Low Dose Oral Steroid in Chronic Rhinosinusitis with Nasal Polyp

Principal Investigator: Dr. Mohd Zul Izzi Bin Fauzi (MMC 63912)

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3 Mr. Amran Bin Mohamad (Co-supervisor; MMC 30417)

4 Assoc. Prof. Dr. Norhayati Mohd Noor (Co-supervisor; MMC 35994)

Background

According to the European Position Paper on Rhinosinusitis and Nasal Polyps (EPOS) 2012, chronic rhinosinusitis (CRS) with or without nasal polyp (NP) in adults is defined as the presence of two or more symptoms, one of which should be either nasal blockage/obstruction/ congestion or nasal discharge (anterior/posterior nasal drip), with or without facial pain/pressure, with or without reduction or loss of smell, for ≥12 weeks, with validation by telephone or interview. Questions on allergic symptoms (i.e. sneezing, watery rhinorrhea, nasal itching, and itchy watery eyes) should be included.[1] CRS with NP (CRSwNP): chronic rhinosinusitis as defined above and bilateral, endoscopically visualized polyps in the middle meatus.

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However, medical treatment options for patients with CRSwNP is limited. Both topical corticosteroids and nasal saline irrigations are recommended as initial medical therapies for affected patients. Intranasal corticosteroids can decrease nasal polyp size, lessen sinonasal symptoms and improve patient quality of life.[7] Oral corticosteroids (OCS) also can reduce polyp size and improve symptoms. However, duration and dose of OCS vary from various studies. There are also no recommendations of what would be considered a "standard" dose and duration of OCS. Antibiotics may be useful in treating infectious exacerbations of CRSwNP, but clinically significant efficacy (i.e. polyp shrinkage) in large, randomized trials is lacking. Patients with significant sinonasal disease and/or those who fail medical management should be evaluated for sinus surgery. A retrospective analysis, a delay in over five years from initial CRS diagnosis to sinus surgery was associated with greater post-operative health care utilization compared to when surgery was performed within 12 months of diagnosis. Functional endoscopic sinus surgery can improve sinonasal symptoms evidenced by improvement seen in sinus CT scan.[8]

OCS is commonly used and considered a mainstay of treatment in the management of s CRSwNP. Many rhinologists considered the used of OCS is a key component of "maximal" medical therapy.[9] OCS have several adverse effects such as hyperglycemia, hypothalamic-pituitary-adrenal axis suppression, gastrointestinal disturbance, dyspepsia, insomnia, mood disturbance, headache, increased appetite, fatigue, backache, acne and oedema. Hissaria at el showed most of the side effects were infrequent and no different in those with placebo except for insomnia.[10] There is a risk of osteonecrosis after a short course of oral steroid, but this

appears to be extremely rare. Vaidyanathan at el found adrenal suppression and alteration of bone metabolism appear to be transient.[11] Basal and dynamic adrenal function as well as marker of osteoblast return to baseline after stopping oral prednisolone.

Literature review

Currently, there are many prescribtion habit for prescribing oral steroids in the management of CRSwNP amongst rhinologist in Hospital USM and in MOH hospital. There are different in term of dose and duration of oral steroids prescribtion. The most common prescription habits are tapering dose and low dose (25mg or 30mg) for 2weeks duration. The heterogeneity also occur amongts the tapering dose group which differ in the starting dose and dose of tapering such as 60mg for 4days then a reduction of 5mg daily for total duration of 2weeks , some give 50mg daily for 3days then tapering 10mg every 3days for total duration of 2weeks.

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Devyani Lal from Department of Otolaryngology-Head and Neck Surgery, Loyola University Medical Center, Maywood, Illinois had done retrospective case series on targeted medical therapy for Chronic rhinosinusitis using tapering dose steroid (60, 40, 20 and 10 mg for three days for each dose) showed 51% complete endoscopic and symptomatic resolution.[12]

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Rationale of the study

1. We hypothesize that low dose steroid can have a good outcome in our population. In reality, in the daily practice, there is actually no consensus in which dose of OCS used for medical treatment of CRSwNP.
2. Cost-effectiveness is better with the low dose with an almost similar outcome.
3. We can reduce the confusion of tapering dose steroid and has better compliance in our population.

General objective

To compare the efficacy between tapering dose and low dose oral steroid in patients with chronic rhinosinusitis with nasal polyps (CRSwNP)

Specific objectives

1. To compare the symptom severity scores using the 22-Item Sino-nasal Outcome Test (SNOT-22) between tapering dose and low dose oral steroid in patients with CRSwNP.
2. To compare symptom severity scores using the Total Nasal Symptom Score (TNSS) between tapering dose and low dose oral steroid in patients with CRSwNP.

3. To compare the endoscopic findings using Lund-Kennedy score between tapering dose and low dose oral steroid in patients with CRSwNP.
4. To describe the adverse effects of oral steroid between tapering dose and low dose oral steroid in patients with CRSwNP.

Hypotheses

1. The symptom severity scores using the 22-Item Sino-nasal Outcome Test (SNOT-22) is not much different after 6weeks and 3months followup between CRSwNP patient taking the tapering dose and low dose oral steroid.
2. The Total Nasal Symptom Score (TNSS) between tapering dose and low dose oral steroid in patients with CRSwNP after 6weeks and 3months followup make no big difference.
3. In tapering dose patients, polyp size score by endoscopic findings will show more improvement than low dose oral steroid patients.
4. CRSwNP patient taking low dose oral steroids will show less adverse effect than tapering dose group.

Methodology

Study design

This is a balanced randomisation, two-armed, non-blinded interventional parallel-group study conducted in Hospital USM. The intervention group will receive tapering dose oral steroid and the control group will receive low dose steroids.

Source population

Patients attending Otorhinolaryngology-Head and Neck Surgery (ORL-HNS) clinic Universiti Sains Malaysia Hospital (Hospital USM).

Study population

All CRSwNP patients aged 18 years old and older attending ORL-HNS clinic, Hospital USM, who meet the inclusion/exclusion criteria.

Study subject

All consented CRSwNP patients aged 18 years old and older attending ORL-HNS clinic, Hospital USM, who meet the inclusion/exclusion criteria.

Study area

The study will be conducted in the ORL-HNS clinic, Hospital USM for patient recruitment

Inclusion criteria:

1. CRSwNP based on the clinical history and confirmed by direct visualization via nasal endoscopy
2. Not been treated with OCS before or has not taken oral steroid in the past six months
3. No previous endoscopic sinus surgery

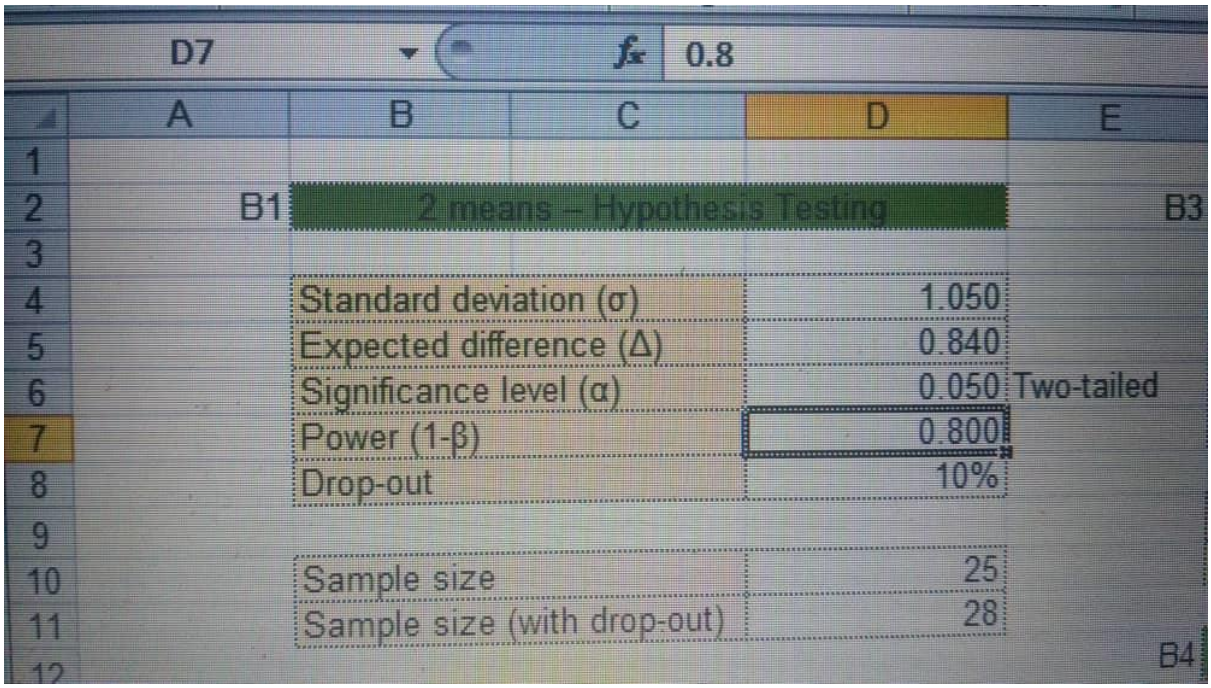
Exclusion criteria:

1. Presence of cystic fibrosis, Kartagener's syndrome, Young syndrome, antrochoanal polyp, inverted papilloma or any malignancy
2. Pregnant and lactating women
3. Uncontrolled diabetes mellitus
4. Uncontrolled hypertension
5. Presence of cataract or glaucoma

Sample size estimation

The sample sizes were calculated using the Excel sample size calculator for comparing two means.

Sample size estimation based on the specific objective (i) (SNOTT-22)

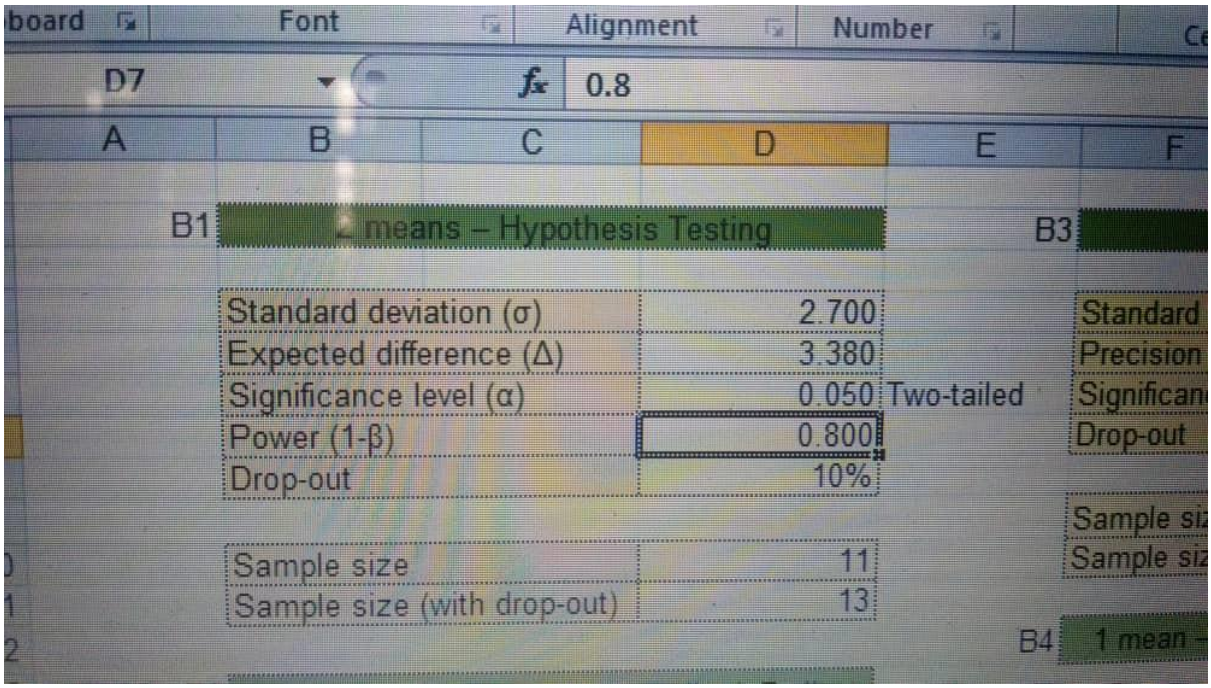


Therefore, for specific objective (i),

Sample size, n = 25 + 10% drop-out

= 25 + 3 = **28 subjects** for each group

Sample size estimatiion based on the specific objective (ii) (TNSS)

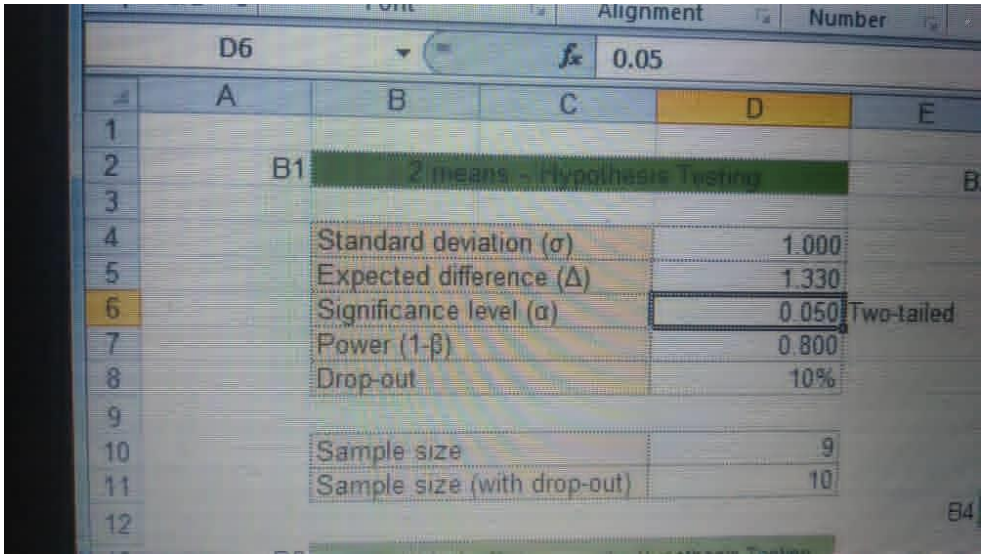


Therefore, for specific objective (ii),

Sample size, n = 11 + 10% drop-out

= 11 + 2 = **13 subjects** for each group

Sample size estimatiion based on the specific objective (iii) (Endoscopic finding/ polyp size)



Therefore, for specific objective (iii),

Sample size, n = 9 + 10% drop-out

= 9 + 1 = **10 subjects** for each group

Since specific objective (iv) is using a descriptive analysis, no sample size needed.

In conclusion, we estimate that a sample size of **28 participants in each group** (Group A and Group B) of our study would be powered at greater than 80% with a 2-tailed α value of 0.05 (Total N=28 participants x2 groups = **56 participants**). This sample size is base of the calculation of the specific objective (i) which the largest sample calculation amongst the specific objective.

Grouping of subjects

Patients will be assigned to two treatment groups. Group A (intervention) will receive oral prednisolone in tapering doses (60, 40, 30, 20 and 10 mg) with each dose taken daily for three days except for 10 mg, which will be taken in a single dose for 2 days. Group B (controlled) will receive 25 mg daily for 14 days. Oral prednisolone will be standardized for 14 days in both groups.

In Clinical Practice Guidelines of management of rhinosinusitis in adolescents and adults in malaysia issued in 2016 has stated short term OCS (25mg/day for two weeks) is significantly more effective than placebo in reduction of nasal polyp size and hyposmia score. However, this statement is only referred to only one randomized controlled trial (RCT) of Vaidyanthan et al published in 2011. So we decide to take this prescribtion as controlled group.

Both groups will receive the same intranasal steroid, which is mometasone nasal spray (2 sprays in each nostril twice daily) and tablet clarithromycin 250 mg twice daily for two weeks then 250 mg daily for 4 weeks.

Randomization and concealment allocation

Block of 4 randomization computered generation is used to randomly allocate between the 2 groups. The allocation sequence was concealed from the researcher enrolling and assessing participants in sequentially numbered, opaque, sealed and stapled envelopes. The randomly sealed opaque envelopes contained the code and dosage of oral steroids will be distributed by the assistant (who are not directly involved with the study) to the investigator only after the enrolled participants completed all baseline assesment and it was time to allocate the invention. Both the patient and the investigator are not blind to this trial. The patient has to know how to take the medication properly and the physician has to properly explain on how to take the medication.

History and General ORL Examination

The demographic information including age, gender, race, occupation and area of residence will be obtained from the patients. Symptoms of rhinosinusitis which include rhinorrhea, nasal blockage, postnasal drip, sneezing and nasal itchiness will be recorded as well as the duration of symptoms.

The severity of CRS symptoms will be classified into mild, moderate and severe based on Total Nasal Symptom Score (TNSS) and Sino-nasal Outcome Test (SNOTT 22). Other relevant medical histories like asthma and eczema, allergic history, history of nasal surgery, family history of atopy, smoking history and drug history will be documented.

General ORL examination including nasoendoscopy will be performed using 2.8mm rigid scope (zero degrees) in a sitting position. Physicians will score the findings of endoscopic examination according to the Modified Lund-Kennedy score in which the endoscopic appearance of both nasal fossae are rated for polyp, oedema and discharge as 0-2 depending on severity. Polyp size was scored using Meltzer clinical scoring system ie "1" for visualized small polyps in the middle meatus, "2" for polyps reaching below the inferior border of the middle turbinate, "3" for polyps extended from middle meatus without complete obstruction and score "4" for massive nasal polyposis. Polyp size was scored as 1 to 4 for each side of the nostril and the bilateral polyp grade was obtained as the sum of the individual units for the left and right nasal cavities (max: 8) The nasoendoscopy is a part of routine ORL examination and it may give discomfort to some patients. All these data will be recorded in the study proforma.

Detailed methodology

The subjects for cases will be recruited from those attending ORL-HNS clinic as described in ' Study Population and Sample', who meet the inclusion/exclusion criteria. The consent form used in this study will need approval by USM Research Ethics Committee. The informed consent will be gained from all subjects before their participation in this study. This study will not involve any vulnerable subjects.

Once the subject is consented to join the trial, he will be examined and research tool has to be completed (as described in "History and ORL examination). After completed the examination, the investigator will be given an enveloped as describe in 'randomization' by an assistant which patient will be prescribed the medication according to the group he/she was randomly recruited. 6 weeks and 12 weeks follow-up appointment will be given to the subject.

The questionnaire of SNOT-22 score, total nasal symptoms score and nasoendoscopy assessing the polyp size will be performed at:

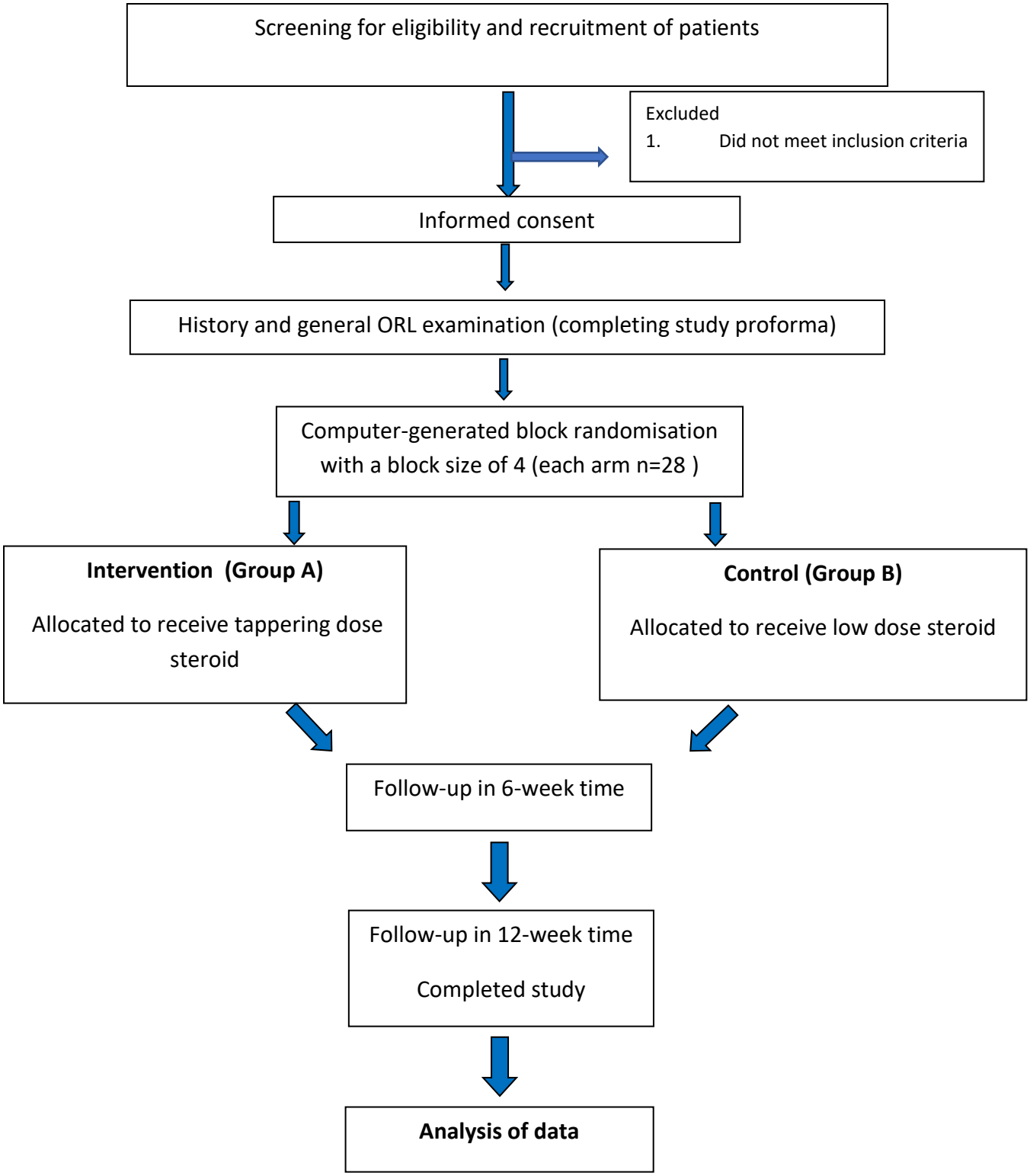
1. initial presentation (at 0 week);
2. 2nd follow-up (at 6 week)
3. 3rd follow-up (at 12 week).

The adverse effects of both different prescriptions of the OCS will also be recorded at 6 and 12 weeks follow-up.

RESEARCH TOOLS

1. Study proforma (Appendix 1) – will be filled in by investigator
2. Total Nasal Symptom Score (TNSS) (Appendix 2) – will be filled in by investigator
3. Sino-nasal Outcome Test (SNOTT-22) (Appendix 3) – will be filled in by patients with the assistance from the investigator/doctors

Flow chart of study



Statistical analysis

Data will be entered and analyzed using SPSS version *25.0*. Descriptive statistics will be used to summarise the socio-demographic characteristics of subjects. Numerical data will be presented as mean (SD) or median (IQR) based on their normality distribution. Categorical data will be presented as frequency (percentage). Repeated measure analysis of covariance (RM ANCOVA) will be performed.

Expected results

For specific objective (i-iii), independent t test and paired t-test will be used.

Table 1. shows comparison of SNOT-22 score, TSS score and Lund-Kennedy score for tapering dose vs low dose OCS treatment in CRSwNP patients

Variables	**Group A (Mean SD)**		**Group B (Mean SD)**		**Mean difference (95% CI)**
	Pre-treatment	**Post-treatment**	**Pre-treatment**	**Post-treatment**	
SNOT-22 score					
TSS score					
Lund-Kennedy score					

Legends: Group A is tapering dose; Group B is low dose OCS

For specific objective (iv), descriptive analysis will be used.

Table 2. shows side effects for tapering dose vs low dose OCS treatment in CRSwNP patients

Side effects	**Group A** (n=28)	**Group B** (n=28)
Insomnia		
Mood disturbance		
Headache		
Dyspepsia		
Increased appetite		
Fatigue		
Backache		
Diarhea/ GI disturbance		
Acne		
Edema (feet/ face)		

Legends: Group A is tapering dose; Group B is low dose OCS. The values will be presented as numbers .